INFLUENCE OF OBESITY-RELATED GENOTYPE ON WEIGHT LOSS SUCCESS, CHANGES IN BODY COMPOSITION, BIOCHEMICAL MARKERS, AND QUALITY OF LIFE WHILE PARTICIPATING IN A 6-MONTH WEIGHT LOSS PROGRAM

A Dissertation

by

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ABSTRACT

The purpose of this study was to determine whether genotype of some obesity-related genes (FABP2, PPARG, ADRB2, ADRB3) impacts health outcomes from participation in a 6-month weight loss program. Fifty-one overweight/obese women (41.8 ± 12.1 yrs, 35.3 ± 8.0 kg/m^2) were randomly assigned to diet based on genotype, true or false match. Dietary intervention included two hypocaloric (week 1: 1400 kcal/d, weeks 2-24: 1500 kcal/d), moderate protein (45% kcal from protein) diets with variations in carbohydrates and fat (LC- 20:35, MC- 30:25). Participants performed a resistance-exercise program four days/week, and 10,000 steps/day three days/week. Anthropometrics, body composition, REE, dietary data, biochemical markers, and psychosocial evaluation were collected monthly. VO_2peak, muscular strength and endurance were assessed at baseline, 3- and 6-months. All measures were analyzed with repeated measures MANOVA. Significant genotype effects and trends favoring false matches were observed for body weight (F-5.6±5.0, T-5.0±5.0 kg, p=0.10), fat free mass (F-0.4±2.3, T-0.8±2.3 kg, p=0.09), android total mass (F-849.1±882.8, T-669.7±855.4 grams, p=0.05), android fat mass (F-627±583, T-459±480 grams, p=0.07), gynoid fat free mass (F+3.0±665, T-199±534 grams, p=0.09), and fasting insulin (T+1.9±5.3, F+0.2±5.1 microIU/mL, p=0.04). Significant time x genotype interactions and trends favoring false were observed for triglycerides (T-9.9±62.3, F-35.5±49.1 mg/dL, p=0.05). Genotype effect favoring true was observed for android fat free mass (T-210.5±451.7, F-222.0±463.8 grams, p=0.04), gynoid total mass (T-878±978, F-852±1073 grams, p=0.09), and hip circumference (T-5.1±5.5, F-4.9±3.7 cm, p=0.07). Significant genotype

x diet interaction and trend was observed in favor of true MC for LDL (TMC-15.8±26.7, FMC-8.6±34.2, FLC+3.7±28.1, TLC+10.1±26.3 mg/dL, p=0.02) and cholesterol (TMC-26.0±32.1, FMC-23.5±32.0, FLC+7.0±31.8, TLC+8.5±35.8 mg/dL, p=0.06). Overall, false matches experienced greater improvements in body composition, fitness, and biochemical markers.

DEDICATION

To my amazing parents, family, and friends, I am blessed to have you all in my life. Thank you for believing in me. I could not have accomplished this without your love, support, and encouragement.

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NOMENCLATURE

BW	Body Weight
BMI	Body Mass Index
CHO	Carbohydrate
DXA	Dual X-Ray Absorptiometry
FM	Fat Mass
FFM	Fat Free Mass
HC	Hip Circumference
HDL	High Density Lipoprotein Cholesterol
Kcal	Kilocalorie
LDL	Low Density Lipoprotein Cholesterol
REE	Resting Energy Expenditure
TG	Triglycerides
VO_2max	Peak Aerobic Capacity
WC	Waist Circumference
MC	Moderate Carbohydrate, Adequate Fat, Moderate Protein Diet
LC	Low Carbohydrate, Adequate Fat, Moderate Protein Diet

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CHAPTER I

INTRODUCTION AND RATIONALE

Background

In the United States, two-thirds of all adults are classified as overweight or obese.[1] Currently, obesity is attributed to an interaction among multiple components, including physiological, metabolic, behavioral, social, and genetic factors.[2] The latter has received significant attention as of late, with new findings from Genome Wide Association Studies identifying possible candidate genes related to the cause of obesity.[3-6] Identification of candidate genes associated with obesity is useful in determining both pharmacological treatment and optimal dietary intervention for weight loss.

Dietary prescription based on genotype is an example of genetic profiling. Genetic profiling is used frequently in oncology to help determine treatment routes and predict clinical outcomes.[7] Regarding obesity, the use of genetic profiling as a method to dictate treatment is a novel idea in its infancy.

Few weight loss interventions to date have assigned dietary prescriptions based on genotype.[7-9] Among the investigations conducted, the genetic profile used in the trial by Dopler-Nelson and colleagues demonstrated the most effective results.[9] However, genotype matching to dietary intervention in this trial was retrospective. Therefore more research is warranted prospectively testing the genetic profile used in Dopler-Nelson and colleagues trial (FABP2 (rs1799883), PPARG2 (rs1801282), ADRB3 (rs4994C3), ADRB2 (rs1042713 and rs1042714)) in relation to dietary prescription and health

outcomes from weight loss interventions to validate the profile for use in a clinical setting.

Statement of the Problem

Will prospective matching to dietary intervention based on variants within the following genetic profile, FABP2 (rs1799883), PPARG2 (rs1801282), ADRB3 (rs4994C3), ADRB2 (rs1042713 and rs1042714), demonstrate improved health outcomes in apparently healthy, sedentary, overweight/obese women assigned to their diet group based on genotype (true match) in comparison to participants assigned to their diet group based on the opposite of their genotype (false match)?

Purpose

The purpose of this study was to determine if participants truly matched to diet intervention based on genotype demonstrated greater health outcomes in comparison to participants falsely matched to diet intervention based on genotype.

General Study Overview

Fifty-one, overweight or obese, apparently healthy, sedentary women were matched to a diet intervention based on variations in allele patterns within the following genetic profile: FABP2 (rs1799883), PPARG2 (rs1801282), ADRB3 (rs4994C3), ADRB2 (rs1042713 and rs1042714). DNA was collected from buccal cheek swabs and samples were sent out to Interleukin Genetics (Waltham, Ma) for genotyping. Once genotyping results were obtained, participants were randomly assigned to either a dietary intervention that aligned with their genotype (true match) or a dietary intervention that did not align with their genotype (false match).

The two diets prescribed in this investigation varied in carbohydrate (CHO) content, such that one diet was a moderate CHO diet (30% kcal CHO) and the other was a low CHO diet (20% kcal CHO).[10-12] Both diets were adequate in fat content, 25% kcal fat in moderate CHO diet and 35% kcal fat in low CHO diet, and moderate in protein content, 45% kcal from protein.[11,12] The diets were also hypocaloric in nature, 1400 kcal/d prescribed for week one and 1500 kcal/d prescribed for weeks two through 24. The variation in CHO and fat content is consistent with previous weight loss interventions suggesting similar variations in relation to candidate genes within the genetic profile.[13-25] Additionally, the use of a moderate protein diet in conjunction with the Curves exercise program (Curves International, Waco TX) is consistent with previous weight loss interventions conducted in the Exercise and Sport Nutrition Laboratory.[26-28]

Along with a dietary intervention, the exercise intervention used was the Curves exercise program (Curves International, Waco TX). The Curves exercise program consisted of a circuit-style training regimen including hydraulic resistance machines interspersed with calisthenic exercise or Zumba dance. Participants completed four, 30-minute, Curves workouts, including one of the four workouts interspersed with Zumba dance. In addition to exercise on the Curves circuit, participants were instructed to achieve 10,000 steps per day on the days they were not exercising on the Curves circuit (three days per week). A pedometer was provided to assist with tracking step count.

The dependent variables included the following: diet assignment; body weight, body composition as determined with the Hologic Discovery W QDR series Dual

Energy X-ray Absorptiometry (Waltham, Ma); resting energy expenditure and peak oxygen consumption with the Parvo Medics TrueMax 2400 Metabolic Measurement System (Sandy, UT); waist and hip circumference; resting heart rate and blood pressure; lower and upper body maximal strength and endurance; serum panels to determine fasting insulin, glucose, HOMA-IR, glucose to insulin ratio, and blood lipid profile; dietary intake via four-day food logs; step count from the pedometer via weekly physical activity log; and psychosocial evaluation. All measures were collected monthly from baseline to completion of six months with the exception of peak oxygen consumption, and lower and upper body muscular strength and endurance, which were measured at baseline, end of three months and six-months. Exercise compliance at the Curves circuit was measured daily via circuit attendance and collection of peak and average heart rate during each workout.

Data were analyzed with SPSS statistical software package, version 22 (Chicago, IL). ANOVA or MANOVA with repeated measures was used to assess the data. Data is presented as mean ± standard deviation. This study was funded by Interleukin Genetics (Waltham, MA) and Curves International, (Waco, TX).

Hypotheses

H_1: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will be observed among body composition variable.

H_2: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will be observed for visceral adipose tissue depots.

H_3: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will be observed for fat deposition.

H_4: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will be observed among anthropometric variables.

H_5: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will be observed for resting energy expenditure.

H_{o6}: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will not be observed for cardiorespiratory fitness.

H_{o7}: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will not be observed for muscular strength.

H_{o8}: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will not be observed for muscular endurance.

H_9: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will be observed among blood lipids.

H_{o10}: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will not be observed among markers related to insulin resistance.

H_{o11}: Statistically significant interactions (time x genotype and/or time x genotype x diet) in favor of true matches will not be observed among variables related to psychosocial evaluation.

Delimitations

The following guidelines will be followed:

1. One hundred and ninety one sedentary, apparently healthy women, between the ages of 18 and 60 years, with a BMI greater than 22 kg/m^2 will be recruited from College Station/Bryan and Texas A & M University.
2. Participants have not participated in a planned exercise program within three months prior to screening for eligibility to participate in this weight loss study.
3. Participants were not currently exercising more than 30 minutes per day, three times per week, at the time of screening.
4. Participants did not experience a weight change of ± 7 pounds within the three months prior to screening for eligibility to participate in this weight loss study.
5. Participants were not pregnant or nursing during the preceding 12 months, nor were they planning to become pregnant during the proceeding 12 months at time of screening for eligibility to participate in the study.
6. Participants did not have any uncontrolled metabolic disorders.
7. Participants were not currently taking thyroid, hyperlipidemic, hypoglycemic, anti-hypertensive, or androgenic medications prior to the start of the study.
8. Within the three months prior to the start of the study, participants were not taking ergogenic levels of nutritional supplements that may have affected muscle mass, anabolic/catabolic hormones levels, or weight loss.
9. All individuals were willing to participate in a regular, moderate, exercise program.

10. All eligible participants attended a familiarization session in the Exercise and Sport Nutrition Laboratory, where they were briefed on the rationale, testing protocols, and requirements of the study. After reviewing the informed consent, all interested participants signed the informed consent, completed a questionnaire related to subjective rating of carbohydrate intolerance (carbohydrate intolerance questionnaire), and completed a general health screening form for review by a research nurse. After paperwork was complete, height, weight, resting heart rate, blood pressure, and buccal cheek swab samples were collected.

Limitations

1. Recruitment of participants in this study is limited to the Bryan/College Station area of Texas.
2. The Eating Satisfaction Survey, included within the psychosocial questionnaires provided, has yet to be validated.
3. Dietary data collected was self-reported via four-day food logs.

Assumptions

1. Participants will honestly and accurately answer all screening questions to determine eligibility for participation in the study.
2. Participants will honestly and accurately complete the general health screening form and carbohydrate intolerance questionnaire.
3. Prior to each testing session, participants will fast for 10-12 hours, abstain alcohol consumption and non-steroidal anti-inflammatory use for 24 hours, and refrain from exercise for 48 hours.

4. Participants will honestly and accurately complete the four-day food records and one-week activity log upon submission at each monthly testing session.
5. Participants will comply with their assigned diet regimen and exercise protocol.
6. The sample population will be normally distributed.
7. All testing procedures will be performed consistently among lab personnel.

CHAPTER II

LITERATURE REVIEW*

Excessive energy intake, poor diet quality, and insufficient energy expenditure is directly associated with weight gain resulting in obesity and adverse health outcomes. It is clear a single cure-all approach for weight loss does not exist; thus more efforts in personalized nutrition via genetic profiling have been investigated. The purpose of this literature review is to present the prevalence, health consequences, and etiology associated with obesity, demonstrate the relationship between genetics and obesity, explain how genetic profiling may improve weight loss outcomes, and identify five potential candidate genes for use in genetic profiling to promote weight loss and improve health outcomes.

Prevalence of Obesity

The obesity epidemic has gained the national spotlight regarding the prevalence, health consequences, and contributing factors of the disease. According to the most recent data from the National Health and Nutrition Examination Survey (NHANES) 2011-2012, in the United States more than two-thirds of adults aged 20 years and older, 68.5%, are classified as overweight or obese (BMI > 24.9 kg/m^2), with one-third alone,

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34.9%, classified among the three grades of obesity (grade 1 = 30-34.9 kg/m^2, grade 2 = 35-39.9 kg/m^2, grade 3 = $\geq$ 40 kg/m^2).[1] Obesity, including excess accumulation of visceral adipose tissue, is associated with increased risk of cardiovascular and metabolic diseases and conditions.[29-33]

Health Consequences and Obesity

Cardiovascular

According to the Centers for Disease Control, annually, one in four deaths in the United States is attributed to heart disease.[34] A positive relationship has been demonstrated between BMI and risk of coronary artery disease, atherosclerosis, and heart failure.[35-37] In a prospective, international, multicenter investigation conducted by Labounty and colleagues[36], increased BMI demonstrated a stronger association with coronary artery disease in comparison to smoking, dyslipidemia, type 2 diabetes and hypertension. Investigators concluded that a "strong and consistent" relationship exists between increased BMI and the severity, extent, and prevalence of coronary artery disease.[36]

Kenchaiah and colleagues[37], also found a significant association between increased BMI and heart failure risk. Women classified as overweight demonstrated a 50% increased risk for heart failure in comparison to normal weight women, whereas, risk of heart failure in obese women doubled in comparison to normal weight women.[37] Outcomes for increased risk differed in men; thus, one may conclude that women classified as overweight or obese are at greater risk of heart failure in comparison to overweight or obese men.

The positive relationship between obesity and risk of heart disease and heart failure may be attributed to obesity-induced dyslipidemia. Dyslipidemia may be characterized as increased plasma triglycerides (TG) and free fatty acids, decreased high-density lipoprotein levels (HDL), and an increase in low-density lipoprotein levels (LDL).[38,39] According to a recent review conducted by Franssen and colleagues[38], dyslipidemia associated with obesity has consistently demonstrated a positive relationship with risk for heart disease and is considered a contributing risk factor.

Along with dyslipidemia, in comparison to lean patients, obese patients are more likely to present with hypertension.[40] Chronic hypertension may result in damage to the heart and coronary arteries, which increases one's risk of developing atherosclerosis, heart disease, heart failure, heart attack and stroke. [41] Multiple investigations have demonstrated a relationship between weight loss in obese individuals and reduction in antihypertensive medication and blood pressure.[40,42-45] Taken together obesity increases one's risk of dyslipidemia and hypertension, which may lead to adverse cardiovascular conditions.

Endocrine and Renal

Along with cardiovascular conditions, onset of obesity is associated with adverse endocrine and renal conditions. Insulin resistance and subsequent onset of type 2 diabetes is directly associated with obesity, in particular increased visceral adiposity.[46,47] The combination of visceral adiposity and an obese state may be attributed to the following mechanisms: adipocytes become resistant to the anti-lipolytic effect of insulin, leading to increased plasma free fatty acids, resultant hepatic gluconeogenesis, muscle

and hepatic insulin resistance and impaired insulin secretion; further over accumulation of visceral fat cells produce adipokines associated with inducing insulin resistance, inflammation, and formation of atherosclerotic plaques.[47] Thus obesity may result in type 2 diabetes and, if not pre-existing, lead to the development of dyslipidemia and atherosclerosis.

If left untreated or poorly controlled, chronic hyperglycemia may develop into neuropathy and lead to amputation, retinopathy and result in blindness, and/or nephropathy and result in chronic kidney disease. If further noncompliance or poor control continues with chronic kidney disease, this increases risk of end stage renal disease.[48,49]

Etiology of Obesity

Originally, the onset of obesity was solely attributed to a positive energy balance such that energy intake exceeded energy expenditure of basal metabolic needs, thermic effect of food, lifestyle and physical activity. Currently, obesity is attributed to an interaction among multiple factors, including physiological, metabolic, behavioral, social, and genetic factors.[2] Attention to genetic factors has gained recent attention as of late and has demonstrated notable relationships that may contribute to the epidemic.

Genetics and Obesity

There are two types of genetic conditions related to obesity, monogenic and polygenic obesity. Monogenic obesity is classified as rare genetic variants that result in extreme measures of obesity.[50] In this form of obesity, a causative effect is demonstrated such that one gene is considered the culprit of the condition.[51] Prader-Willi, syndrome is

an example of a condition within monogenic obesity.[52] Examples of genetic variants associated with monogenic obesity include single nucleotide polymorphisms (SNPs) in the melanocortin-4 receptor (MC4R), propiomelanocortin (POMC), leptin gene and leptin receptor gene.[50-52]

In contrast to monogenic obesity, polygenic obesity is classified as a summation of effects from multiple SNPs.[50] Polygenic obesity is referred to as common obesity and consists of the majority of cases of obesity. The discovery of polygenic obesity may be attributed to the start of genome-wide association studies (GWAS). The method within GWAS is unbiased and thorough, enabling determination of associations between target disease phenotypes and common variations in the genome.[51] This method scans a set of SNP markers from 0.1 to 5 million in size and tags SNPs that demonstrate variation in haplotypes within a target region. From the tagged SNPs, one may determine where variations occur within the genome.[51]

With use of GWAS, identification of countless candidate genes associated with BMI classification of obesity, unfavorable blood lipid profiles and body fat distribution have been identified.[3-6] This information enables research within the areas of nutrigenomics and nutrigenetics. Nutrigenomics focuses on how diet and other lifestyle factors influences the expression of genes over time.[53] The influence of baseline genotype on the response to caloric restriction within a weight loss program is considered nutrigenetics, also commonly referred to as genetic profiling.[53]

Genetic Profiling (Nutrigenetics)

The concept of genetic profiling to classify or predict clinical outcomes and disease states is used frequently with microarray analyses in oncology.[7] Within a clinical setting, genotypes associated with metabolism, transport of nutrients, removal of toxins, and protection from antioxidants are analyzed to determine a pattern of baseline genetic variation.[8] Determining baseline variation in candidate genes provides insight regarding clinical intervention, diet, and exercise.[8] This practice is relatively new in the arena of weight loss, with few studies to date assessing baseline genetic profile in relation to health outcomes after participating in a weight loss intervention.[7-9] (Appendix A)

In a retrospective analysis conducted by Mutch and colleagues[7], a smaller sample size from a larger European multicenter study, the Nutrient-Gene Interactions in Human Obesity-Implications for Dietary Guidelines Trial (NUGENOB; www.nugenob.org), was assessed in regards to baseline genotype and response to the weight loss intervention. Briefly, within the NUGENOB 10-week intervention, 771 obese (average BMI ~ 35 kg/m^2) participants, with an average age of approximately 35 years old, were randomly assigned to a hypocaloric diet (~600 kcal deficit) consisting of either a low fat, high carbohydrate (CHO) diet (20-25% kcal fat, 60-65% kcal CHO, 15% kcal protein), or a moderate fat, low CHO diet (40-45% kcal fat, 40-45% kcal CHO, 15% kcal protein). Three-day weighed food logs were collected at baseline and 10 weeks, and participants were in weekly contact with a Registered Dietitian (RD) to assist with dietary compliance.

Mutch and colleagues[7] selected 53 participants from the NUGENOB trial who

were closely matched in baseline characteristics. This smaller sample of participants were then classified as responders or non-responders based on their success in the NUGENOB intervention. Responders exhibited an 8-10 kg weight loss by the end of the intervention, whereas non-responders exhibited less than four kilograms of weight loss. Genotype was determined from microarray analysis of adipose biopsies collected at the start of the study. The following candidate genes were identified as having significantly different allele patterns between responders and non-responders at baseline: transmembrane protein 132A (TMEM132A), quinolinate phosphoribosyltransferase (QPRT), claudin 5 (CLDN5), prostaglandin D2 synthase (PTGDS), endothelial cell adhesion molecule (ESAM), fibromodulin (FMOD), family with sequence similarity 69 B (FAM69B), interferon alpha-inducible protein 27 (IF127).[7] Taken together, these findings suggest that the identified candidate genes are associated with success in the aforementioned weight loss intervention.[7]

Similarly, Dopler-Nelson and colleagues[9] retrospectively categorized participants to their dietary interventions, i.e. true match to diet or false match to diet, based on baseline genotype in a smaller sample from a large, 12-month, randomized controlled trial, The AtoZ Weight Loss Trial.[9,54] Summarily, within the AtoZ Weight Loss Trial, 311 obese (average body fat percentage ~40%) participants, with an average age of about 40 years old, were randomly assigned to one of the following commercial weight loss programs: Atkins: $\leq$ 20 g/d CHO for 2-3 mo, then $\leq$ 50 g/d CHO; Zone: 40% kcal CHO, 30% kcal fat, 30% kcal protein; LEARN: 55-60% kcal CHO and < 10% kcal saturated fat; Ornish: $\leq$ 10% kcal fat).[54] Weekly dietary education was provided for two

months by an RD. Three-day food records were collected at baseline, and then randomly around two, six, and twelve months. Additionally, anthropometrics, body composition, blood pressure, and blood sample were collected at baseline, two, six, and twelve months.[54]

Dopler-Nelson and colleagues[9] contacted all participants in the AtoZ Weight Loss Trial regarding retrospective genetic analysis. Of all 311 participants contacted, 101 individuals participated in the retrospective genetic profiling study. Genotyping was determined via buccal cheek swabs to assess five genetic variants among the following four candidate genes: fatty acid binding protein (FABP2, rs1799883), peroxisome-proliferator activated-receptor gamma 2 (PPARG2, rs1801282), beta-3 adrenergic receptor (ADRB3, rs4994C3), beta-2 adrenergic receptor (ADRB2, rs1042713 and rs1042714). Findings determined that individuals who were truly matched to their dietary intervention based on genotype experienced a 5.3 percent loss in body weight (BW) over 12-months versus 2.3 percent BW in false matches ($p < 0.05$).[9] True matches to the programs lowest in CHO (Atkins) and fat (Ornish) experienced 6.8% total weight loss in comparison to 1.4% in false matches. Additionally, true matches experienced a significant reduction in waist circumference ($p=0.01$) and triglycerides ($p=0.007$), and an increase in HDL ($p=0.01$).

In addition to the retrospective analyses, Arkadianos and colleagues[8] conducted the only investigation to our knowledge where participants were matched prospectively to a dietary intervention based on genotype at baseline. Ninety-three patients from the Dr. Arkadianos Clinic participated in an intervention approximately 11-months in

length. All participants followed a low saturated fat, low glycemic index, Mediterranean-style diet. With typical macronutrient distribution range of the Mediterranean diet consisting of approximately 38% kcal CHO, 46% kcal fat, and 16% kcal protein.[8] Fifty obese (22 female, 28 male, average BMI 32 kg/m^2) participants, aged approximately 45 years old, received specific alterations in their dietary prescription based on genetic variants within the candidate gene of interest (nutrigenetic group), whereas 43 participants (18 female, 25 male, average BMI 32 kg/m^2) simply followed the prescribed Mediterranean-style diet (control group). In addition to diet, exercise routines were provided and consistent among all participants. Participants attended regular appointments with their physician at the clinic where BW was measured and a fasting blood sample was collected at baseline and completion.[8] Genotyping was determined by Buccal cheek swabs. Results from buccal cheek swabs included variants among the following candidate genes: 5,10-methylenetetrahydrofolate reductase (MTHFR, rs1801131, 677C>T), 5-methyltetrahydrofolate-homocysteine methyltransferase reductase (MTRR, 66A>G), 5-methyltetrahydrofolate-homocysteine methyltransferase (MTR, 275A>G), cystathione-beta-synthase (CBS, 699C>T); glutathione s-transferase MI (GSTMI, deletion), glutathione s-transferase theta 1 (GSTT1, deletion), glutathione s-transferase pi (GSTP1, 313A>G, 341C>T); SOD2 (-28C>T), SOD3 (760C>G), nitric oxide synthase (NOS3, 894G>T); vitamin D receptor (VDR, CTaqIT, TBsmIC, TFokIC), collagen type 1 alpha 1 (COLIA, G SpI T); tumor necrosis factor alpha (TNFalpha, -308G>A), interleukin 6 (IL6, 1595C>G), nitric oxide synthase 3 (NOS3, 894G>T); cholesteryl ester transfer protein (CETP, 279G>A), lipoprotein lipase (LPL,

1595C>G), apolipoprotein C-3 (APOC3, 3175C>G); angiontensin I convertin enzyme (ACE, INS/DEL), and peroxisome-proliferator activated-receptor gamma 2 (PPARG2, Pro12Ala).[8]

There were no significant differences among participants in age, sex, BMI, fasting blood lipids and blood glucose at baseline. Upon completion of the study, change in BMI between approximately three to ten months of the intervention was not significant; however, after about ten months, BMI decreased 5.6% (1.93 kg/m^2) in the nutrigenetic group versus a 2.2% gain (0.51 kg/m^2) in the control group ($p < 0.023$). After 90 days, among the participants with pre-diabetes, 57% of individuals in the nutrigenetic group and 25% of individuals in the control group demonstrated a significant reduction in fasting blood glucose ($p < 0.046$).[8] Overall these findings support use of genetic profiling to personalize nutrition and optimize weight loss and maintenance in comparison to random assignment to a diet for weight loss. Additionally, findings suggest benefits for use of genetic profiling in patients with pre-diabetes such that these patients experience improved insulin sensitivity when genetically matched to a diet to promote weight loss.

As previously mentioned, few investigations have assessed the relationship between baseline genotype and weight loss success after participation in an intervention. Candidate genes assessed among investigations have been relatively inconsistent. More research assessing a consistent group of candidate genes will be helpful to determine if genetic profiling is analytically and clinically valid.[55] Between the investigations retrospectively matching genotype to diet, Dopler-Nelson and colleagues demonstrated

the most practical intervention and genetic profile while demonstrating clear significant effects.[9] In the one investigation prospectively matching genotype to diet, significant effects were not exhibited until after about ten months of intervention.[8] Considering the profound results found with the genetic profile used by Dopler-Nelson and colleagues, further research with use of this genetic profile is warranted. The following section will review candidate genes within the genetic profile suggested by Dopler-Nelson and colleagues (FABP2, rs1799883; PPARG2, rs1801282; ADRB3, rs4994C3; ADRB2, rs1042713 and rs1042714), specifically in relation to association with obesity, weight loss interventions, and potential use in genetic profiling to optimize nutrition for weight loss. (Appendix B)

Candidate Genes

FABP2 (rs1799883)

Association with Obesity

Intestinal fatty acid binding protein 2 (FABP2) is a protein located in the cytosol of intestinal epithelial cells and is associated with long-chain fatty acid metabolism.[56] At rs1799883 a transition occurs at codon 54 resulting in replacement of alanine (Ala) with threonine (Thr).[57] The wild-type allele pattern for FABP2 is Ala/Ala, whereas the mutant-type is Ala/Thr or Thr/Thr. In most populations, the allelic frequency of Thr at codon 54 is 30%.[57] Multiple investigations have demonstrated differences in baseline biochemical markers related to glucose and lipid metabolism favoring the wild-type allele pattern.[57-59] All of these investigations conducted genotyping with peripheral leukocytes.

In an investigation assessing 122 overweight and obese (BMI > 25 kg/m^2) men and women (average age 48 ± 16 years) where diet was controlled prior to collection of biochemical markers, those with the mutant-type allele pattern demonstrated significantly higher circulating levels of fasting glucose and insulin.[59] Additionally, in another investigation assessing 55 morbidly obese men and women, those with mutant-type allele pattern had significantly higher levels of fasting insulin, HOMA, leptin, and lower levels of adiponectin.[57]

Along with this, Albala and colleagues[58] compared baseline FABP2 rs1799883 genotype and fasting levels of glucose, insulin, HOMA, blood lipids, and inflammatory markers between obese and normal weight individuals. Thirty-three obese women (BMI > 30 kg/m^2) were compared to 30 normal weight women (BMI 18.5-24.9 kg/m^2), all with an average age of about 37 years old. Regarding genotype, a significant difference in the number of obese females carrying the mutant-type allele pattern was demonstrated in comparison to normal weight women. As expected, obese women had significantly higher levels of fasting glucose, insulin, HOMA, triglycerides, total cholesterol, and TNFα in comparison to normal weight women. In obese participants, those homozygous for the Thr allele, one of the mutant-type allele patterns, demonstrated significantly higher levels of insulin, TNFα, and leptin.[58]

Collectively, evidence suggests that obese individuals are more likely to contain the mutant-type allele patterns of FABP2 at rs1799883. Consequently, the mutant-type allele patterns demonstrate an association with markers of insulin resistance and abnormal lipid profile. Thus assessment of baseline allelic variants in FABP2 rs1799883

in relation to health outcomes after a weight loss intervention is justified to determine optimal interventions, especially in individuals with the mutant-type allele pattern.

Weight Loss Interventions

Multiple investigations have demonstrated varying health outcomes after implementation of diet and exercise intervention for weight loss in individuals containing the FABP2 rs1799883 mutant-type allele patterns.[13-16,60] In a two-month randomized, clinical trial conducted by de Luis and colleagues[14], 204 apparently healthy, obese (average BMI 34.3 ± 4.8 kg/m^2) men and women (50 males and 154 females), with an average age of 46.5 ± 15.7 years, were randomly assigned to either a hypocaloric moderate fat diet (1500 kcal/d, 27% kcal fat, 52% kcal CHO, 20% kcal protein) or hypocaloric low CHO diet (1507 kcal/d, 36% kcal fat, 38% kcal CHO, 26% kcal protein). Aerobic exercise consisting of 60 minutes per day, three days per week was encouraged. Three-day food records were collected at baseline and two-months to determine dietary compliance. Anthropometric measurements and blood samples were collected at baseline and two months. Genotyping was determined from peripheral leukocytes. Overall, from baseline to two months all participants experienced significant loss in BW and fat mass (FM) ($p < 0.05$). Regardless of diet group, a significant reduction in cholesterol, TG, insulin, and leptin was demonstrated in the wild-type allele pattern, with no significant changes in mutant-type allele pattern. However, participants with the mutant-type allele pattern who followed the low CHO diet experienced a significant reduction in FM ($p < 0.05$).[14]

Similarly, Martinez-Lopez and colleagues[13] also conducted a two-month weight loss intervention utilizing a moderate fat diet in 109 overweight and obese (BMI > 25 kg/m^2) men and women (20 male, 89 female), with mean age of 38.6 ± 11.3 years. The diet consisted of 1000 kcal/d for women and 1200 kcal/d for men, with 30% kcal from fat, 55% kcal CHO, 15% kcal protein. Additionally, participants were required to consume less than 200 mg dietary cholesterol per day, 25 grams per day of fiber and two grams per day from plant stanols/sterols. Exercise was not included in this intervention. To assess dietary compliance, an RD collected 24-hour dietary recalls at baseline, one month, and two months. Anthropometric measurements and blood samples were collected at baseline, one month, and two months. Genotyping was derived from peripheral leukocytes. Significant reductions in BW, BMI, body fat percentage (BF%), waist circumference (WC), waist-to-hip ratio (WHR), systolic blood pressure, fasting glucose, TG, total cholesterol, high-density lipoprotein (HDL), very low-density lipoprotein (VLDL), and insulin was exhibited in all participants ($p < 0.05$). Additionally, a significantly greater reduction in BW, BMI, WC, WHR, and c-reactive protein was demonstrated in individuals with the mutant-type allele patterns ($p < 0.05$).[13]

Along with this, de Luis and colleagues[16,60] conducted two, three-month weight loss investigations testing varying fat content within the dietary interventions in order to determine the influence of genotype and response to treatment. In the first investigation, 111 obese participants, with average BMI of 30.7 ± 7.1 kg/m^2 and an average age of 49.7 ± 10.1 years, consumed a diet consisting of 1459 kcal/d, with 34.4% kcal fat, 45.7% kcal CHO, 19.9% kcal protein. Fat content was further divided into 21.8% kcal from

saturated fat, 55.5% from monounsaturated fats (MUFA), and 22.7% from polyunsaturated fats (PUFA) (seven grams per day omega-6 fatty acids and two grams per day omega-3 fatty acids).[16] Two to three hours of walking per week was encouraged as aerobic exercise. Dietary intake was assessed via three-day food records at baseline and three months, and weekly dietary monitoring by an RD via phone call. Anthropometric measurements and blood samples were collected at baseline and three months. Genotyping was determined via peripheral leukocytes. All in all a significant decrease in BW, BMI, fat free mass (FFM), and systolic blood pressure were demonstrated in all participants from baseline to three months ($p < 0.05$). Individuals with the mutant-type allele pattern experienced greater reductions in BMI, BW, FFM, FM, and WC ($p < 0.05$). Interestingly only individuals with the mutant-type allele patterns demonstrated significant decrease in total cholesterol, LDL, insulin and HOMA after three months ($p < 0.05$).[16]

In the second investigation, 122 apparently healthy, obese (average BMI 37.4 ± 6.1 kg/m^2, average age 47.8 ± 11.9 years) males and females were assessed.[60] The dietary protocol was slightly different from the aforementioned protocol such that higher amounts of MUFAs were included as opposed to PUFAs. The diet was composed of 1342 kcal/d, 34.1% kcal fat, 46.6% kcal CHO, 19.2% kcal protein. Fat content was further divided into 21.7% kcal from saturated fat, 67.5% kcal as MUFA and 10.8% kcal PUFA. Three-day food records were collected at baseline and three months to determine dietary compliance. Exercise, genotyping, and measurement protocols were identical to the previously mentioned trial.[16] In this trial all participants demonstrated a significant

decrease in BW, BMI, and WC ($p < 0.05$). In contrast to the previously mentioned investigation, individuals with the wild-type allele pattern demonstrated significant reduction in FM, along with fasting insulin and leptin levels ($p < 0.05$).[60]

Finally, in another three-month weight loss intervention conducted by de Luis and colleagues[15], 69 apparently healthy, obese participants (average BMI 34.1 ± 5.1 kg/m^2), with an average age of 45.5 ± 16.6 years, consumed a hypocaloric diet consisting of 1520 kcal/d, 25% kcal fat, 52% kcal CHO, 23% kcal protein. Aerobic exercise was encouraged for 60 minutes at least three days per week. Three-day food records were collected at baseline and three-months to determine dietary compliance. Anthropometric measurements, blood sample, and maximal oxygen consumption was measured at baseline and three months. All Genotyping was determined via peripheral leukocytes. All participants demonstrated a significant reduction in BW, BMI, WC, and increase in oxygen consumption between baseline and three months ($p < 0.05$). Individuals with the wild-type allele pattern demonstrated a greater decrease in FM, LDL and leptin levels in comparison to those with the mutant-type allele pattern ($p < 0.05$). However, individuals with the mutant-type allele pattern demonstrated more significant reduction in fasting glucose at three months ($p < 0.05$).[15]

Overall, health outcomes from weight loss interventions in relation to FABP2 rs1799883 genotype have been variable. Among the two-month weight loss interventions, de Luis and colleagues[14] demonstrated greater reductions in biochemical markers related to lipid and CHO metabolism in carriers of the wild-type allele pattern, yet greater reductions in fat mass in individuals with the mutant-type allele pattern.

Similarly Martinez-Lopez and colleagues[13] demonstrated favorable outcomes in anthropometrics in individuals carrying the mutant-type allele pattern, but biochemical changes were not significantly different between genoytpe. It is possible the degree of caloric restriction may have influenced the minor variations in results, i.e. ~1500 kcal/d versus 1000-1200 kcal/d. In the three-month weight loss interventions, varying responses in relation to genotype were demonstrated pending on the type of fat included in the diet, MUFA versus PUFA.[16,60] Additionally, when fat content was not controlled, mutant-type allele pattern was associated with improvements in fasting glucose, whereas wild-type allele pattern was associated with improvements in LDL cholesterol, FM, and fasting leptin levels.[15] Considering these findings, it is evident that varying dietary compositions elicit different outcomes pending FABP2 rs1799883 genotype.

FABP2 rs1799883 and Genetic Profiling

The mutant-type allele pattern at rs1799883 of FABP2 has been associated with adverse glucose and lipid metabolism.[57-59] Additionally, this genotype is more prevalent in obese individuals.[57-59] Collectively, when considering dietary prescription to optimize weight loss, evidence supports a lower CHO, moderate fat, and adequate protein diet to improve markers of body composition in overweight and obese individuals carrying the mutant-type allele patterns.[13-16] Furthermore, a moderate CHO, lower fat, and adequate protein diet may be helpful for individuals with the wild-type allele pattern to improve body composition and fasting blood lipid levels.[15] Considering this, use of FABP2 rs1799883 may be useful as a marker within a genetic profile to optimize nutrition for weight loss.

PPARG2 (rs1801282)

Association with Obesity

Peroxisome proliferator-activated receptor gamma-2 (PPARG2) is an isoform of the peroxisome proliferator-activated receptor gamma gene and consists of an additional 28 amino acids at its amino terminus.[61] PPARG2 is primarily located in adipocytes and plays an important role in adipocyte differentiation.[62-64] A missense mutation in PPARG2 occurs at codon 12 of exon B in rs1801282 and consists of a transition of alanine (Ala) for proline (Pro).[64] The wild-type allele pattern for PPARG2 is Pro/Pro, whereas the mutant-type is Pro/Ala or Ala/Ala. In contrast to FABP2 rs1799883, the allelic frequency of Ala varies among populations; for example, the frequency among Caucasians is about 11%, whereas the frequency among Asians is about 9%.[65,66] A strong association between mutant-type allele patterns and more favorable body composition, blood lipid profile, and insulin sensitivity has been demonstrated in normal-weight, middle-aged and elderly men and women in comparison to individuals with the wild-type allele pattern.[61,64] Interestingly, the opposite association has been demonstrated in overweight/obese individuals.[65-68]

In an investigation conducted by Cole and colleagues[65], baseline PPARG2 rs1801282 genotype, anthropometric, and biochemical measurements were assessed in 921 overweight/obese (BMI > 28 kg/m^2), middle-aged (38-40 years old) Mexican-Americans who were part of a population-based family study of atherosclerotic risk factors associated with atherosclerosis (San Antonio Family Heart Study). BMI, WC, WHR, body composition via bioelectrical impedance, and a fasting blood sample were

collected. Genotyping was determined from peripheral leukocytes. Overall, mutant-type allele patterns demonstrated significantly higher BMI (p=0.011), WC (p=0.028), and leptin levels (p=0.021) in comparison to individuals with the wild-type pattern.[65]

Similarly, Kim and colleagues[66] assessed 1,051 overweight (BMI of 25.6 ± 0.12 kg/m^2) Korean women aged 27 ± 0.2 years old. Body composition measures were collected via bioelectrical impedance, and fat distribution measures via CT scan for 471 of the participants. Blood samples were collected to determine blood lipid profile and genotyping. Individuals with the mutant-type allele pattern had significantly higher BW (p=0.012), BMI (p=0.012), WHR (p=0.001), BF% (p=0.025), abdominal fat area, abdominal subcutaneous fat, and visceral fat (p=0.001).

Along with investigations exclusively in overweight and obese individuals, Robitaille and colleagues[68] assessed normal weight, overweight, and obese individuals from a cohort of the Quebec family study including 720 adults (313 men and 407 women), with an average age of approximately 44 years old, of French-Canadian descent. Body composition via CT scan, WC, and a blood sample were collected. Genotyping was determined from lymphoblastoid cell lines. When adjusted for age and gender, regardless of baseline weight status, individuals with mutant-type allele pattern exhibited higher BMI (p=0.04), FM (p=0.009), WC (p=0.03), visceral adipose tissue (p=0.01), and subcutaneous adipose tissue (p=0.001).[68]

Similarly, Milewicz and colleagues[67] compared overweight/obese women to normal weight counterparts within 318 postmenopausal women, 50-60 years old. Body composition determined by DXA scan, BW, WC, and blood sample were collected.

Genoytping was determined via peripheral leukocytes. In comparison to normal weight individuals, obese individuals with mutant-type allele pattern demonstrated higher total cholesterol ($p < 0.001$), LDL ($p < 0.001$), and TG ($p < 0.001$). Aside from these findings, no other significant differences between weight status or genotype among BW and body composition measures were observed.[67]

Furthermore, from a longitudinal perspective, a retrospective population study was conducted assessing genotype and weight change throughout the life cycle in 311 participants (145 men and 166 women).[69] Weight was measured at birth, seven years of age, 20 years of age, and the age of the study, which was approximately 41 years. Genotyping was determined from peripheral leukocytes. Individuals homozygous for the mutant-type allele pattern (Ala/Ala) demonstrated higher birth weight ($p=0.031$), weight at seven years of age ($p=0.016$), and weight at study age ($p=0.073$). Individuals with either mutant-type allele pattern demonstrated significantly higher ponderal index (birth weight in kg/birth length in m^3) ($p=0.04$) and waist circumference at study age ($p=0.04$).[69]

Jointly, a strong association has been demonstrated between PPARG2 rs1801282 mutant-type allele pattern in relation to degree of obesity, fat deposition, and adverse blood lipid profile in overweight/obese individuals.[65-68] When comparing overweight/obese individuals to normal weight individuals, those with the mutant-type allele pattern, regardless of weight status, demonstrated higher BW and adverse parameters of body composition.[68] Additionally, in the post-menopausal age group, when comparing normal weight to overweight/obese women, overweight/obese women

with the mutant-type allele pattern demonstrated significantly greater markers of blood lipids.[67] Moreover, findings from a longitudinal, retrospective study suggests the mutant-type allele pattern in PPARG2 rs1801282 may serve as a predictor for weight gain throughout the life cycle. These findings support increased susceptibility to overweight/obese weight status, adverse body composition and abnormal blood lipid profiles in individuals carrying the mutant-type allele pattern of PPARG2 rs1801282; thus further research is warranted in this population to determine optimal intervention to promote weight loss, improved body composition and blood lipid profile.

Weight Loss Interventions

In spite of the aforementioned findings, few investigations have assessed the association between baseline PPARG2 rs1801282 genotype and response to weight loss interventions. In an investigation conducted by Lindi and colleagues[20], 490 overweight/obese men and women (average BMI 31.1 ± 4.6 kg/m^2, aged 40-68 years old) with pre-diabetes were assessed for baseline PPARG2 rs1801282 genotype in relation to health outcomes after participating in the Finnish Diabetes Prevention Study. Briefly, the Finnish Diabetes Prevention Study included 522 participants who were randomized into a control group or lifestyle intervention group.[70] A diet consisting of less than 30% calories from fat, less than 10% calories from saturated fat and 15 grams of fiber consumed per 1000 calories was prescribed, with no specific instruction regarding total caloric intake, and macronutrient range for CHO and protein. Participants met with an RD for dietary education/counseling seven times within the first year and every three months over the last two years. Additionally, 30 minutes of exercise per day

was encouraged. Dietary data from three-day food records, anthropometric measurements, and a blood sample was collected at baseline and at three years. Genotyping was determined via peripheral leukocytes.[70]

At three years, within the control group, participants homozygous for Ala allele had significantly greater chance of developing type 2 diabetes, a 2.36 fold odds ratio, in comparison to individuals with the wild-type allele pattern.[20] In the intervention group, while the risk of developing type 2 Diabetes was higher in individuals homozygous for Ala in comparison to those with the wild-type allele pattern, the difference in risk was not significant. Moreover, within the intervention group, individuals homozygous for Ala allele experienced a significant reduction in body weight in comparison to those with the wild-type allele pattern ($p=0.043$). While not statistically significant, heterozygotes for Ala also exhibited greater reduction in body weight in comparison to individuals with the wild-type allele pattern.[20]

Along with this investigation in patients with pre-diabetes, Franks and colleagues[18] demonstrated similar findings in the Diabetes Prevention Program conducted in the United States. Briefly, the U.S Diabetes Prevention Program was a multi-centered, randomized controlled trial.[71] Participants were randomized to a control group, a medication group, and a lifestyle intervention. The medication group received 850 mg twice daily of metformin along with annual individual meetings, 20-30 minutes in length, emphasizing consumption of healthy diet and participation in a regular exercise program. The lifestyle intervention included a 16-session curriculum covering diet, exercise, and behavior modification. The curriculum included individual meetings

with study personnel for the first 24 weeks, then monthly sessions thereafter for the remainder of the study. Participation in 150 min of physical activity per week was prescribed.[71] Further, in both groups dietary prescription was based on the National Cholesterol Education Program step 1 diet (500-1000 kcal/d reduction, 55% kcal CHO, < 30% kcal fat with 8-10% kcal from saturated fat, ~15% kcal protein, and < 300 mg/d cholesterol).

Franks and colleagues[18] reported on data collected in one year of the program in 3,234 obese (average BMI 34.1 kg/m^2, average age of 51 years) men and women. Genotyping for all participants was determined via peripheral leukocytes. Consistent with previously mentioned findings, individuals with mutant-type allele pattern demonstrated significant reduction in body weight in the drug group ($p=0.01$) and lifestyle intervention ($p=0.04$) in comparison to individuals with the wild-type allele pattern.[18]

In addition, Curti and colleagues[21] assessed baseline genotype of PPARG2 rs1801282 along with FTO rs9939609 and PPARG ApoA1 -75G/A in a 9-month weight loss intervention in 18-80 year old, apparently healthy, overweight/obese (BMI 30.4 ± 0.48 kg/m^2) males and females. Participants received lifestyle coaching every three months consisting of dietary education/counseling for a healthy diet, and encouragement for participation in greater than 150 minutes per week of physical activity. At baseline and nine months, 24-hour food recalls were collected to determine dietary compliance, physical activity was assessed with the International Physical Activity Questionnaire, and BW, BMI, blood pressure, WC, and blood samples were collected. Genotyping was

determined from whole blood samples. Regarding PPARG2 rs1801282 genotype, outcomes demonstrate a significant reduction in blood pressure favoring the mutant-type allele patterns ($p < 0.001$). All participants experienced a significant reduction in BW ($P < 0.001$), WC ($p=0.01$), fasting blood glucose ($p=0.041$), fasting insulin ($p < 0.001$), apolipoprotein B ($p < 0.001$), and increased HDL ($p < 0.001$).[21] Favorable trends for the mutant-type allele pattern were demonstrated for WC and fasting blood glucose, whereas favorable trends for the wild-type allele pattern were demonstrated for fasting insulin.

Similarly, Garaulet and colleagues[19] assessed baseline PPARG2 rs1801282 in relation to weight loss outcomes in 1465 apparently healthy, overweight/obese (BMI 25-40 kg/m^2), males and females, aged 20-65 years old. Length of the study was individualized depending on how long it took each participant to reach goal weight. Individual goal weight was determined considering a weight loss of 0.5-1 kg per week. The Harris-Benedict Equation was used to calculate energy needs including an activity factor; for weight loss, 600 kcals were deducted from the predicted energy needs to promote weight loss. In addition, participants were instructed to consume 50% of their kcal from CHO, 35% kcal fat (< 10% kcal saturated fat, 20% MUFA), and 15-20% kcal protein. Overall this resulted in a 1200-1800 kcal diet for women and 1500-2000 kcal diet for men. Participants met with an RD weekly for group education sessions. The exercise intervention included 10,000 steps per day along with daily physical activity of moderate-intensity for 30 minutes or more. Dietary data was collected via 24-hour diet recalls; BW, body composition via bioelectrical impedance, WC, HC, and blood pressure were measured at start and finish of each individual's study time. Genotyping

was determined from whole blood samples. Overall, a significant interaction between heterozygote carriers, a mutant-type allele pattern, was demonstrated between fat intake and weight loss ($p < 0.001$). When consuming a lower fat diet, individuals with the mutant-type allele patterns demonstrated greater percentage of weight loss from baseline in comparison to those with the wild-type allele pattern ($p=0.286$); additionally, when consuming a higher fat diet (> 42.6% kcal fat), those with the mutant-type pattern demonstrated less weight loss from baseline in comparison to individuals with the wild-type pattern ($p=0.037$).[19]

Finally, Nicklas and colleagues[72] conducted an 18 month trial, including six months of weight loss intervention followed by 12 months of follow up in 70 postmenopausal (average age 61 years old), apparently healthy, obese (average BMI ~31 kg/m^2) women. For the six-month weight loss intervention, participants were instructed to reduce caloric intake by 250-350 kcal/d, with no specific instruction regarding macronutrient distribution. In addition, participants attended weekly group meetings with an RD for dietary instruction, education, and counseling. Along with the dietary component, the exercise component included walking on a treadmill at 50-60% measured heart rate reserve one day per week in the investigator's laboratory, and walking two days per week outside of the lab. Measures at baseline and six months include the following: BW, body composition via DXA scan, maximal oxygen uptake, resting metabolic rate via indirect calorimetry, and blood sample. Genotyping was determined from whole blood samples. Of all the measures collected, significant reductions from baseline to six months were only exhibited in BW, fasting glucose and

insulin favoring individuals with the wild-type allele pattern ($p < 0.001$). Individuals with the mutant-type allele pattern also demonstrated significant reduction in fat oxidation.[72]

As for the 12-month follow up portion of the study, for the first six months of this time participants attended group sessions with an RD bi-weekly to discuss healthy lifestyle change. Participants were encouraged to continue progress for the last six months and return for BW measurements after six months.[72] Upon completion of the12 month maintenance period, incidence of weight regain was significantly higher in women with the mutant-type allele pattern (5.4 ± 0.8 kg in mutant-type versus 2.8 ± 0.4 kg in wild-type, $p < 0.01$).[72]

Among all weight loss interventions conducted, the majority of evidence supports greater reductions in BW, improvements in body composition, and improvements in fasting blood glucose associated with PPARG2 rs1801282 mutant-type allele pattern in both apparently healthy overweight/obese individuals and overweight/obese individuals with pre-diabetes. [18-21,72] In contrast, Nicklas and colleagues[72] demonstrated significant reduction in BW, fasting blood glucose, and insulin levels favoring individuals with the mutant-type allele pattern. Differences in health outcomes regarding genotype may be attributed to length of intervention and/or degree of caloric restriction, suggesting individuals with the wild-type allele pattern may improve health outcomes in a shorter period of time with less caloric restriction, whereas those with the mutant-type allele pattern may require longer interventions with a more intense dietary protocol.

PPARG2 rs1801282 and Genetic Profiling

The role of PPARG2 in adipocyte differentiation and fat metabolism is supported by significant associations demonstrated between baseline genotype and degree of obesity, body composition, and blood lipid profile in overweight/obese indivudals.[65-68] Regarding weight loss, the majority of investigations demonstrated greater outcomes in individuals with the mutant-type allele pattern.[18-21] These investigations included similar exercise prescriptions, emphasizing at least 30 minutes per day, five days per week, of cardiovascular activity. In addition, dietary prescription consisted of a hypocaloric, lower-fat, moderate CHO, and adequate protein diet specifically in individuals carrying the mutant-type allele pattern of PPARG2 rs1801282. Therefore, preliminary evidence supports the use of baseline PPARG2 rs1801282 genotype to optimize dietary prescription within a weight loss program.

ADRB3 (rs4994)

Association with Obesity

Beta-3-adrenergic receptor (ADRB3) is located primarily in adipocytes and plays a role in lipid metabolism and thermogenesis.[73,74] A missense mutation in rs4994 at codon 64 results in the replacement of tryptophan for arginine.[74] The wild-type allele pattern of ADRB3 is homozygous for tryptophan, Trp/Trp, whereas the mutant-type allele patterns include arginine and can be homozygous, Arg/Arg, or heterozygous, Trp/Arg.

In a quantitative meta-analysis conducted in over 9000 participants across diverse populations, regardless of weight classification, heterozygous carriers of the

mutant-type allele pattern exhibited a significantly greater BMI in comparison to individuals with the wild-type allele pattern.[74] Along with this, more recent investigations comparing normal weight to overweight/obese males and females have also demonstrated increased BF%, visceral adipose tissue (VAT), WC, WHR, decreased HDL levels, and impaired glucose tolerance in carriers of the mutant-type allele patterns.[75-77]

Furthermore, in an investigation comparing 131 obese (BMI > 30 kg/m^2), premenopausal women to 256 age-matched non-obese women, the obese individuals with the mutant-type allele pattern exhibited significantly higher fasting BG, total cholesterol, TG, and lower HDL in comparison to obese individuals with wild-type allele pattern.[78] Interestingly, no significant differences for body composition, fat distribution, blood pressure, fasting BG, insulin, and blood lipid levels were demonstrated between genotype in non-obese weight participants.[78]

Overall, a strong association has been demonstrated between ADRB3 rs4994 mutant-type allele patterns and adverse health effects in overweight/obese individuals. Considering this strong association, along with ADRB3's role in lipid metabolism, research is warranted assessing health outcomes from a weight loss intervention in relation to ADRB3 rs4994 genotype.

Weight Loss Interventions

While multiple investigations have assessed baseline ADRB3 rs4994 genotype in relation to health outcomes after participation in a weight loss intervention, findings regarding genotype are mixed. In an investigation conducted by Rawson and

colleagues[79], 34 obese (BMI > 30 kg/m^2), postmenopausal (average age 57 years), Caucasian women were prescribed a 1200-calorie diet based on the step two diet plan from the National Cholesterol Education Program (500-1000 kcal/d reduction, 55% kcal CHO, < 30% kcal fat with < 7% kcal from saturated fat, ~15% kcal protein, and < 200 mg/d cholesterol).[80] An exercise component was not included in this intervention. Length of study was dependent on how long it took each participant to reach her goal weight, which was based on the Metropolitan Life Insurance Tables. Average length of study for participants was approximately 13.5 months. Measures from baseline to completion of the study included BW and body composition via doubly labeled water technique. Genotyping was determined from peripheral leukocytes. Interestingly, all participants experienced a significant reduction in body mass, BMI, BF%, FFM, and FM from baseline to completion ($p < 0.05$), with no genotype x time interactions observed.[79]

In addition, Shiwaku and colleagues[81] also did not find significant differences in health outcomes between ADRB3 rs4994 genotype and health outcomes after participation in a weight loss intervention. Seventy-six apparently healthy, normal and overweight (BMI > 21 kg/m^2) Japanese women aged 35-69 years old participated in a three-month weight loss program that included individualized dietary counseling promoting caloric restriction from baseline dietary intake, with no specific prescription regarding macronutrient intake. The exercise component of the program consisted of 7,000 steps per day measured with a pedometer. Additionally, participants attended supportive group therapy sessions with study personnel emphasizing implementation of healthy lifestyle habits.[81] Body composition measurements, BW, and a blood sample

were collected at baseline and three months. Genotyping was determined from peripheral leukocytes. As mentioned previously, no significant differences in ADRB3 rs4994 genotype were demonstrated in anthropometric measures or biochemical markers from baseline to three-months; all participants exhibited significant reductions in WC, HC, tricep skinfold measurement, blood pressure, BW, HDL LDL to HDL ratio, and phospholipids from baseline to completion of the study ($p < 0.05$).[81]

Similarly, Tahara and colleagues[82] conducted a three-month behavioral weight loss intervention in 57 apparently healthy, normal and overweight/obese Japanese men (BMI > 23 kg/m^2), with an average age of 48 years old. The dietary intervention consisted of individual meeting(s) with an RD at least once during the study for dietary counseling to promote consumption of a healthier, lower calorie diet in comparison to baseline diet. Additionally, the exercise intervention included 10,000 steps per day measured with a pedometer. Corresponding with the previously mentioned trial,[79] a behavioral intervention was also included in this trial. The behavioral intervention consisted of three group meetings (baseline, mid-point, and completion of the study) emphasizing healthy lifestyle habits. In order to determine compliance with the diet and exercise interventions, a battery of questionnaires were provided at completion of the study. Additionally, BW and WC were measured once per week throughout the duration of the study, and genotyping was determined via peripheral leukocytes. Consistent with aforementioned studies,[79,81] while all participants experienced significant reductions in anthropometric measures from baseline to three-months ($p < 0.05$), no significant differences were identified between ADRB3 rs4994 genotype.[82]

Furthermore, Bea and colleagues[83] retrospectively assessed baseline genotype of three common mutations of beta-adrenergic receptor (ADRB2, ADRA2B, ADRB3) in response to health outcomes from a block-randomized controlled lifestyle intervention. This investigation is different from previously mentioned trials[79,81,82] such that there was no dietary component within the weight loss intervention, solely an exercise component. This secondary analysis included 148 apparently healthy, normal and overweight/obese (BMI > 21 kg/m^2) postmenopausal women, with an average age of 56 years. The lifestyle intervention was 12-months in length, where participants were randomized at baseline to an exercise group or control group. The exercise intervention consisted of high-intensity resistance training and moderate impact weight-bearing exercise for 75 minutes, three days per week. Individuals completed two sets of six to eight repetitions at 70-80% one repetition maximum (1 RM). Participant's 1 RM was adjusted every six to eight weeks as strength improved. Body composition was measured via DXA at baseline and 12 months. Genotyping was determined from buccal cheek swabs. Regarding ADRB3 rs4994 polymorphism, as reported in previous studies with dietary and/or lifestyle interventions, no significant differences were exhibited between ADRB3 rs4994 genotype and changes in body composition from baseline to 12 months. Additionally, all ADRB3 rs4994 genotypes lost significant and equivalent BF%.[83]

In contrast to the previously mentioned studies demonstrating no significant differences between ADRB3 rs4994 genotype after diet, exercise, and/or behavioral intervention,[79,81-83] some investigations have found significant differences between ADRB3 genotype and health outcomes after a weight loss intervention.[17,22,23] Phares and

colleagues[22] conducted a six-month weight loss intervention within 70 apparently healthy, overweight (average BMI 28 kg/m^2), Caucasian men and women (29 men, 41 women), aged 50-75 years old. The dietary intervention was not hypocaloric, but included a macronutrient distribution range recommended by the American Heart Association (55% kcal CHO, 30% kcal fat, 15% kcal protein). The exercise intervention consisted of endurance exercise three days per week and progressed in intensity and duration for the first ten weeks of the trial, i.e. 50-70% individual VO_2max starting with 20 minutes of exercise and progressing to 40 minutes. For the last 14 weeks, participants trained at 70% VO_2max for 40 minutes and also included 45-60 minutes of walking on one day during the weekend. Dietary compliance was measured from three-day food records collected at baseline, two, four, and six months. Measures at baseline included blood sample for genotyping, VO_2max, oral glucose tolerance test, and body composition via DXA scan. At six months, body composition was measured once more. Regarding the ADRB3 rs4994 genotype, while all participants exhibited a significant reduction in BF%, FM, and percent trunk mass from baseline to six months, individuals with the mutant-type allele pattern demonstrated greater reduction in BF% ($P=0.027$), FM ($p=0.037$), and percent trunk fat ($p=0.03$) in comparison to individuals with the wild-type allele pattern.[22]

Although Phares and colleagues[22] exhibited a significant difference between ADRB3 rs4994 genotype in favor of the mutant-type allele pattern, other investigations have demonstrated the opposite.[17,23] In a three-month weight loss intervention conducted by Lee and colleagues[23], 80 apparently healthy, overweight (BMI 25-30 kg/m^2),

Japanese women, aged 40-69 years old, attended weekly dietary counseling sessions with an RD regarding reduction of baseline energy intake. In addition, participants completed 60 minutes of supervised, moderate-intensity, aerobic exercise weekly along with 10,000 steps per day as measured with a pedometer. Dietary compliance was measured with two-day food records collected at baseline and three months. Additionally, BW, tricep and subscapular skinfold thickness, WC, BF% as determined by the Brozek equation, and a blood sample was retrieved at baseline and three months. Genotyping was determined from peripheral leukocytes. Overall, while all participants experienced a significant reduction in BW, BMI, BF%, WC, and total cholesterol from baseline to three months ($p < 0.01$), participants with the wild-type allele pattern also demonstrated significant reductions in HDL ($p < 0.05$), LDL ($p < 0.05$), and TG ($p < 0.01$). Moreover, participants with the wild-type allele pattern demonstrated greater reductions in BW and BMI ($p < 0.01$).

Similarly, a more recent three-month investigation was conducted in 260 apparently healthy, obese (average BMI 37 kg/m^2) men and women (55 men, 166 women), with an average age of approximately 45 years old.[17] Participants were randomized into two hypocaloric diet groups with similar macronutrient distributions (approximately 1400 kcal/d, 45% kcal CHO, 35% kcal fat, 20% kcal protein). The difference between diet groups remained in the content of MUFA versus PUFA. The MUFA group included a dietary prescription of 67.5% fat calories as MUFA and 10.8% fat calories as PUFA, while the PUFA group included 55.5% fat calories from MUFA and 22.7% fat calories from PUFA. The exercise intervention consisted of 60 minutes

per day of aerobic activity, three days per week. At baseline and three months, the following measures were collected: three-day food records, BW, blood pressure, body composition via bioelectrical impedance, and a blood sample. Additionally, genotyping was determined by peripheral leukocytes. As demonstrated in previous investigations, all participants experienced significant reductions in BMI, BW, FM, and WC from baseline to completion ($p < 0.05$), regardless of genotype or diet group. Individuals with the wild-type allele pattern following the PUFA diet also demonstrated a significant reduction in BG, insulin, HOMA, TC, LDL, and TG from baseline ($p < 0.05$). When comparing genotypes within the diet groups, reductions in WC were significantly greater in mutant-type following the MUFA diet ($p < 0.05$), whereas reductions in BMI were greater in wild-type allele pattern ($p < 0.05$). In the PUFA diet, participants with the mutant-type allele pattern exhibited greater reductions in BW, WC, and fasting insulin ($p < 0.05$), whereas participants with the wild-type allele pattern exhibited greater reductions in BMI, FM, WHR, and calculated HOMA ($p < 0.05$).[17]

Conclusively, evidence exists regarding baseline ADRB3 rs4994 genotype and response to weight loss interventions. Among investigations that demonstrated no significant differences between baseline genotype and response to intervention, this may be attributed to less-rigorous diet and exercise protocols.[79,81-83] For example, half of these investigations did not include a specific dietary prescription, rather dietary counseling with the objective of reducing overall energy intake.[81,82] Furthermore, while Rawson and colleagues included a specific dietary prescription, no exercise intervention was included; the opposite was done in the investigation for Bea and colleagues.[79,83]

Therefore, evidence suggests inclusion of a specific dietary and exercise prescription is necessary to determine if a relationship exists between baseline ADRB3 rs4994 genotype and health outcomes after a weight loss intervention.

Among the interventions that have demonstrated significant differences between genotype, the findings are inconsistent.[17,22,23] Within the investigation that demonstrated health outcomes in favor of the mutant-type allele pattern, these results may be attributed to lack of caloric restriction within the intervention.[22] Additionally, since this investigation was six-months in length in comparison to three-months in the investigations favoring the wild-type allele pattern, it is possible that the mutant-type allele pattern may be associated with long-term benefits, whereas the wild-type allele pattern is associated with acute response to weight loss intervention. Thus current evidence suggests that individuals with the wild-type allele pattern may experience greater health outcomes in comparison to the mutant-type allele pattern when following a hypocaloric, moderate fat diet, and participating in 60 minutes of moderate to high intensity aerobic activity three days per week for at least three months.

ADRB3 rs4994 and Genetic Profiling

A strong association has been demonstrated between the mutant-type allele pattern of ADRB3 rs4994 and prevalence of obesity.[74-76,78,84] Considering ADRB3's exclusive location in adipocytes and primary role in lipid metabolism, dietary manipulation of fat intake specifically may be useful in improving health outcomes in individuals participating in a weight loss intervention. Among weight loss interventions, current evidence suggests the necessity of a specific dietary and exercise component

within the investigation to promote weight loss. Regarding the dietary component, evidence suggests a hypocaloric, moderate CHO, higher fat, adequate protein diet to promote improvements in body composition in individuals with the mutant-type allele pattern. Further, increase PUFA content within the diet may improve body composition and biochemical markers related to glucose and lipid metabolism in individuals with the wild-type allele pattern. Regarding the exercise component, it appears as though participation in 60 minutes of moderate to high intensity aerobic activity three days per week for at least three months is necessary.

ADRB2 (rs1042713 and rs1042714)

Association with Obesity

Beta-2-adrenergic receptor (ADRB2) is a G-protein coupled receptor that is widely distributed across the body in adipocytes.[85] The influence of catecholamines on the adrenergic receptors, specifically ADRB2, modulates lipolysis and lipogenesis.[86] Two of the most common genetic mutations associated with ADRB2 occur at codon 16 and 27.[86] At codon 16 (rs1042713)**,** arginine (Arg) replaces glycine (Gly). The allele pattern homozygous for glycine (Gly/Gly) is considered the wild-type allele pattern, whereas the allele patterns including arginine (Arg/Gly, Arg/Arg) are considered the mutant-type. The frequency of the mutation varies depending on the population. For example, allelic frequency of arginine in Europeans is about 51-64% whereas the frequency in East Asians is 71-85%. Additionally the frequency of mutation is most common in women.[86] At codon 27 (rs1042714), glutamic acid (Glu) replaces glutamine (Gln).[86] Thus homozygous carriers of glutamine (Gln/Gln) contain the wild-type pattern,

and carriers of glutamic acid (Glu/Gln, Glu/Glu) are considered mutant-type. At the global level, the frequency of the mutation is about 30%.[86]

Considering the high frequency of mutation at codons 16 and 27, role in lipid metabolism, and subsequent influence on energy expenditure, ADRB2 genotype at codons 16 and 27 may serve importance in relation to weight status.[87] Current evidence suggesting an association between ADRB2 and obesity is mixed. Two meta-analyses assessing men and women of varying populations, ages, and weight classifications did not demonstrate any significant associations between mutations of ADRB2 at codon 16 or 27 and increased risk of obesity or adverse health markers associated with obesity.[86,88]

In contrast, regarding the mutation at codon 16 (rs1042713), two investigations, conducted in men and women demonstrated a significant association between the wild-type allele pattern and prevalence of obesity.[89,90] Additionally, a significantly higher BMI, WC, HC, WHR, total cholesterol, LDL, TG, leptin and insulin levels were demonstrated in individuals with the wild-type allele pattern.[90] Along with these findings, two longitudinal studies, one over a six year time period and one over a 23 year time period, conducted in men and women, demonstrated a significant association between obesity in men carrying the wild-type allele pattern, and obesity in women carrying the mutant-type allele pattern.[87,91] In a five year longitudinal study conducted in individuals who were normal weight at baseline, significant increases in BMI, WHR, FM, and BP were exhibited after five years in men and women carrying the glycine allele, which is part of the wild-type and heterozygous mutant-type allele patterns.[92]

Furthermore, the mutation at codon 27 (rs1042714) has also shown significant associations with obesity. In two recent meta-analyses, the presence of the mutant-type allele pattern demonstrated a significant association with obesity risk, with increased risk in Asians, Pacific Islanders, and American Indians.[86,88] In investigations comparing normal weight to overweight/obese individuals, regardless of weight, individuals homozygous for the mutant-type allele pattern demonstrated significantly ($p < 0.05$) higher BMI,[85,89,93] WC and HC,[85] TG,[85,89,93] fasting leptin and insulin,[85] and incidence of type 2 diabetes.[89] Moreover, a higher risk of obesity was demonstrated in individuals homozygous for the mutant-type allele pattern.[89,93] In the previously mentioned five year longitudinal study, significant increases in BMI, WHR, FM, and BP were exhibited after five years in men and women carrying the mutant allele patterns.[92]

Interestingly, only one investigation to date has assessed an interaction between the aforementioned mutations in ADRB2. Prior and colleagues[94] exhibited significantly greater BMI, weight, BF%, intra-abdominal fat, fasting BG, and 120 minute post-prandial glucose in obese, middle-aged women with the glycine allele at codon 16 (Gly16) and glutamine allele at codon 27 (Gln27).[94]Additionally, individuals with Gly16 and glutamic acid at codon 27 had the lowest oxygen consumption during a submaximal exercise test. These findings suggest individuals with the wild-type allele pattern of both ADRB2 polymorphisms or heterozygous mutant-type allele pattern of the mutation at codon 27 may be at greater risk of obesity and adverse health markers associated with obesity.

Overall, current evidence suggests an association between obesity and carriers of the glycine allele at codon 16 (wild-type or heterozygous mutant-type) and glutamic acid allele at codon 27 (heterozygous or homozygous mutant-type). The only investigation to date demonstrating a synergistic effect between these mutations in ADRB2 suggests prominent adverse health effects in the presence of the glycine allele at codon 16.[94] Due to the aforementioned associations with obesity and known role of ADRB2 in regards to thermogenesis and lipid metabolism, further research regarding ADRB2 genotype at codon 16 and 27 in relation to success in a weight loss intervention is warranted.

Weight Loss Interventions

Few investigations have assessed the relationship between baseline genotype of the common mutations of ADRB2 and health outcomes from a weight loss intervention. Regarding the mutation at codon 27, Bea and colleagues[83], as previously mentioned with respect to ADRB3, demonstrated significant increases in lean soft issue in individuals with the mutant-type allele patterns. As demonstrated among weight loss trials related to ADRB3, the exercise intervention included in Bea and colleagues trial is the most rigorous prescription among all of the studies assessing baseline ADRB2 polymorphisms in response to a weight loss intervention.

The remaining weight loss trials assessing health outcomes in relation to baseline ADRB2 genotype at codon 16 and 27 consist primarily of dietary interventions, with some guidance/encouragement for participation in regular physical activity. In a 12-month intervention exclusively assessing changes in relation to codon 27 genotype, 62 apparently healthy, obese (BMI > 30 kg/m^2), postmenopausal (average age ~39 years

old) women were prescribed a very low calorie diet for three months, with no specific instruction regarding macronutrient intake, for three months followed by a nine month weight maintenance period.[24] The very low calorie diet consisted of approximately 750 kcals/d, delivered primarily through meal replacement products, for the first three months, and participants attended weekly group sessions with an RD.[24] The following nine months consisted of monthly group nutrition classes covering different nutrition topics to assist with weight maintenance and healthy eating habits. As for the exercise component, participants were instructed to keep a daily physical activity log including activity type, duration, and perceived intensity. At baseline, three months, and 12 months, BW, WC, and body composition via DXA were measured. Additionally, baseline genotyping was determined from whole blood samples. As a whole, all participants lost weight and experienced favorable changes in body composition. A significant reduction in gynoid body fat percentage favoring the wild-type allele pattern versus homozygous mutant-type allele pattern was demonstrated ($p < 0.03$).[24]

Additionally, Saliba and colleagues[95] conducted a seven week dietary intervention assessing outcomes related to baseline genotype of mutations at codon 27 and codon 16. In this trial, 109 apparently healthy, obese (average BMI 30-34.9 kg/m^2), premenopausal (average age 30-39 years old) women were prescribed individualized diets consisting of a 600 kcal deficit based on estimated energy requirements, with no specific prescription regarding macronutrient intake. The dietary intervention consisted of three individual counseling sessions and two group sessions. As for the exercise component, participants attended one group session that provided information regarding

increasing physical activity from baseline. BW was measured at baseline and seven weeks and baseline genotyping was determined from whole blood samples. Overall, no significant differences were exhibited between health outcomes and polymorphisms of ADRB2 at codon 16 or 27.[95]

Furthermore, a three month dietary intervention in 78 apparently healthy, obese (34 ± 2.8 kg/m^2), premenopausal (average age 36.7 ± 7 years old) women, provided individualized diets for participants based on a 600 kcal deficit from the individual's estimated energy requirements multiplied by an activity factor of 1.3 (low physical activity).[25] Participants also attended weekly dietary counseling sessions with an RD. Unfortunately no exercise component was included in this study. The following measures were collected at baseline and completion of the study: three day weighed food records, BW, body composition via DXA, WC, and resting metabolic rate. Additionally, baseline genotyping was determined via a buffy coat. By the end of the intervention, no significant changes in outcomes were demonstrated among allele patterns at codon 16; however, a trend in change in BW and FM was exhibited favoring individuals with the wild-type allele pattern. At codon 27, individuals with the mutant-type allele patterns demonstrated significantly greater reductions in BW ($p=0.002$) and LM ($p=0.001$) in comparison to wild-type allele pattern.[25]

In contrast, in a five month diet only intervention exclusively assessing the mutation at codon 16, no significant differences were exhibited between allele patterns and health outcomes.[96] In this investigation, 150 apparently healthy, overweight and obese (BMI 27-38 kg/m^2) men and women (39 males, 111 females), aged 20-50 years

old were prescribed a very low calorie diet for two months, followed by instruction to maintain the newly achieved body weight for the last three months. The diet consisted of a formula containing 50 g CHO/d, 7 g fat/d, 52 g protein/d (~500 kcal/d), along with unlimited non-starchy vegetable intake. No exercise component was included in this study. At baseline, two months, and five months, BW and body composition via the BOD POD were measured. Genotyping was determined at baseline via a buffy coat. . While all participants experienced significant reductions in BW, BMI, FM, percent FM, WC, and hip circumference ($p < 0.001$) from baseline to five months, no significant differences were found between genotypes.[96]

Collectively, the relationship between allelic variants of ADRB2 at codon 16 and codon 27 in relation to health outcomes and success in a weight loss intervention are inconclusive. Of the three investigations that assessed polymorphisms at codon 16, only one investigation demonstrated a trend in BW and FM loss favoring the wild-type allele pattern,[25] with the other trials demonstrating no significant differences in outcomes between genotype.[95,96] These differences may be attributed to varying lengths of study and dietary protocols. Additionally, only one of the investigations addressed physical activity.[95]

Regarding the five trials that assessed polymorphisms at codon 27, only one investigation demonstrated a greater reduction in BW with the mutant-type allele pattern.[25] Further, inconsistent findings regarding changes in lean mass with regards to the mutant-type allele pattern exist, with one trial demonstrating a reduction in lean mass[25] and another exhibiting an increase.[83] These findings may be attributed to

variances in methodologies, such that the latter trial consisted only of an exercise intervention, while the former solely implemented dietary intervention. Interestingly, in an investigation including diet and exercise, gynoid body fat percentage was reduced in individuals with the wild-type allele pattern.[24] In contrast to the increased prevalence of obesity demonstrated in individuals with the mutant-type allele pattern, it appears as though individuals with the wild-type allele pattern experience greater weight loss when following a hypocaloric diet. Moreover, individuals with the mutant-type allele pattern have exhibited greater improvements in body composition when exercise has been included in the intervention.

ADRB2 rs1042713 and rs1042714 and Genetic Profiling

As mentioned previously, on account of the high frequency of mutation at codons 16 and 27, role in lipid metabolism, and subsequent influence on energy expenditure, baseline allelic patterns in these sequences of ADRB2 may serve importance in relation to weight status.[87] The wild-type allele pattern at codon 16 has been associated with overweight/obesity status and related adverse health effects.[87,89-92] Equitably, there is evidence to suggest implementation of a hypocaloric diet to promote improved measures of body composition in individuals with the wild-type allele pattern at codon 16.[25] In contrast, the mutant-type allele patterns at codon 27 have more frequently been associated with overweight/obese weight status.[85,86,88,89,92,93] Current evidence suggests implementation of a hypocaloric diet along with an exercise prescription to promote improved measures of body composition in individuals with the mutant-type allele pattern.[24,25,83]

Summary: Genetic Profiling and Weight Loss Interventions

Determining baseline variation in candidate genes provides insight regarding clinical intervention, diet, and exercise.[8] Among the few investigations that have used genetic profiling in correspondence with weight loss interventions, the candidate genes assessed have been relatively inconsistent.[7-9] However, the genetic profile used by Dopler-Nelson and colleagues (FABP2, rs1799883; PPARG2, rs1801282; ADRB3, rs4994C3; ADRB2, rs1042713 and rs1042714) demonstrated clear, significant effects.[9] Furthermore, research supports a strong association between each polymorphism in this profile and obesity/obesity-related adverse health outcomes. [57-59,65-68,74-78,85-89,91-93] Collectively, within a weight loss intervention, evidence suggests implementation of a hypocaloric diet with variations in fat and CHO content pending allelic pattern of the gene, and inclusion of an exercise component.[13-16,18-21,17,22-25,83] Thus, more weight loss interventions genotyping for FABP2 (rs1799883), PPARG2 (rs1801282), ADRB3 (rs4994C3), and ADRB2 (rs1042713 and rs1042714) together to dictate dietary intervention, while including an exercise component, may be useful in improving health outcomes from participation in a weight loss intervention.

CHAPTER III

METHODS

Participants

Fifty-one, apparently healthy, sedentary, overweight and obese (41.8 ± 12.1 yrs, 35.3 ± 8.0 kg/m^2, 45.1 ± 4.8% body fat) women were recruited from College Station/Bryan Texas (see Appendix C for recruitment flyer). This investigation was approved by the Texas A&M University Institutional Review Board, #2013-0737F. Participants were randomly assigned to a dietary intervention that either aligned with their genotype (true match) or did not align with their genotype (false match). Inclusion criteria consisted of the following: individuals with a BMI greater than 22 kg/m^2, individuals who were not currently participating in a planned exercise program; individuals who had not been exercising for more than 30 minutes per day, three days per week; individuals that did not experience a weight increase or decrease of seven pounds within three months; individuals who were not taking ergogenic levels of nutritional supplements that may have affected muscle mass, anabolic/catabolic hormone levels, or weight loss; and individuals who were not pregnant, nursing, or planning to become pregnant during the next 12 months. Additionally, individuals were not included if they had an uncontrolled metabolic disorder.

Study Site

The familiarization session, testing sessions, and circuit workouts were conducted at the Exercise and Sport Nutrition Laboratory (ESNL) at Texas A&M

University. The Exercise and Sport Nutrition Laboratory is part of the Department of Health and Kinesiology within the College of Education and Human Development.

Experimental Design

Individuals who met the eligibility criteria and were interested in participating followed the study protocol outlined in Table 1. Buccal cheek swabs collected at the familiarization session were shipped to Interleukin Genetics (Waltham, MA) for genotyping. Once genotyping results were received (~6-10 weeks post familiarization session), individuals still interested in participating were randomly assigned to a dietary intervention that either aligned with their genotype (true matches to diet) or did not align with their genotype (false matches to diet). Participants completed seven testing sessions overall including a baseline testing session, with each session approximately four weeks apart. The exercise protocol was conducted at baseline, mid-point (end of three months), and completion (end of six months) of the study.

Sample Size Calculation

A power analysis was conducted to determine goal sample size for this investigation and was built from previous research conducted in our laboratory utilizing similar diet and exercise intervention and Dopler-Nelson and colleague investigation. The analysis was set at >0.80 and was based on change in fat mass between diet groups from previous research in our lab, and body weight change between genotype in Dopler-Nelson and colleagues investigation. Overall, the goal sample size for the present investigation was 80 participants.

Independent and Dependent Variables

Independent variables in this investigation included baseline genotype and exercise intervention. Exercise compliance was determined by attendance rate at the Curves Exercise Circuit along with measurement of peak and average heart rate during each workout. Assignment to dietary intervention was dependent on baseline genotype, and dietary compliance was determined from four-day food records submitted at each monthly testing session. Other dependent variables included body weight, height, resting energy expenditure, body composition, waist and hip circumference, resting heart rate and blood pressure, peak oxygen consumption, upper and lower body muscular strength and endurance, biochemical data (insulin, glucose, triglycerides, total cholesterol, HDL, LDL), and psychosocial parameters. The monthly psychosocial evaluation conducted included the following questionnaires: Rosenberg Self-Esteem Scale, Social Physique Anxiety Scale (SPAS), Eating Satisfaction Survey, and Multidimensional Body-Self Relations Questionnaire- Appearance Scales.

Table 1: Study protocol

Familiarization	Baseline (T1)	4 Weeks (T2)	8 Weeks (T3)	12 Weeks (T4)	16 Weeks (T5)	20 Weeks (T6)	24 Weeks (T7)
Familiarization Session	Diet Record Review	Diet Record Review	Diet Record Review	Diet Record Review	Diet Record Review	Diet Record Review	Diet Record Review
Complete Paperwork	IPAQ[a]	IPAQ[a]	IPAQ[a]	IPAQ[a]	IPAQ[a]	IPAQ[a]	IPAQ[a]
Review Medical History	Body Weight	Body Weight	Body Weight	Body Weight	Body Weight	Body Weight	Body Weight
Physical Exam	Hip & Waist Measure	Hip & Waist Measure	Hip & Waist Measure	Hip & Waist Measure	Hip & Waist Measure	Hip & Waist Measure	Hip & Waist Measure
Genetic Screening	Resting Energy Expenditure	Resting Energy Expenditure	Resting Energy Expenditure	Resting Energy Expenditure	Resting Energy Expenditure	Resting Energy Expenditure	Resting Energy Expenditure
Determination of Qualifications to Participate	Resting BP[b] and HR[c]	Resting BP[a] and HR[b]	Resting BP[a] and HR[b]	Resting BP[a] and HR[b]	Resting BP[a] and HR[b]	Resting BP[a] and HR[b]	Resting BP[a] and HR[b]
Randomized Diet Assignment: MC (30%C, 25%F, 45% P) LC (20%C, 35%F, 45% P)	Body Composition	Body Composition	Body Composition	Body Composition	Body Composition	Body Composition	Body Composition
Phase I – 1,400 kcals/d for 1 week	Fasting Blood	Fasting Blood	Fasting Blood	Fasting Blood	Fasting Blood	Fasting Blood	Fasting Blood
Phase II – 1,500 kcals/d for 23 weeks	Maximal Cardiopulmonary Exercise Test	Survey Completion[d]	Survey Completion[d]	Maximal Cardiopulmonary Exercise Test	Survey Completion[d]	Survey Completion[d]	Maximal Cardiopulmonary Exercise Test
	1 rep and 80% 1 rep Bench Press and Leg Press			1 rep and 80% 1 rep Bench Press and Leg Press			1 rep and 80% 1 rep Bench Press and Leg Press
	Survey Completion[d]			Survey Completion[d]			Survey Completion[d]

[a]International Physical Activity Questionnaire; [b]Blood Pressure; [c]Heart Rate; [d]Social Physical Anxiety Scale, Rosenberg Self-Esteem Scale, Body Image (Multidimensional Body-Self Relations Questionnaire- Appearance Scales), and Eating Satisfaction Survey, MC - Moderate Carbohydrate diet, LC – Low Carbohydrate diet

Familiarization Session

Individuals that expressed interest in participating in the study attended a familiarization session at the ESNL. At the start of the session, individuals were screened for eligibility (Appendix D). All eligible participants received the following information verbally from the study coordinator: purpose and rational of the study, review of study requirements, review of study protocol for each testing session followed by a guided tour of the lab. Next individuals were instructed to read the informed

consent form (Appendix E). Interested individuals signed the informed consent, and completed a general health history questionnaire (Appendix F). Upon completion of paperwork, height, weight, resting heart rate and blood pressure were measured. Buccal cheek swabs for genotyping were also collected at this time.

Upon completion of the familiarization session, the research nurse reviewed all general health history questionnaires and measures collected at the session (i.e. resting heart rate, blood pressure, and calculated BMI). Pending history and current measurements, some participants were required to submit a physician clearance (Appendix G) per nurse's evaluation prior to participating in the study.

Genotyping

Buccal cheek swabs were collected at the familiarization session after individuals signed the informed consent. Once at least 40 samples were collected, samples were shipped to Interleukin Genetics Inc. (Waltham, MA) for genotyping within their CLIA (Clinical Laboratory Improvements Amendments) certified molecular genetics laboratory. Here DNA was extracted from buccal cheek swabs (Puritan, Gilford, ME) using standard procedures for the five polymorphisms of interest (rs1801282, rs1799883, rs1042714, rs4994, and rs1042713). Of note, the following polymorphisms genotyped are functional SNPs with clinical significance (ADRB3 rs4994, ADRB2 rs1042713 and rs1042714). Before polymerase chain reactions (PCR), DNA was diluted to adjust concentrations within a range compatible with multiplex PCR conditions. Single Nucleotide Polymorphism (SNP) genotyping was done by the single-base extension (SBE) method using the SNP stream instrument and chemistry (Beckman Coulter, Brea,

CA) with SNPs multiplexed as needed to avoid interference. The multiplex PCR were treated with exonuclease I and shrimp alkaline phosphatase (USB). The SBE reaction was performed per manufacturer's protocol, and "tagged" products were hybridized to a microarray plate. The SNPstream instrument was used to read the plates and the SNPstream software was used to determine initial allele calls, which were confirmed by a technician.

Approximately six to ten weeks after sending samples to Interluekin Genetics Inc. (Waltham, MA) for genotyping, results were provided to the ESNL lab coordinator and study coordinator via email. Genotyping results included the following information: allelic variant within each polymorphism as notated with the Human Genome Variation Society (HGVS) nomenclature, mutation patterns for each individual, suggested diet based on genotype (low fat, low CHO, or balanced diet), suggested exercise intensity (high or moderate metabolic equivalents).

Dietary Protocol

Moderate CHO/Adequate Fat/Moderate Protein Diet (MC)

Participants assigned to this dietary intervention followed the Curves Complete® diet program. The diet consisted of a1400 kcal/d prescription for the first week of the program and 1500 kcal/d for the remaining 23 weeks of the program. The macronutrient distribution range consisted of the following: 30% kcal CHO, 25% kcal fat, 45% kcal protein. In order to follow the diet, participants received a Curves Complete® online diet program account. Within the diet program, personalized menus were generated based on the individual's response to a food preference questionnaire prompted at start up of the

account. Participants were able to change their food preferences at any time, which would in turn alter menus. Additionally participants were able to change meal and snack options within the menus through the online program. All participants received instruction on how to use the online program from the study coordinator, who was a Registered Dietitian. Furthermore, a free application for the online diet program was available for Android and iPhone users to assist with dietary compliance. Table 2 outlines the dietary protocols prescribed.

Low CHO/Adequate Fat/Moderate Protein Diet (LC)

The caloric prescription within this dietary intervention was consistent with the prescription in the moderate CHO diet (1400 kcal/d for one week, 1500 kcal/d for 23 weeks). The macronutrient distribution range consisted of the following: 20% kcal CHO, 35% kcal fat, 45% kcal protein (Table 2). In order to follow the diet, participants were provided a menu booklet for each caloric phase of the diet. Serving sizes were quantified based on the Diabetic Exchange System. The study coordinator provided all participants instruction on how to use the exchange system to substitute food items within the menus per individual taste preference.

Table 2: Dietary protocol

Time	Total kcal/d	Macronutrients	%/d	g/d	kcal/d	g/kg/d (90 kg)
Moderate Carbohydrate, Adequate Fat, Moderate Protein (MC)						
1 week	1400	CHO	30	105	420	1.17
		Fat	25	39	250	0.43
		Protein	45	158	630	1.75
23 weeks	1500	CHO	30	113	450	1.25
		Fat	25	42	375	0.47
		Protein	45	169	675	1.88
Low Carbohydrate, Adequate Fat, Moderate Protein (LC)						
1 week	1400	CHO	20	60	280	0.78
		Fat	35	54	490	0.6
		Protein	45	158	630	1.75
23 weeks	1500	CHO	20	75	300	0.83
		Fat	35	58	525	0.65
		Protein	45	169	675	1.88

Protocol Nomenclature

The nomenclature for each diet is based on accepted macronutrient distribution cut-offs within the literature.[10-12] A low carbohydrate diet is defined as less than 30% kcals from CHO, therefore one of the diets is considered a low CHO diet, 20% kcal CHO, while the other is considered moderate CHO, 30% kcal CHO.[10,11] The fat content of both diets is considered adequate as the percent kcals falls within the recommended macronutrient distribution range according to the dietary guidelines (20-35% kcals fat). Finally, a high protein diet is defined as greater than 55% kcals from protein, thus the current dietary prescription is considered moderate.[11,12]

Genotype Matching to Diets

Based on genotyping results, suggested diets consisted of low CHO, low fat, or balanced diet. Individuals with suggested diet of balanced diet were offered participation in a different weight loss study conducted in the lab at that time. Regarding the suggested diet of low CHO, the true match for this suggest was the low CHO, adequate fat, moderate protein diet (20% kcal CHO, 35% kcal fat, 45% kcal protein). The true

match for the suggested low fat diet was the moderate CHO, adequate fat, moderate protein diet (30% kcal CHO, 25% kcal fat, 45% kcal protein). Relative to LC, MC contained less fat deeming this as the appropriate diet assignment to use within this intervention.

Dietary Supplements

All participants received a monthly supply of dietary supplements upon completion of each testing session, including baseline testing. The daily supplement package consisted of a calcium and vitamin D supplement, a standard women's multivitamin and mineral supplement, and an omega-3 fatty acid supplement. Participants were instructed to take these supplements daily with food (Tables 3-5).

Table 3: Calcium and vitamin D supplement

Nutrient	Daily Dose	% Daily Value
Vitamin D (cholecalciferol)	400 IU	100%
Calcium (calcium citrate tetrahydrate & calcium citrate malate)	800 mg	80%
Magnesium Oxide	300 mg	75%
Zinc Gluconate	7.5 mg	50%
Copper	2 mg	100%
Manganese	2 mg	100%

Table 4: Omega-3 fatty acid supplement

Nutrient	Daily Dose	% Daily Value
Calories	20	N/A
Calories from Fat	20	N/A
Total Fat	2 g	2%
Cholesterol	0 mg	0%
Eicosapentaenoic Acid	320 mg	N/A
Docosahexaenoic Acid	200 mg	N/A

Table 5: Multivitamin and mineral supplement

Nutrient	Daily Dose	% Daily Value
Vitamin A (50% beta-carotene; 50% retinyl acetate)	5000 IU	100%
Vitamin C	200 mg	333%
Vitamin D (cholecalciferol)	1600 IU	400%
Vitamin E	30 IU	100%
Vitamin K	80 mcg	100%
Thiamin	50 mg	3333%
Riboflavin	50 mg	2941%
Niacin	50 mg	250%
Vitamin B-6	50 mg	2500%
Folic Acid	400 mcg	100%
Vitamin B-12	50 mcg	833%
Biotin	300 mcg	100%
Pantothenic Acid	50 mg	500%
Calcium Carbonate	500 mg	50%
Magnesium Oxide	100 mg	25%
Zinc Oxide	15 mg	100%
Selenium	200 mcg	286%
Copper	2 mg	100%
Manganese	2 mg	100%
Chromium	120 mcg	100%
Molybdenum	75 mcg	100%
Blend: alpha-lipoic acid; green tea leaf extract; bilberry, elderberry, black currant, and blueberry fruit powders; resveratrol	70 mg	N/A
Hyaluronic acid & Collagen	50 mg	N/A
Phosphatidylserine & Choline	20 mg	N/A
Cranberry Concentrate	20 mg	N/A
Inositol	10 mg	N/A
Silicon Dioxide	4 mg	N/A
Boron	2 mg	N/A
Lutein	950 mcg	N/A
Lycopene	950 mcg	N/A
Zeaxanthin	190 mcg	N/A
Astaxanthin	50 mcg	N/A
Vanadium	10 mcg	N/A

Exercise Protocol

All participants followed the Curves International® (Waco, TX) exercise program which consisted of circuit-style training with hydraulic resistance machines, interspersed with calisthenic exercise three times per week and Zumba dance one time per week. Each workout was 30 minutes in length. The Curves circuit was comprised of 13 hydraulic resistance machines along with a personalized kiosk system, CurvesSmart®, that increased resistance provided by each machine based on baseline

resistance settings, performance from previous workouts, and frequency of workouts (i.e.- every day versus every other day). All 13 machines together provided a full-body resistance workout.

Prior to beginning the exercise protocol and after baseline testing, participants met with study personnel to set up their personal account in the CurvesSmart® Kiosk at the Curves exercise circuit in the ESNL. At this time, participants reviewed the circuit exercise protocol, learned proper form and technique for each machine, and calibrated each machine based on current strength. The exercise protocol for the circuit on calisthenic exercise days included two laps around the circuit, with 30 seconds of repetitions per machine followed by 30 seconds of calisthenic exercise led by a Jillian Michaels® video. The exercise protocol for the circuit on Zumba exercise days included one lap around the circuit, with one minute of repetitions per machine followed by one minute of Zumba dance led by a certified Zumba instructor. During each workout on the Curves circuit, participants wore a Polar FT4 Heart Rate Monitor (Lake Success, NY) to keep track of exercise intensity and circuit attendance for compliance. In addition to following the Curves Exercise Program, participants were provided with a standard pedometer and instructed to reach a goal of 10,000 steps per day on the days they were not exercising on the circuit.

Testing Session Procedures

Pre-Testing Guidelines

Participants received reminder emails from the study coordinator both one-week and 24 hours prior to each testing session. The one-week reminder email included the

following instruction: fast for 10-12 hours, inhibit alcohol consumption and use of non-steroidal anti-inflammatory drugs for 24 hours, refrain from exercise for 48 hours, wear articles of clothing and accessories without metal secondary to the DXA scan, and bring in completed four-day food records (blank documents attached to email). The one-week reminder emails for the exercise sessions also included direction to wear comfortable clothing and sneakers for participation in exercise testing. The email sent 24-hours prior to the session included a reminder of the session time and direction to bring in completed four-day food records and one-week activity log (blank documents attached to the email). Upon arrival to the ESNL for testing sessions, study personnel confirmed adherence to pre-testing guidelines and collected the four-day food logs for review.

Anthropometrics

At the familiarization session, height was measured to the nearest hundredth of an inch using the Health-O-Meter Professional 500KL scale (Alsip, IL). Weight was measured to the nearest tenth of pound using the aforementioned scale at the familiarization session, baseline-testing session, and all monthly testing sessions with use of the same scale. At baseline and all monthly testing sessions waist and hip circumference was measured to the nearest tenth of an inch with standard measuring tape using methods described in the American College of Sports Medicine's Guidelines for Exercise Testing and Prescription.[97]

Resting Energy Expenditure

After measuring body weight, resting energy expenditure (REE) was measured using an open-circuit method of indirect calorimetry with the ParvoMedics TrueMax

2400 Metabolic Measurement System (Parvomedics Inc, Sandy, UT). At the start of each testing session day, quality control (QC) calibration procedures were performed for gas calibration and flowmeter calibration. The gas analyzer was calibrated against known concentrations. The flowmeter calibration was conducted with the Hans Rudolph series 5530 three-liter syringe (Hans Rudolph Inc., Kansas City, MO) following standard procedures. Per manufacturer, the coefficient of variation for the device is ±2% in apparently healthy individuals. In order to measure REE, participants rested comfortably in a bed with their legs resting on a padded box while under a metabolic hood to measure pulmonary exchange. Expiration passively diffused from the metabolic hood through tubing to the metabolic cart where gas exchange was measured. The test lasted approximately 20 minutes in length. The five time points with a rate of oxygen consumption and carbon dioxide expiration varying no more than five percent after the first ten minutes of the test were averaged for principle variables of interest (i.e.- oxygen consumption in L/min, resting energy expenditure in kcal/d, respiratory quotient).[98,99]

Dual Energy X-Ray Absorptiometry

Upon completion of the REE, the next measure commonly performed was the dual energy X-ray absorptiometry (DXA) scan via the Hologic Discovery W QDR series DXA system (Waltham, MA). At the start of each testing session day, QC calibration procedures were performed on the DXA via scan of a phantom spine (Discovery W-Caliber Model DPA/QDR-1 anthropometric spine phantom). In order to determine change in bone mineral density, body composition, visceral adipose tissue, android and gynoid fat deposition from baseline, DXA scans were performed monthly on all

participants. The DXA scan provided low-dose radiation via an x-ray scan of the entire body excluding the head, thus participants were required to complete a radiation consent form at each testing session prior to the scan (Appendix H). Each DXA scan exposed participants to 1.5 mRs. By the end of the study, participants were exposed to a total of 10.5 mRs of radiation. This amount of radiation exposure is less than the amount of radiation one is exposed to after living in College Station, TX for one year. The maximum x-ray radiation dose permitted per year for non-occupational reasons is 500 mRs.

For the test participants were instructed to remove all articles of clothing containing metal prior to the scan. Participants were supine on the scan table and lined up within the scanning field, with their feet taped inwards in order to capture accurate image of the hip girdle. Participants were instructed to close their eyes when the arm of the machine passed overhead. The test lasted approximately six minutes in length. The mean coefficient of variation for all scans throughout the study were between 0.31-0.33% with a mean intra-class correlation of 0.935.

Resting Heart Rate and Blood Pressure

Resting heart rate was typically measured after the DXA scan, while the participant was still in the supine position, as determined by palpating the radial or ulnar artery. Resting blood pressure was measured thereafter with a mercurial sphygmomanometer (American Diagnostic Corporation, model #AD-720, Hauppuage, NY) following standard procedures.

Blood Collection

Fasting blood samples were collected at baseline and each monthly testing session. Participants were fasted for 8-12 hours prior to each blood draw and blood was drawn following standard phlebotomy procedures. Upon collecting blood samples, one tube was spun in the Heraeus Megafuge 40R centrifuge (ThermoFisher Scientific, Inc) immediately at 3500 rpm for 10 minutes in order to obtain a peripheral leukoctye sample. The remaining three tubes sat out at room temperature for 15 minutes. After 15 minutes, two tubes were spun in the aforementioned centrifuge following the same procedures to obtain serum samples, and one tube was kept as whole blood. Serum, peripheral leukocytes, and whole blood samples were pipetted from the collection tube to micro-centrifuge tubes and stored in a freezer at -80° C for later analyses.

In order to measure glucose, triglycerides, total cholesterol, LDL, and HDL levels from serum samples, the Cobas C 111 (Roche Diagnostics, USA) was used following manufacturer instructions. The tested intra-assay coefficient of variation for these variables was approximately less than 3% along with a inter-assay coefficient of variation of less than 2%.[100] In addition, serum samples were used to measure fasting insulin levels from a commercially available enzyme linked immunoabsorbent assay (ELISA) kit (ALPCO Diagnostics, Salem, NH). Within the procedures for the ELISA kit, a BioTek ELX-808 Ultramicoplate reader (BioTek Instruments Inc, Winooski, VT) was used with an optical density of 450 nm against known standard curve while following standard procedures from the BioTek Gen5 Analysis software. The intra-assay coefficient of variation has been shown to range from 5.1-10.3%, and the inter-assay

coefficient of variation ranges from 6.7-16.6%. Glucose to Insulin ratio was calculated by dividing glucose (mg/dL) by insulin (μIU/L). Taking the product glucose (mmol/L) and insulin (μIU/L) and dividing it by 22.5 calculated Homeostatic Model of Assessment for Insulin Resistance (HOMA-IR).[101]

Peak Aerobic Capacity

At baseline, end of three months, and end of six months, participants completed a graded exercise test on a treadmill following the Bruce protocol in order to measure fitness via peak aerobic capacity.[97] At the start of each testing session day, QC calibration procedures were performed for gas calibration and flowmeter calibration. The gas analyzer was calibrated against known concentrations. The flowmeter was calibrated with the Hans Rudolph series 5530 three-liter syringe (Hans Rudolph Inc., Kansas City, MO) following standard procedures. The coefficient of variation for calibration procedures was ±2% for gas and flowmeter. The ParvoMedics TrueMax 2400 Metabolic Measurement System (Parvomedics Inc, Sandy, UT) was used to measure oxygen consumption. Additionally, a 10-lead echocardiogram (ECG) was included to monitor tracing for safety purposes (Nasiff Cardio Card Electrocardiograph, Nasiff Associates Inc, Central Square NY).

While the participant was standing, BioProtech t716 electrodes (BioProtech Inc, Tuston, CA) were placed at 10 sites surrounding the heart. The 10 sites included the following: right and left subclavicular fossa (RA, LA), fourth intercostal space at the right and left sternal border (V1, V2), fifth intercostal space at the mid-clavicular line (V4), half-way between the fourth intercostal space at the left sternal border and fifth

intercostal space at the mid-clavicular line (V3), fifth intercostal space at the anterior axillary line and midaxillary line (V5, V6), and right and left abdominal line (RL, LL). Prior to electrode placement, the given area was wiped down with an alcohol swab and Trace Prep 2236 (3M Red Dot) to improve trace quality.

Once electrodes were placed on the participant, she was instructed to lie down on an exam bed for lead placement. Upon placement of the leads while the participant was still in the supine position, rating of perceived exertion (RPE) based on the Borg Scale was recorded.[97] Additionally resting heart rate and blood pressure was measured and recorded, and an ECG was printed and reviewed by lab personnel to ensure safe conditions for the test. Next the participant was instructed to stand up and walk towards the TrackMaster tmx425c treadmill (Full Vision Inc., Newton, KS). Once the participant was standing comfortably on the treadmill, the Bruce protocol was reviewed, along with obtainment of a second RPE, heart rate and blood pressure measurement, and printed ECG for review. Thereafter the participant was outfitted with nose clips and a sterile mouthpiece equipped with a headpiece for support and tubing to connect to the metabolic cart for expired gas analysis.

Prior to initiation of the Bruce protocol, a two-minute warm-up at two miles per hour and zero percent incline was completed. During the graded exercise test, variables of interest (i.e.- ventilation, carbon dioxide production, respiratory quotient, and oxygen consumption) were measured constantly from expiration with the electronic flowmeter, and oxygen and carbon dioxide analyzers. Expiration was collected from the Hans Rudolph 2700 series two-way non-breathing valve that was attached to the mouthpiece.

Furthermore, RPE, heart rate, blood pressure, and ECG were collected at the end of every stage. The participant continued the test until she felt as if she was unable to continue, which was considered her peak aerobic capacity. At this time, RPE, ECG, heart rate and blood pressure was obtained prior to removal of nose clips and headgear. After this point, the participant began the recovery stage, which consisted of a three-minute walking cool down on the treadmill and three-minute seated recovery. At the end of each recovery point, RPE, ECG, heart rate and blood pressure were collected.

Upper and Lower Body Muscular Strength and Endurance

Participants completed leg press and bench press exercises at baseline, end of three months, and end of six months to determine upper and lower body strength and endurance. Muscular strength was measured by determining the participants one repetition maximum (1 RM). Muscular endurance was determined by the number of repetitions the participant could complete at 80% of her 1RM. A standard hip sled leg press (Nebular Fitness, Versailles, OH) and bench press (Nebula Fitness, Versailles, OH) was used. For the leg press, the same sled and foot position was individualized and consistent among all exercise testing sessions.

Protocol for muscular strength was consistent for upper and lower body tests. The participant completed two sets of 10 repetitions with no weight on the sled or bench press bar, with two-minute rest in between. Thereafter, weight was added to the sled or bar and the participant completed one repetition. After a two-minute rest more weight was added and the protocol continued until failure to lift the last weight added to the sled or bench press bar. Once 1RM was identified, the participant was provided a four-minute

rest, and then completed as many repetitions as possible, while still maintaining correct form, at 80% of her 1RM.

Food Log and Activity Log

Participants were instructed to complete and bring in four days of food records, including three weekdays and one weekend day, for every testing session (Appendix I). At the familiarization session participants were provided with detailed instruction on how to complete a food record. The following was included as instruction for completing food records: record all foods and beverages containing calories; record the food item, quantity consumed, and how it was prepared; for combination foods prepared at home (i.e. a sandwich) provide quantities and preparation method for each component of the food (i.e.- two slices whole wheat bread, 3 oz grilled chicken, 1 tbsp light mayonnaise); if the food item is from a fast food restaurant, simply record the name of the item and size/quantity consumed (i.e. Chic-Fil-A, 8 piece grilled nuggets). Food records were entered and analyzed with Food Processor Nutrition Analysis Software Version 10.12.0 (ESHA Nutrition Research, Salem OR).

Participants also completed a one-week activity log, which included type of lifestyle and physical activity, perceived intensity of each activity, duration of each activity, and total step count for each day of the week. The one-week activity log was submitted at every testing session. Detailed instructions on how to complete this log were included on the document.

Psychosocial Evaluation

Participants completed a battery of psychosocial questionnaires at each testing session throughout the study. Instructions on how to complete each questionnaire were provided on the document.

Rosenberg Self-Esteem Scale

The Rosenberg Self-Esteem Scale is a global method to assess self-esteem.[102] The survey consists of 10 statements that require a response on a scale of one to four, with one designating strong agreement with the statement and four designating strong disagreement. The survey is scored on a scale of 10-40, with lower scores indicating lower self-esteem and vice-versa. The correlation for reliability is 0.88.[103] (Appendix K)

Social Physique Anxiety Scale

The Social Physique Anxiety Scale (SPAS) assesses an individual's anxiety related to his or her physique via a 12 question survey.[104] Individuals are instructed to rank how they feel towards each statement related to physique and appearance on a scale of one to five, with one indicating "not at all true" and five indicating "extremely true." Increased anxiety related to physique is associated with an increased score. The SPAS has demonstrated a strong correlation for reliability, $r = 0.82$, with women.[104] (Appendix L)

Eating Satisfaction Survey

The Eating Satisfaction Survey measures the severity of six symptoms related to quality of dietary intervention via a 10-point likert scale, with 0 indicating no symptoms and 10 indicating severe symptoms. The six symptoms included in this survey are

appetite, hunger, satisfaction from food, feeling of fullness, amount of energy, and overall quality of diet. As mentioned previously the Eating Satisfaction Survey has not been validated; however, the survey was developed by Curves International® thus the survey was used to maintain consistency among other Curves studies conducted within the ESNL.[105] (Appendix J)

Body Image

The Multidimensional Body-Self Relations Questionnaire- Appearance Scales (MBSRQ-AS) is a validated assessment for one's perception of body image.[106] The survey consists of 34 statements in which the individual is instructed to rank each statement on a scale of one to five, with one indicating definite disagreement and five indicating definite agreement. The instrument covers the following domains with reliability correlation in parentheses: appearance evaluation (0.88), appearance orientation (0.88), overweight preoccupation (0.73), self-classified weight (0.70), and body area satisfaction (0.77).[106,107] (Appendix M)

International Physical Activity Questionnaire

The International Physical Activity Questionnaire (IPAQ) is a globally validated survey instrument used to assess lifestyle and physical activity of adults aged 15-69 years old over a seven day period.[108,109] This instrument consists of 27 questions among five domains. The domains included are as follows: occupational activity, transportation-related activity, housework and maintenance activity, leisure time activity, and total time spent sitting. Response to each question within each domain is evaluated based on a metabolic equivalent (METs) of the associated activity in order to determine one's

average weekly activity. The reliability correlation is approximately 0.8.[110] (Appendix N)

Statistical Analyses

All data was analyzed with SPSS statistical software package, version 22 (Chicago, IL). One-way ANOVA or MANOVA with repeated measures and a confidence level set at alpha 0.05 was used to assess the data. The repeated measures MANOVA was 2 x 2 x 7, with diet (MC or LC) and genotype (true or false match) as the between subjects factors and time (baseline, 4, 8, 12, 16, 20, 24 weeks) as the within subjects factor. Tukey's least significant difference analyses were utilized for interactions to identify where statistically significant differences or trends were obtained. Furthermore, Cohen's d effect sizes were calculated from partial eta squared values for observed statistical trends following the methods outlined in Jacob Cohen's text book.[111]

A total of 1,305 variables were analyzed with 66,555 data points total. Of the 66,555 data points collected among all participants who completed the study, only 203 data points were missing, representing 0.3% of the data points. Thus missing data points were replaced via linear interpolation method for variables pertaining to body composition, resting energy expenditure, fitness, and dietary intake. Last observed value carried forward (LOCF) method was used to present missing data points pertaining to fasting glucose and blood lipid profile. Additionally, LOCF was used for the psychosocial questionnaires of one participant at one time point where a testing session was missed.

Multivariate analyses are expressed with the Wilks' Lambda distribution and probability levels from univariate tests are based on the Greenhouse-Geisser test to control for sphericity. Data pertaining to means at each time point and time effects are presented as mean ± standard deviation and group means are presented as mean ± standard error. Data in figures include delta change from baseline and are presented as mean ± standard deviation.

CHAPTER IV

STUDY OUTCOMES

Baseline Characteristics

Fifty-one women completed the 24-week intervention. Twenty-nine women were randomly assigned to a diet that aligned with their genotype (true match) and 22 women were randomly assigned to a diet that did not align with their genotype (false match). Within the true matches (T), 16 women followed the moderate CHO, adequate fat, moderate protein diet (MC) and 13 women followed the low CHO, adequate fat, moderate protein diet (LC). Within the false matches (F), 7 women followed the MC diet and 15 women followed the LC diet. Analyses from one-way ANOVA revealed no significant differences between groups at baseline for age (41.8±12.1 yrs), height (162.3±6.8 cm), weight (94.1±21.8 kg), BMI (35.3±8.0), fat mass (40.0±13.3 kg), fat free mass (47.2±8.4 kg), body fat percentage (45.1±4.8), waist circumference (96.7±13.4 cm), and hip circumference (123±16.2 cm). This investigation was performed in accordance with the Declaration of Helsinki and approved by the Texas A&M University Institutional Review Board (#2013-0737F). Figure 1 represents the consort diagram of the study. Table 6 represents baseline characteristics for participants within each group.

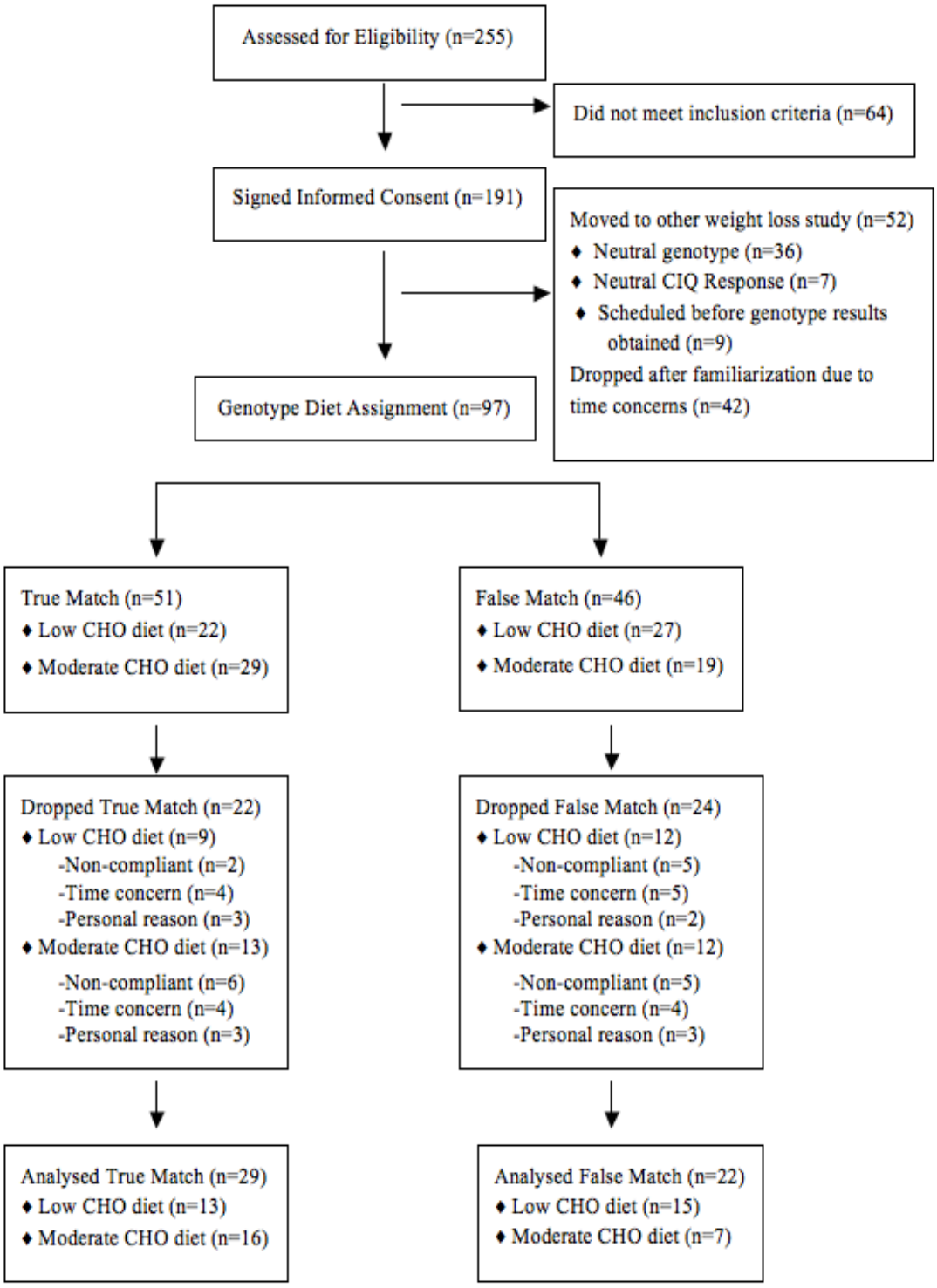

Figure 1: Consort diagram
CIQ = Carbohydrate Intolerance Questionnaire

Table 6: Baseline characteristics

Variable	Mean	T-MC	T-LC	F-MC	F-LC	P-value
Age (yrs)	41.8 ± 12.1	39.9 ± 13.2	41.5 ± 11.3	37.1 ± 12.2	46.3 ± 11.1	0.33
Height (cm)	162.3 ± 6.8	160.0 ± 4.5	161.0 ± 7.8	166.3 ± 7.9	164.1 ± 6.8	0.12
Weight (kg)	94.1 ± 21.8	88.0 ± 15.6	91.4 ± 24.6	101.2 ± 15.4	99.5 ± 26.7	0.38
BMI (kg/m^2)	35.3 ± 8.0	33.6 ± 8.0	34.9 ± 7.9	36.9 ± 7.0	36.7 ± 8.8	0.68
Fat Mass (kg)	40.0 ± 13.3	36.8 ± 9.6	38.1 ± 14.7	43.2 ± 9.1	44.1 ± 16.7	0.36
Fat Free Mass (kg)	47.2 ± 8.4	45.1 ± 6.5	46.4 ± 9.8	51.1 ± 6.6	48.4 ± 9.5	0.40
Body Fat (%)	45.1 ± 4.8	44.2 ± 4.6	44.1 ± 5.5	45.5 ± 3.7	46.6 ± 4.7	0.43
Waist (cm)	96.7 ± 13.4	95.9 ± 12.3	93.6 ± 12.8	98.7 ± 13.2	98.9 ± 15.7	0.74
Hip (cm)	123 ± 16.2	119 ± 12.4	119 ± 15.6	126 ± 11.9	128 ± 20.8	0.31

Data presented as Mean ± SD. Significance level $p < 0.05$. T = true match. F = false match. MC = moderate CHO. LC = low CHO. Mean (n = 51), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). BMI = Body Mass Index.

Dietary Intake

Absolute Energy and Macronutrient Intake

Repeated measures MANOVA analyses revealed a Wilks' Lambda effect of time (p=0.00) with no significant interactions for time x genotype (p=0.59), time x diet (p=0.75), and time x genotype x diet (p=0.76). Univariate analyses revealed a significant effect of time for total energy, CHO, fat, and protein intake. In reference to total energy, CHO, and fat intake, a significant linear relationship was observed such that all participants significantly decreased consumption of energy, daily grams of CHOs and fat from baseline to completion (Energy -520±498 kcal/d, p=0.00; CHO -81.1±73.3 g/d, p=0.00; fat -28.0±27.3 g/d, p=0.00). In addition, a significant linear relationship was observed for protein intake where intake increased from baseline to completion (+21.3±33.7 g/d, p=0.00) for all participants. Further, no significant interactions were observed for time x genotype, time x diet, and time x genotype x diet.

A trend in genotype effect for CHO intake was observed, where false matches consumed less grams of CHOs per day at each time point in comparison to true matches (p=0.08, η^2_p=0.063, d=0.84). The large effect size suggests a strong relationship between

genotype and CHO intake. A trend in genotype x diet interaction with a large effect for energy was observed in T-LC ($p=0.06$, $\eta^2_p=0.071$, $d=0.92$). At 16 weeks T-LC energy intake was significantly less from baseline, with a trend in difference from their genotype counterpart, F-MC. From baseline to completion T-LC exhibited the greatest reduction in energy intake (-580±521 kcal/d) followed by T-MC (-560±566 kcal/d), F-LC (-557±464 kcal/d), and F-MC (-244±343 kcal/d). A trend in genotype x diet interaction with a large effect was also observed for fat intake, where a greater reduction in fat intake from baseline to completion was exhibited in F-LC (-34.2±31.2 g/d), followed by T-MC (-30.0±24.5 g/d), T-LC (-24.2±27.6 g/d), and F-MC (-17.4±13.2 g/d) ($p=0.06$, $\eta^2_p=0.072$, $d=0.93$).

Relative Energy and Macronutrient intake

Multivariate analyses revealed an overall Wilks' Lambda effect of time ($p=0.00$) with no significant time x genotype ($p=0.59$), time x diet ($p=0.67$), or time x genotype x diet interaction ($p=0.84$). Univariate analyses revealed a significant effect of time for relative intake of kcals ($p=0.00$), grams of CHO ($p=0.00$), protein ($p=0.00$), and fat ($p=0.00$). From baseline to completion all participants exhibited a linear reduction in relative intake of kcals (-4.7±5.7 kcal/kg/d, $p=0.00$), CHO (-0.8±0.8 g/kg/d, $p=0.00$), and fat (-0.3±0.3 g/kg/d, $p=0.00$), along with a linear increase in intake of protein (+0.3±0.4 g/kg/d, $p=0.00$). There were no significant interactions for time x genotype, time x diet, or time x genotype x diet. Furthermore, there was a significant genotype effect for relative intake of CHOs such that individuals in the true match group consumed less g/kg of CHOs per day at each time point, and exhibited a greater reduction in CHOs

from baseline to completion in comparison to false matches (T -0.9±0.9, F -0.7±0.7 g/kg/d, p=0.02). There were no other significant effects for genotype, diet, or genotype x diet interaction.

Macronutrient Intake as Percent of Total Intake

An overall Wilks' Lambda effect of time (p=0.00) was observed with a trend in time x genotype x diet interaction consisting of a moderate relationship (p=0.09, η^2_p=0.031, d=0.60). No significant interactions for time x genotype (p=0.35) and time x diet (p=0.50) were observed. Univariate analyses revealed a significant effect of time for percent calories consumed from CHO (p=0.00), protein (p=0.00), and fat (p=0.004). From baseline to completion of the study percent of total energy consumed from CHO decreased linearly (-10.6±12.3 %kcal CHO, p=0.00) for all participants, whereas percent of total energy consumed from protein increased linearly (+15±8.5 % kcal protein, p=0.00). Fat intake demonstrated a significant quadratic relationship over time, where intake decreased from baseline to 3-months, then increased slightly from 3-6 months, but remained less at 6-months in comparison to baseline (baseline-3-months: -5.1±8.3 % kcal fat, 3-6 months: +1.1±8.6 % kcal fat, baseline-6-months: -4.1±8.8 % kcal fat,; p=0.004, p_q=0.01). There were no significant interactions for time x genotype, time x diet, and time x genotype x diet. However, there was a trend in genotype effect, along with a strong relationship, for percent total calories consumed from CHOs such that true matches demonstrated a slightly greater reduction in percent of total calories consumed from CHOs at each time point and from baseline to completion (T -10.8±12.1, F -10.4±12.8 % kcal CHO; p=0.07, η^2_p=0.069, d=0.88). Additionally, there were no

significant effect of diet or interaction for genotype x diet observed between subjects. Tables 7-9 represent absolute energy and macronutrient intake, relative energy and macronutrient intake, and macronutrient intake as percent of total intake respectively in each group throughout the study.

Exercise and Activity Log

One-way ANOVA analyses demonstrate no significant differences between groups for the total number of workouts completed (T-MC 82±13, T-LC 80±13, F-MC 73±13, F-LC 83±11, p=0.30) or percentage of workouts completed (T-MC 85±13, T-LC 83±13, F-MC 76±13, F-LC 86±11 %, p=0.30). Among workouts completed, there was no significant difference for average heart rate (T-MC 136±13, T-LC 136± 2, F-MC 143±18, F-LC 134±15 bpm, p=0.50) or peak heart rate between groups (T-MC 163±14, T-LC 162±12, F-MC 173±15, F-LC 160±17 bpm, p=0.30). Compliance with inclusion of step data on the weekly activity log was poor; therefore we were unable to analyze this data.

Table 7: Absolute macronutrient intake observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Energy Intake (kcal/d)	T-MC	1,779±576	1,260±261	1,342±263	1,309±305	1,302±324	1,228±258	1,220±209	1,349±60	T=0.00
	T-LC	1,891±516	1,462±336	1,336±320	1,453±464	1,213±317$^{\wedge}$	1,302±350	1,311±245	1,423±67$^{\delta}$	G=0.78
	F-MC	1,772±304	1,269±224	1,340±293	1,438±340	1,509±352	1,393±387	1,528±318	1,464±91	D=0.40
	F-LC	1,623±468	1,284±402	1,187±337	1,258±420	1,231±466	1,228±407	1,066±375	1,268±62	G×D=0.06
	T	1,829±543	1,351±309	1,339±285	1,373±384	1,262±318	1,262±299	1,261±226	1,386±45	T×G=0.42
	F	1,671±721	1,279±349	1,236±325	1,315±397	1,320±445	1,280±399	1,213±414	1,366±55	T×D=0.25
	MC	1,777±502	1,263±245	1,342±265	1,348±314	1,365±339	1,278±303	1,314±280	1,406±55	T×G×D=0.65
	LC	1,747±500	1,367±377	1,256±332	1,349±444	1,223±397	1,262±376	1,180±339	1,346±46	
	Time	1,761±496	1,320±325*	1,295±304*	1,348±387*	1,287±375*	1,270±342*	1,240±318*		
CHO Intake (g/d)	T-MC	183.8±77.4	117.3±48.9	111.6±34.5	119.2±36.7	103.8±45.2	107.7±38.5	102.1±36.4	120.8±9.1	T=0.00
	T-LC	194.0±67.9	106.6±47.8	115.7±63.2	126.6±80.3	95.3±44.9	96.1±48.6	99.7±63.8	119.2±10.1	G=0.08
	F-MC	159.7±60.5	94.5±13.6	100.5±42.6	116.6±45.8	118.0±63.9	99.1±47.9	115.2±63.5	114.8±13.8	D=0.18
	F-LC	155.3±55.5	77.2±42.3	78.2±31.8	69.3±27.6	74.6±40.4	84.1±48.7	69.1±34.0	86.8±9.4	G×D=0.23
	T	188.4±72.2	112.5±47.8	113.4±48.5	122.5±59.1	100.0±44.5	102.5±42.9	101.0±49.6	120.0±6.8	T×G=0.35
	F	156.7±55.7	82.7±36.2	85.3±36.1	84.4±40.2	88.4±51.8	88.9±47.8	83.8±49.1	100.8±8.4$^{\gamma}$	T×D=0.49
	MC	176.4±72.2	110.3±42.4	108.2±36.5	118.4±38.7	108.1±50.5	105.1±40.6	106.1±45.1	117.8±8.3	T×G×D=0.52
	LC	173.3±63.5	90.9±46.5	95.6±51.6	95.9±64.1	84.2±43.1	89.7±48.1	83.3±51.5	103.0±6.9	
	Time	174.7±66.9	99.7±45.3*	101.3±45.4*	106.1±54.8*	95.0±47.6*	96.6±45.1*	93.6±49.6*		
Protein Intake (g/d)	T-MC	79.4±25.8	93.9±26.5	97.4±16.3	94.3±24.1	103.9±36.3	93.3±19.6	94.6±21.9	93.8±5.4	T=0.00
	T-LC	81.9±17.8	114.8±32.9	99.8±25.9	100.8±26.5	93.4±33.9	105.0±37.2	98.7±21.8	99.2±6.0	G=0.43
	F-MC	84.6±18.1	106.5±34.7	103.1±20.5	113.4±27.6	107.6±26.9	100.4±33.0	125.1±25.1	105.8±8.2	D=0.82
	F-LC	72.9±22.5	103.3±35.9	103.9±35.3	110.4±44.8	100.2±40.1	96.2±34.1	95.8±38.4	97.5±5.6	G×D=0.29
	T	80.5±22.2	103.3±30.9	98.5±20.8	97.2±24.9	99.2±35.0	98.5±38.9	96.5±21.5	96.5±4.1	T×G=0.41
	F	76.6±21.5	104.3±34.8	103.6±30.8	111.3±39.4	102.5±35.9	97.5±33.0	105.1±36.8	101.6±5.0	T×D=0.26
	MC	81.0±23.4	97.7±29.1	99.2±17.4	100.1±26.1	105.0±33.1	95.4±23.9	103.9±26.5	99.8±4.9	T×G×D=0.48
	LC	77.1±20.6	108.6±34.4	102.0±30.8	105.9±37.1	97.0±36.8	100.2±35.2	97.1±31.3	98.3±4.1	
	Time	78.8±21.8	103.7±32.3*	100.7±25.4*	103.3±32.4*	100.6±35.1*	98.1±30.4*	100.2±29.1*		
Fat Intake (g/d)	T-MC	73.7±26.2	45.5±17.3	51.9±17.0	47.1±17.6	46.0±11.7	43.6±12.3	43.7±11.2	50.2±3.0	T=0.00
	T-LC	78.6±32.7	58.4±24.0	48.4±20.3	49.5±14.9	48.2±12.9	52.0±19.6	54.4±15.1	55.6±3.3	G=0.73
	F-MC	75.1±15.4	48.3±15.6	54.0±14.8	51.3±18.7	58.2±16.1	62.3±25.0	57.7±17.3	58.1±4.5	D=0.71
	F-LC	71.0±28.7	50.4±15.2	47.3±17.4	49.3±21.0	45.8±19.3	50.4±24.4	36.7±19.1^{bcd}	50.1±3.1$^{\delta}$	G×D=0.06
	T	75.9±28.8	51.3±21.2	20.3±18.3	48.2±16.2	47.0±12.1	47.4±16.2	48.5±14.0	52.9±2.2	T×G=0.54
	F	72.3±25.0	49.8±15.0	49.4±16.6	50.0±19.9	49.7±18.9	54.2±24.6	43.3±20.7	54.2±2.7	T×D=0.47
	MC	74.1±23.1	46.4±16.5	52.5±16.1	48.4±17.6	49.7±14.1	49.3±18.7	47.9±14.5	54.2±2.7	T×G×D=0.39
	LC	74.5±30.3	54.1±19.8	47.8±18.5	49.4±18.1	46.9±16.4	51.1±21.9	44.9±19.3	52.9±2.3	
	Time	74.3±27.0	50.6±18.6*	49.9±17.4*	49.0±17.7*	48.2±15.3*	50.3±20.3*	46.3±17.2*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$ (univariate), γ trend in genotype effect $p > 0.05$ and $p < 0.1$, δ trend in genotype x diet interaction $p > 0.05$ and $p < 0.1$ (Tukey LSD), ^ significant difference compared to baseline (Tukey LSD). Letter superscripts indicate significance ($p < 0.05$) from Tukey LSD post hoc analyses: [b]significant difference from T-MC, [c]significant difference from T-LC, [d]significant difference from F-MC, [e]significant difference from F-LC.

Table 8: Relative macronutrient intake observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Energy Intake (kcal/kg/d)	T-MC	20.5±6.5	14.9±3.3	16.3±4.5	16.0±4.4	15.9±3.9	15.2±4.4	15.0±3.5	16.2±1.0	T=0.00
	T-LC	21.7±7.1	17.7±6.9	15.8±4.1	17.0±4.3	14.9±6.3	15.8±5.8	15.7±3.2	17.0±1.1	G=0.13
	F-MC	17.8±3.7	13.2±3.6	14.2±4.4	14.9±3.1	16.0±5.2	14.8±5.1	15.8±3.4	15.3±1.6	D=0.89
	F-LC	17.3±6.8	14.0±5.2	13.5±5.6	14.5±6.1	13.6±5.0	13.9±5.8	12.5±6.4	14.2±1.1	G×D=0.47
	T	21.0±6.7	16.2±5.3	16.0±4.3	16.4±4.3	15.4±5.0	15.5±5.0	15.3±3.3	16.6±0.8	T×G=0.38
	F	17.4±5.9	13.8±4.7	13.8±5.1	14.6±5.3	14.4±5.1	14.2±5.5	13.6±5.8	14.7±0.8	T×D=0.25
	MC	19.7±5.8	14.4±3.4	15.6±4.5	15.7±4.0	15.9±4.2	15.1±4.5	15.3±3.4	15.8±0.9	T×G×D=0.85
	LC	19.3±7.2	15.8±6.3	14.6±5.0	15.6±5.4	14.2±5.6	14.8±5.8	14.0±5.3	15.6±0.8	
	Time	19.5±6.5	15.1±5.2*	15.0±4.8*	15.7±4.8*	15.0±5.0*	14.9±5.2*	14.6±4.6*		
CHO Intake (g/kg/d)	T-MC	2.1±0.8	1.4±0.7	1.4±0.6	1.5±0.6	1.3±0.5	1.3±0.6	1.3±0.5	1.5±0.1	T=0.00
	T-LC	2.2±0.9	1.2±0.6	1.3±0.7	1.5±0.9	1.1±0.6	1.1±0.5	1.2±0.6	1.4±0.1	G=0.02
	F-MC	1.6±0.7	0.9±0.3	1.1±0.6	1.2±0.6	1.3±0.7	1.3±0.6	1.2±0.6	1.2±0.2	D=0.24
	F-LC	1.7±0.7	0.9±0.5	0.9±0.4	0.8±0.3	0.8±0.4	1.1±0.5	0.8±0.4	1.0±0.1	G×D=0.53
	T	2.2±0.8	1.3±0.7	1.4±0.6	1.5±0.7	1.2±0.5	1.2±0.6	1.2±0.6	1.4±0.1	T×G=0.30
	F	1.6±0.7	0.9±0.5	0.9±0.5	0.9±0.5	1.0±0.6	1.0±0.5	0.9±0.5	1.1±0.1Γ	T×D=0.45
	MC	2.0±0.8	1.3±0.6	1.3±0.6	1.4±0.6	1.3±0.6	1.1±0.5	1.2±0.5	1.3±0.1	T×G×D=0.57
	LC	1.9±0.9	1.0±0.6	1.1±0.6	1.1±0.7	1.0±0.5	0.9±0.6	1.0±0.6	1.2±0.9	
	Time	1.9±0.8	1.2±0.6*	1.2±0.6*	1.2±0.7*	1.1±0.5*	1.1±0.6*	1.1±0.6*		
Protein Intake (g/kg/d)	T-MC	0.9±0.3	1.1±0.3	1.2±0.3	1.1±0.3	1.3±0.4	1.2±0.3	1.2±0.3	1.1±0.1	T=0.00
	T-LC	1.0±0.3	1.4±0.7	1.2±0.6	1.3±0.6	1.2±0.7	1.4±0.8	1.2±0.5	1.2±0.1	G=0.55
	F-MC	0.9±0.2	1.1±0.4	1.1±0.3	1.2±0.3	1.1±0.4	1.1±0.4	1.3±0.4	1.1±0.2	D=0.61
	F-LC	0.8±0.3	1.2±0.5	1.2±0.6	1.3±0.7	1.1±0.6	1.1±0.5	1.1±0.7	1.1±0.1	G×D=0.70
	T	0.9±0.3	1.3±0.6	1.2±0.4	1.2±0.5	1.2±0.5	1.2±0.6	1.2±0.4	1.2±0.1	T×G=0.50
	F	0.8±0.3	1.1±0.5	1.2±0.5	1.3±0.6	1.1±0.5	1.1±0.5	1.2±0.6	1.1±0.1	T×D=0.35
	MC	0.9±0.3	1.1±0.3	1.1±0.3	1.2±0.3	1.2±0.4	1.1±0.3	1.2±0.3	1.1±0.1	T×G×D=0.69
	LC	0.9±0.3	1.3±0.6	1.2±0.6	1.3±0.6	1.2±0.7	1.2±0.7	1.2±0.6	1.2±0.1	
	Time	0.9±0.3	1.2±0.5*	1.2±0.5*	1.2±0.5*	1.2±0.5*	1.2±0.5*	1.2±0.5*		
Fat Intake (g/kg/d)	T-MC	0.8±0.3	0.5±0.2	0.6±0.3	0.6±0.2	0.6±0.2	0.5±0.2	0.5±0.2	0.6±0.04	T=0.00
	T-LC	0.9±0.4	0.7±0.4	0.6±0.2	0.6±0.2	0.6±0.2	0.6±0.2	0.6±0.2	0.7±0.05	G=0.39
	F-MC	0.7±0.1	0.5±0.2	0.6±0.2	0.5±0.1	0.6±0.2	0.7±0.3	0.6±0.2	0.6±0.07	D=0.92
	F-LC	0.8±0.4	0.6±0.2	0.5±0.3	0.6±0.3	0.5±0.2	0.6±0.3	0.4±0.3	0.6±0.05	G×D=0.40
	T	0.9±0.3	0.6±0.3	0.6±0.2	0.6±0.2	0.6±0.2	0.6±0.2	0.6±0.2	0.6±0.03	T×G=0.48
	F	0.8±0.3	0.5±0.2	0.5±0.2	0.6±0.3	0.5±0.2	0.6±0.3	0.5±0.3	0.6±0.04	T×D=0.42
	MC	0.8±0.3	0.5±0.2	0.6±0.2	0.6±0.2	0.6±0.2	0.6±0.2	0.6±0.2	0.6±0.04	T×G×D=0.41
	LC	0.8±0.4	0.6±0.3	0.5±0.2	0.6±0.2	0.5±0.2	0.6±0.3	0.5±0.3	0.6±0.03	
	Time	0.8±0.3	0.6±0.3*	0.6±0.2*	0.6±0.2*	0.6±0.2*	0.6±0.2*	0.5±0.2*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$ (univariate), Γ significant genotype effect $p < 0.05$

Table 9: Percent total kcals from macronutrients observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
CHO Intake (% total kcal)	T-MC	42.3±9.5	37.3±12.8	33.7±7.7	37.2±8.3	32.8±8.3	35.3±7.3	33.1±9.7	36.0±2.0	T=0.00
	T-LC	42.2±7.7	29.7±12.3	33.5±13.3	35.0±14.7	30.9±10.1	29.5±11.3	29.5±12.4	32.9±2.2	G=0.07
	F-MC	36.9±8.6	30.9±4.9	29.2±7.8	33.4±12.0	30.7±11.8	27.4±9.2	29.2±11.4	31.1±3.0	D=0.28
	F-LC	40.0±9.4	26.0±10.6	27.5±9.8	26.0±12.9	26.9±10.0	28.4±11.8	28.3±10.3	29.0±2.1	G×D=0.84
	T	42.3±8.6	33.9±12.9	33.6±10.4	36.2±11.4	31.9±9.0	32.7±9.6	31.4±10.9	34.4±1.5	T×G=0.86
	F	39.0±9.1	27.6±9.4	28.0±9.1	28.3±12.8	28.1±10.5	28.1±10.8	28.6±10.4	30.0±1.8$^{\gamma}$	T×D=0.25
	MC	40.7±9.4	35.3±11.3	32.4±7.9	36.0±9.4	32.1±9.3	32.9±8.6	31.9±10.2	33.5±1.8	T×G×D=0.50
	LC	41.0±8.6	27.8±11.4	30.2±11.7	30.1±14.3	28.8±10.1	28.9±11.3	28.9±11.1	30.9±1.5	
	Time	40.8±8.9	31.2±11.8*	31.2±10.1*	32.8±12.6*	30.3±9.8*	30.7±10.3*	30.2±10.7*		
Protein Intake (% total kcal)	T-MC	19.2±5.2	29.9±8.5	30.9±8.3	30.3±9.4	33.2±5.8	31.6±6.2	32.5±7.9	29.7±1.6	T=0.00
	T-LC	18.6±4.1	34.3±12.0	31.5±10.2	30.7±11.0	32.2±7.7	33.9±9.7	32.1±9.9	30.5±1.8	G=0.22
	F-MC	20.6±5.6	34.1±7.3	32.4±8.9	33.6±10.0	31.7±11.7	31.3±12.7	35.5±11.3	31.3±2.5	D=0.42
	F-LC	19.1±5.2	35.0±6.3	36.1±7.9	37.0±8.3	37.1±9.4	33.7±8.7	37.4±6.9	33.6±1.7	G×D=0.70
	T	18.9±4.6	31.9±10.3	31.1±9.0	30.5±9.9	32.7±6.6	32.6±7.9	32.3±8.7	30.0±1.2	T×G=0.37
	F	19.6±5.2	34.7±6.5	34.9±8.2	35.9±8.8	35.4±10.2	32.9±9.9	36.8±8.3	32.5±1.5	T×D=0.73
	MC	19.6±5.2	31.2±8.3	31.4±8.3	31.3±9.5	32.7±7.8	31.5±8.4	33.4±8.9	30.5±1.5	T×G×D=0.48
	LC	18.9±4.6	34.7±9.2	33.9±9.2	34.1±10.0	34.8±8.9	33.8±9.0	35.0±8.7	32.0±1.2	
	Time	19.2±4.9	33.1±8.9*	32.8±8.8*	32.8±9.8*	33.9±8.4*	32.8±8.7*	34.3±8.7*		
Fat Intake (% total kcal)	T-MC	38.4±6.3	32.5±8.7	35.1±6.1	32.4±5.8	33.8±6.1	32.9±7.5	33.1±6.2	34.0±1.3	T=0.00
	T-LC	38.1±6.5	35.9±12.1	32.2±7.7	33.1±9.4	36.7±5.3	36.4±9.3	38.0±7.7	35.8±1.4	G=0.19
	F-MC	40.2±5.1	34.4±6.2	37.2±9.4	32.7±5.2	36.6±6.3	40.9±10.9	35.3±8.4	36.7±1.9	D=0.49
	F-LC	40.1±6.5	38.9±8.0	36.3±5.9	36.8±8.7	36.0±8.8	37.3±8.4	34.2±7.0	37.1±1.3	G×D=0.65
	T	38.3±6.3	34.1±10.3	33.8±6.9	32.7±7.5	35.1±5.8	34.5±8.4	35.3±7.2	34.9±1.0	T×G=0.51
	F	40.1±6.0	37.5±7.6	36.6±7.0	35.5±7.9	36.2±7.9	38.4±9.2	34.6±7.3	36.9±1.2	T×D=0.33
	MC	38.9±5.9	33.1±7.9	35.7±7.1	32.5±5.5	34.7±6.1	35.3±9.3	33.8±6.8	35.4±1.2	T×G×D=0.24
	LC	39.2±6.4	37.5±10.0	34.4±7.0	35.1±9.0	36.3±7.2	36.9±8.7	36.0±7.4	36.4±1.0	
	Time	39.1±6.1	35.5±9.3	35.0±7.0*	33.9±7.7*	35.6±6.7*	36.2±8.9	35.0±7.2*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$ (univariate), γ trend in genotype effect $p > 0.05$ and $p < 0.1$

Lifestyle Activity

Lifestyle activity was measured monthly via IPAQ. An overall Wilks' Lambda effect of time (p=0.002) was observed, with no significant interaction for time x genotype (p=0.95), time x diet (p=0.37), or time x genotype x diet (p=0.82). Univariate analyses revealed a significant time effect for vigorous intensity MET minutes that was quadratic in nature. Overall participants increased time participating in vigorous intensity activity from baseline to 6-months (+618±1198 min/wk; p=0.00, p_q=0.01). Additionally, a significant time x diet interaction was observed for walking MET minutes (p=0.05). MC exhibited significant reduction in walking MET minutes at each time point from baseline, whereas LC exhibited significant increase in walking MET minutes at each time point from baseline. There were no other significant time effects, time interactions, genotype effects, diet effects, or genotype x diet interactions observed. Table 10 represents intensity of weekly lifestyle activity in each group throughout the study.

Regarding occupational activity, transportation activity, house and garden activity, and leisure-time activity, an overall Wilks' Lambda time effect was observed (p=0.04) with no significant time x genotype (p=0.53), time x diet (p=0.72), or time x genotype x diet (p=0.34) interaction. Univariate analyses revealed significant time effect for leisure-time activity such that all participants increased activity during leisure-time from baseline to completion (+854±1399 min/wk; p=0.002). No other significant effects or interactions were demonstrated within subjects among variables. Further, no significant between subjects effects or interactions were exhibited among variables.

Table 11 represents occupational, active transportation, house and garden and leisure time activity in each group throughout the study.

Finally, regarding total time sitting, overall, there was no significant effect of time (Wilks' Lambda p=0.52) or interaction for time x genotype (p=0.46), time x diet (p=0.24), or time x genotype x diet (p=0.86). Univariate analyses revealed no significant time effect or interactions. A significant effect of diet was observed where MC exhibited less time sitting at each time point in comparison to LC and exhibited the greatest reduction in time spent sitting from baseline to completion of the study (MC -179±169, LC -103±624 min/wk, p=0.03). Table 12 represents total time sitting observed between groups throughout the study.

Anthropometrics and Body Composition

Body Weight, Fat Mass, Fat Free Mass, Body Fat Percentage

An overall Wilks' Lambda effect of time (p=0.00) with no significant interaction for time x genotype (p=0.77), time x diet (p=0.54), or time x genotype x diet (p=0.76) was observed. Univariate analyses revealed a significant time effect for body weight, fat mass, and body fat percentage, such that all participants exhibited a reduction within these variables from baseline to completion (body weight -5.3±5.0 kg, p=0.00; fat mass -4.4±3.7 kg, p=0.00; body fat percentage -2.8±2.7%, p=0.00). For fat free mass, a trend in time with a moderate effect was observed revealing a significant quadratic relationship, where fat free mass decreased from baseline to 3-months, and then increased from 3-6 months returning close to baseline levels (baseline-3-months: -0.9±1.8 kg, 3-6-months: +0.2±1.7 kg, baseline-6 months -0.6±2.3 kg; p_q=0.01, p=0.08, η^2_p=0.044, d=0.64).

Table 10: Intensity of weekly lifestyle activity observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Walking MET Minutes	T-MC	1,947±2,811	1,534±2,514	1,895±2,606	1,390±1,718	1,390±1,720	2,069±2,363	1,412±1,756	1,663±390	T=0.80
	T-LC	889±780	1,168±1,032	1,647±2,828	1,245±1,322	1,773±3,104	1,279±1,404	1,284±2,118	1,327±432	G=0.77
	F-MC	2,334±3,709	2,694±2,534	1,841±1,414	1,339±1,248	1,065±1,026	1,205±872	1,933±2,569	1,773±589	D=0.50
	F-LC	679±711	1,462±1,352	1,583±1,573	1,868±1,931	1,483±1,324	1,734±1,685	1,598±1,587	1,487±403	G×D=0.96
	T	1,509±2,217	1,413±1,991	1,770±2,708	1,199±1,394	1,528±2,440	1,771±2,012	1,399±1,911	1,495±291	T×G=0.46
	F	1,205±2,211	1,854±1,843	1,665±1,496	1,700±1,731	1,350±1,229	1,565±1,474	1,705±1,895	1,630±257	T×D=0.05
	MC	2,065±3,028	1,887±2,522^	1,879±2,275^	1,375±1,561^	1,291±1,526^	1,806±2,044^	1,570±1,991^	1,718±353	T×G×D=0.44
	LC	777±737	1,325±1,201^a	1,613 ±2,199^a	1,579 ±1,676^a	1,618 ±2,284^a	1,523 ±1,550^a	1,453±1,823^	1,407±295	
	Time	1,357±2,179	1,579±1,912	1,733±2,215	1,487±1,613	1,470±1,966	1,650±1,777	1,506±1,882		
Moderate MET Minutes	T-MC	2,128±3,277	2,748±2,780	2,674±4,211	2,635±3,325	2,542±2,888	3,184±5,489	2,072±2,816	2,569±521	T=0.79
	T-LC	1,831±1,830	1,346±1,077	1,556±1,761	1,032±988	1,515±1,152	1,143±1,155	962±816	1,341±578	G=086
	F-MC	2,262±2,371	1,928±2,279	2,196±1,415	2,461±1,241	1,964±1,671	1,854±1,647	1,976±1,662	2,091±788	D=0.30
	F-LC	1,563±1,661	1,798±1,699	2,217±2,687	2,257±1,588	1,581±1,475	2,640±3,943	2,186±1,905	2,035±538	G×D=0.35
	T	1,978±2,733	2,160±2,298	2,206±3,395	1,985±2,668	2,094±2,345	2,332±4,280	1,613±2,234	1,955±389	T×G=0.74
	F	1,785±1,886	1,839±1,847	2,210±2,321	2,322±1,460	1,703±1,510	2,390±3,359	2,119±1,794	2,063±477	T×D=0.96
	MC	2,169±2,976	2,498±2,614	2,528±3,562	2,582±2,822	2,366±2,554	2,779±4,656	2,043±2,482	2,330±472	T×G×D=0.41
	LC	1,688±1,714	1,588±1,437	1,910±2,288	1,688±1,459	1,550±1,311	1,945±3,039	1,618±1,601	1,688±395	
	Time	1,905±2,354	1,998±2,081	2,189±2,916	2,091±2,203	1,918±1,991	2,321±3,834	1,810±2,035		
Vigorous MET Minutes	T-MC	475±1,250	1,037±1,603	1,300±1,612	1,125±1,727	565±1,135	1,115±1,699	993±1,614	944±199	T=0.00
	T-LC	142±253	1,185±1,265	1,022±774	578±697	554±595	818±760	871±853	738±221	G=0.37
	F-MC	0±0	846±447	737±621	647±1273	80±139	486±886	263±450	437±301	D=0.71
	F-LC	37±145	856±653	1,325±1,889	885±741	720±643	1,069±967	832±831	818±205	G×D=0.22
	T	323±961	1142±1449	1183±1315	911±1386	580±928	960±1367	914±1326	841±149	T×G=0.97
	F	25±119	853±585	1138±1603	809±918	516±612	884±962	651±769	627±182	T×D=0.76
	MC	330±1,056	978±1,348	1,129±1,396	979±1,589	417±967	923±1,507	770±1,396	690±180	T×G×D=0.74
	LC	86±205	1,009±980	1,184±1,463	743±725	643±615	953±870	850±826	778±151	
	Time	196±727	995±1,148*	1,159±1,1419*	850±1,187*	541±793*	940±1,187*	814±1,108*		
Total MET Minutes	T-MC	4,550±6,793	5,319±6,311	5,870±7,480	5,150±5,846	4,497±4,599	6,367±8,316	4,476±5,499	5,176±928	T=0.16
	T-LC	2,862±1,845	3,698±1,986	4,225±4,078	2,855±1,773	3,842±2,884	3,241±2,295	3,118±2,605	3,406±1,029	G=0.98
	F-MC	4,596±4,186	5,468±3,781	4,774±2,681	4,447±2,411	3,109±2,497	3,544±2,686	4,171±3,164	4,301±1,403	D=0.43
	F-LC	2,279±1,951	4,116±1,835	5,125±4,763	5,010±3,001	3,784±2,146	5,443±4,843	4,617±3,228	4,339±958	G×D=0.41
	T	3,825±5,280	4,715±4,912	5,159±6,259	4,095±4,665	4,256±3,933	5,063±6,563	3,925±4,495	4,291±693	T×G=0.76
	F	3,016±2,960	4,546±2,597	5,013±4,148	4,831±2,781	3,569±2,226	4,839±4,303	4,475±3,139	4,320±849	T×D=0.56
	MC	4,564±6,020	5,364±5,573	5,536±6,354	4,936±4,999	4,075±4,068	5,508±7,133	4,384±4,834	4,738±841	T×G×D=0.25
	LC	2,550±1,891	3,922±1,882	4,707±4,400	4,010±2,695	3,811±2,467	4,420±3,969	3,921±3,000	3,872±703	
	Time	3,458±4,348	4,572±4,013	5,081±5,328	4,428±3,890	3,930±3,253	4,911±5,585	4,129±3,898		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, ^ significant difference compared to baseline (Tukey LSD), [a]significant difference from MC $p < 0.05$ (Tukey LSD post hoc).

Table 11: Occupational, active transportation, house and garden, and leisure time activities observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Occupation MET Minutes	T-MC	1,948±4,174	990±2,103	1,293±3,085	1,165±1,740	737±1,851	1,579±2,491	1,164±1,869	1,268±399	T=0.35
	T-LC	519±708	893±1349	613±715	369±761	309±380	597±724	353±557	522±442	G=0.68
	F-MC	1,327±2,731	2,304±4,365	1,670±2,674	1,103±2,428	1,221±2,775	1,014±2,110	1,084±2,656	1,389±603	D=0.16
	F-LC	722±1,543	562±918	1,478±3,034	1,073±1,821	444±609	761±997	519±1,219	794±412	G×D=0.87
	T	1,269±3,224	974±1,802	964±2,370	738±1,400	565±1,416	1,123±1,982	773±1,494	895±298	T×G=0.60
	F	915±1,950	1,1116±2,587	1,539±2,861	1,083±1,974	691±1,608	842±1,396	699±1,755	1,092±365	T×D=0.83
	MC	1,759±3,741	1,390±2,932	1,408±2,910	1,146±1,917	884±2,118	1,407±2,349	1,140±2,075	1,328±361	T×G×D=0.32
	LC	628±1,212	715±1,129	1,077±2,279	746±1,451	381±511	685±869	442±957	658±302	
	Time	1,138±2,696	1,020±2,141	1,226±2,561	927±1,671	608±1,476	1,010±1,722	757±1,585		
Transit MET Minutes	T-MC	642±1,105	384±755	959±1,339	842±1,260	426±712	1,167±2,412	481±918	700±242	T=0.56
	T-LC	497±760	473±743	945±2,434	531±759	843±2,060	561±1,039	776±1,862	661±268	G=0.63
	F-MC	820±1,273	424±1,038	768±953	398±760	248±349	325±504	830±1,792	545±366	D=0.93
	F-LC	352±439	658±936	334±376	640±949	463±867	432±686	870±1,236	536±250	G×D=0.96
	T	598±963	439±746	962±1,905	678±1,070	635±1,483	927±1,944	635±1,421	680±181	T×G=0.31
	F	501±801	584±951	472±630	563±883	395±739	398±624	857±1,391	540±221	T×D=0.40
	MC	697±1,132	396±826	901±1,216	707±1,133	372±622	911±2,048	587±1,216	622±219	T×G×D=0.49
	LC	419±602	572±841	618±1,674	589±852	639±1,521	492±853	826±1,528	598±183	
	Time	544±882	493±831	746±1,478	642±980	519±1,199	681±1,1511	718±1,388		
House & Garden MET Minutes	T-MC	1,364±1,907	2,198±2,571	2,062±2,707	1,435±1,517	2,070±2,279	1,994±3,120	1,472±2,090	1,799±359	T=0.86
	T-LC	1,551±1,712	1,106±859	1,196±1,655	826±751	1,321±1,016	903±1,008	764±742	1,095±398	G=0.92
	F-MC	1,331±428	911±393	1,161±751	1,736±998	1,086±1,019	1,194±1,010	1,196±804	1,231±543	D=0.68
	F-LC	1,012±874	1,542±1,664	1,641±1,464	1,825±1,412	1,264±1,402	2,068±3,885	1,728±1,311	1,582±371	G×D=0.22
	T	1,481±1,817	1,734±2,073	1,723±2,327	1,203±1,256	1,734±1,869	1,540±2,477	1,178±1,670	1,447±268	T×G=0.23
	F	1,114±765	1,341±1,407	1,488±1,282	1,797±1,271	1,207±1,271	1,790±3,245	1,558±1,181	1,407±329	T×D=0.98
	MC	1,354±1,591	1,806±2,217	1,788±2,309	1,527±1,364	1,770±2,009	1,750±2,656	1,388±1,781	1,515±325	T×G×D=0.29
	LC	1,263±1,332	1,340±1,346	1,434±1,543	1,361±1,242	1,290±1,216	1,527±2,938	1,280±1,173	1,339±272	
	Time	1,304±1,440	1,550±1,788	1,594±1,913	1,436±1,288	1,507±1,623	1,628±2,789	1,329±1,463		
Leisure Time MET Minutes	T-MC	596±800	1,747±2,828	1,556±1,814	1,708±3,346	1,265±1,707	1,629±1,935	1,359±1,445	1,409±288	T=0.002
	T-LC	295±319	1,226±1,072	1,470±1,095	1,130±1,153	1,369±1,245	1,180±1,086	1,226±1,036	1,128±319	G=0.97
	F-MC	1,117±2,568	1,829±1,356	1,174±572	1,210±1,484	554±796	1,011±1,247	1,062±1,001	1,137±435	D=0.99
	F-LC	193±299	1,355±795	1,671±1,152	1,472±1,096	1,613±1,497	2,181±1,688	1,500±943	1,426±297	G×D=0.41
	T	477±646	1,568±2,222	1,509±1,537	1,476±2,623	1,323±1,518	1,473±1,611	1,340±1,262	1,268±215	T×G=0.91
	F	487±1462	1,506±999	1,513±1,017	1,388±1,203	1,276±1,389	1,809±1,630	1,350±960	1,282±263	T×D=0.12
	MC	754±1,515	1,772±2,440	1,440±1,538	1,557±2,879	1,048±1,507	1,441±1,750	1,269±1,310	1,273±261	T×G×D=0.33
	LC	240±307	1,295±918	1,578±1,110	1,313±1,115	1,500±1,366	1,717±1,504	1,372±978	1,277±218	
	Time	472±1,062	1,510±1,770*	1,516±1,308*	1,423±2,082*	1,296±1,435*	1,592±1,608*	1,326±1,129*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$

Table 12: Total time sitting observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Total Time Sitting (minutes)	T-MC	1,141±453	1,120±488	982±343	1,017±388	1,045±514	1,099±479	992±331	1,057±76	T=0.43
	T-LC	1,262±520	995±288	1,414±940	1,349±546	1,086±413	1,212±388	1,145±378	1,209±84	G=0.90
	F-MC	1,240±453	951±347	892±416	788±419	1,041±583	1,027±345	994±312	991±84	D=0.03
	F-LC	1,282±205	1,233±584	1,402±844	1,161±332	1,209±402	1,290±544	1,193±642	1,253±78	G×D=0.54
	T	1,196±479	1,064±409	1,176±700	1,166±486	1,063±463	1,150±436	1,060±355	1,133±57	T×G=0.67
	F	1,269±295	1,143±529	1,240±764	1,042±394	1,156±459	1,206±497	1,130±559	1,122±70	T×D=0.22
	MC	1,171±445	1,069±449	955±359	947±403	1,044±522	1,077±436	992±319	1,024±69[D]	T×G×D=0.83
	LC	1,273±377	1,122±478	1,407±873	1,248±446	1,152±404	1,254±471	1,170±528	1,231±58	
	Time	1,227±408	1,098±461	1,203±721	1,113±449	1,103±459	1,174±460	1,090±450		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. [D]significant diet effect $p < 0.05$

Thus, while all participants lost body weight, fat mass, and body fat percentage, fat free mass was maintained relatively well throughout the study. Aside from time effects, there were no time x diet, time x genotype, or time x genotype x diet interactions.

A trend in genotype with moderate effect was revealed for body weight where false matches presented with greater body weight at each time point in comparison to true matches and demonstrated a greater reduction in body weight from baseline to 6-months (F -5.6±5.0, T -5.0±5.0 kg, $p=0.10$, $\eta^2_p=0.056$, $d=0.78$). Post-hoc power analyses revealed a required sample size of 690 with a difference of 2.2 kg body weight to detect statistical significance between groups. Additionally a trend in genotype with strong effect for fat free mass was observed where false matches presented with more fat free mass at each time point and experienced better retention in fat free mass from baseline to 6-months (F -0.4±2.3, T -0.8±2.3 kg, $p=0.09$, $\eta^2_p=0.062$, $d=0.83$). Post-hoc power analyses revealed a sample size of 3,181 with a difference of 2.7 kg fat free mass to detect statistical significance between groups. No other significant genotype or diet effects were observed along with no significant interaction for genotype x diet. Table 13 represents body weight, fat mass, fat free mass, and body fat percentage in each group throughout the study. Figures 2-9 represent changes in body weight, fat mass, fat free mass, and body fat percentage between diet and genotype throughout the study. Since we did not observe statistically significant interactions favoring true matches among body composition variables, we reject H_1.

Table 13: Body weight, fat mass, fat free mass, and body fat percentage observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Body Weight (kg)	T-MC	88.0±15.6	86.0±14.6	85.1±14.5	83.7±14.0	83.2±13.8	83.0±13.9	83.2±14.4	84.6±5.2	T=0.00
	T-LC	91.4±24.6	89.3±24.2	88.6±24.1	87.9±23.8	86.8±23.3	86.6±23.1	86.1±22.6	88.1±5.8	G=0.10
	F-MC	101±15.4	99.0±15.5	97.4±16.0	97.2±15.8	96.9±16.0	97.0±15.1	97.6±15.4	98.1±7.9	D=0.97
	F-LC	99.5±26.7	96.8±25.9	95.3±25.4	94.3±25.4	93.6±25.0	93.1±24.9	93.0±25.9	95.1±5.4	G×D=0.60
	T	89.5±19.8	87.5±19.2	86.7±19.1	85.6±18.8	84.8±18.4	84.6±18.3	84.5±18.2	86.4±3.9	T×G=0.57
	F	100.1±23.4	97.5±22.7	96.0±22.4	95.2±22.4	94.6±22.2	94.3±22.0	94.4±22.8	96.6±4.8$^{\gamma}$	T×D=0.32
	MC	92.0±16.4	90.0±15.8	88.9±15.7	87.8±15.6	87.4±15.5	87.3±15.4	87.6±15.8	91.3±4.7	T×G×D=0.43
	LC	95.8±25.6	93.3±25.0	92.2±24.6	91.3±24.4	90.4±24.0	90.1±23.9	89.8±24.2	91.6±3.9	
	Time	94.1±21.8	91.8±21.2*	90.7±20.9*	89.7±20.8*	89.1±20.5*	88.8±20.4*	88.8±20.7*		
Fat Mass (kg)	T-MC	36.4±9.6	34.7±9.2	33.8±8.8	32.8±9.3	32.8±9.8	32.0±8.8	32.5±9.3	33.6±3.3	T=0.00
	T-LC	38.1±14.7	37.0±15.1	36.0±15.0	35.7±14.8	34.4±14.0	34.2±14.4	33.9±14.0	35.6±3.6	G=0.13
	F-MC	43.2±9.1	41.9±9.5	40.4±9.2	39.5±9.6	39.1±9.2	39.5±10.1	39.2±9.6	40.4±5.0	D=0.75
	F-LC	44.1±16.6	42.6±16.6	41.0±16.8	40.4±16.4	39.5±16.7	39.2±16.7	38.7±16.6	40.8±3.4	G×D=0.83
	T	37.1±11.9	35.8±12.0	34.8±11.8	34.1±11.9	33.5±11.4	33.0±11.5	33.1±11.4	34.6±2.5	T×G=0.61
	F	43.8±14.4	42.4±14.5	40.8±14.6	40.1±14.4	39.4±14.5	39.3±14.6	38.8±14.5	40.6±3.0	T×D=0.37
	MC	38.5±9.8	36.9±9.7	35.8±9.3	34.8±9.7	34.7±9.5	34.3±9.3	34.5±9.7	37.0±3.0	T×G×D=0.69
	LC	41.3±15.7	40.0±15.8	38.7±15.9	38.2±15.6	37.1±15.4	36.9±15.6	36.5±15.4	38.2±2.5	
	Time	40.0±13.3	38.6±13.4*	37.4±13.3*	36.7±13.3*	36.0±13.0*	35.7±13.2*	35.6±13.0*		
Fat Free Mass (kg)	T-MC	45.1±6.5	44.9±6.3	44.8±6.4	44.4±6.0	44.1±5.1	44.5±5.9	44.4±5.7	44.6±1.9	T=0.08
	T-LC	46.4±9.8	45.6±9.2	46.0±9.0	45.5±8.9	45.9±9.3	45.9±8.7	45.5±8.1	45.8±2.1	G=0.09
	F-MC	51.1±6.6	49.9±6.0	50.0±6.7	50.9±6.1	51.1±6.6	50.8±5.2	51.8±5.5	50.8±2.9	D=0.64
	F-LC	48.4±9.5	47.5±8.9	47.5±8.1	47.0±8.3	47.3±8.1	47.1±7.9	47.5±8.6	47.5±2.0	G×D=0.31
	T	45.7±8.0	45.2±7.6	45.3±7.6	44.9±7.3	44.9±7.2	45.1±7.2	44.9±6.8	45.2±1.4	T×G=0.24
	F	49.3±8.6	48.2±8.0	48.3±7.6	48.3±7.8	48.5±7.7	48.3±7.2	48.8±7.9	49.1±1.7$^{\gamma}$	T×D=0.49
	MC	46.9±7.0	46.4±6.5	46.4±6.8	46.4±6.7	46.3±6.3	46.4±6.3	46.6±6.5	47.7±1.7	T×G×D=0.21
	LC	47.5±9.5	46.6±8.9	46.8±8.4	46.3±8.4	46.7±8.5	46.5±8.1	46.6±8.2	46.7±1.4	
	Time	47.2±8.4	46.5±7.9*	46.6±7.7*	46.4±7.6*	46.5±7.6$^{\tau}$	46.5±7.3$^{\tau}$	46.6±7.5$^{\tau}$		
Body Fat (%)	T-MC	44.2±4.6	43.1±5.1	42.5±5.6	41.8±6.2	42.1±5.7	41.3±5.6	41.6±5.2	42.4±1.3	T=0.00
	T-LC	44.1±5.5	43.7±5.4	42.7±5.6	42.7±5.9	41.7±5.2	41.5±5.8	41.4±5.8	42.5±1.5	G=0.22
	F-MC	45.5±3.7	46.3±2.7	44.3±3.6	43.2±3.4	42.9±3.4	43.2±4.7	42.6±3.7	44.0±2.0	D=0.74
	F-LC	46.6±4.7	46.1±5.1	45.0±6.1	44.8±6.0	44.0±6.7	43.9±6.7	43.4±6.6	44.9±1.4	G×D=0.83
	T	44.1±4.9	43.4±5.1	42.6±5.5	42.2±6.0	41.9±5.3	41.4±5.6	41.5±5.4	42.5±1.0	T×G=0.34
	F	46.3±4.3	46.2±4.4	44.8±5.3	44.3±5.3	43.7±5.8	43.7±6.1	43.1±5.7	44.4±1.2	T×D=0.58
	MC	44.6±4.3	44.1±4.7	43.0±5.0	42.2±5.5	42.3±4.9	41.9±5.3	41.9±4.7	43.2±1.2	T×G×D=0.55
	LC	45.5±5.1	45.0±5.3	43.9±5.9	43.8±6.0	43.0±6.1	42.8±6.3	42.5±6.2	43.7±1.0	
	Time	45.1±4.8	44.6±5.0	43.5±5.5*	43.1±5.7*	42.7±5.5*	42.4±5.6*	42.2±5.6*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, γ trend in genotype effect $p > 0.05$ and $p < 0.1$, τ trend in time effect from baseline $p > 0.05$ and $p < 0.1$ (univariate)

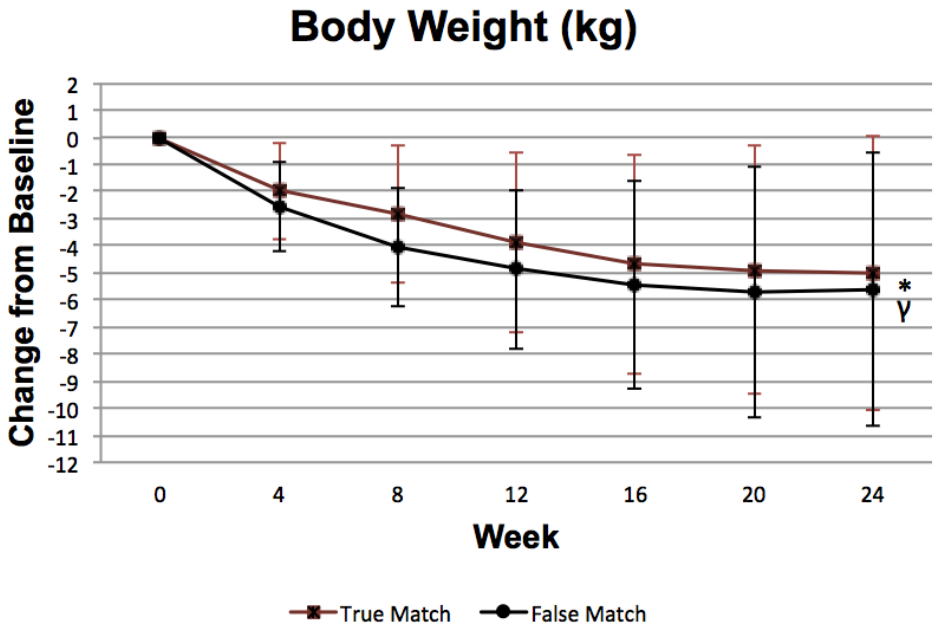

Figure 2: Delta change in body weight observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$), γ trend in genotype effect $p > 0.05$ and $p < 0.1$

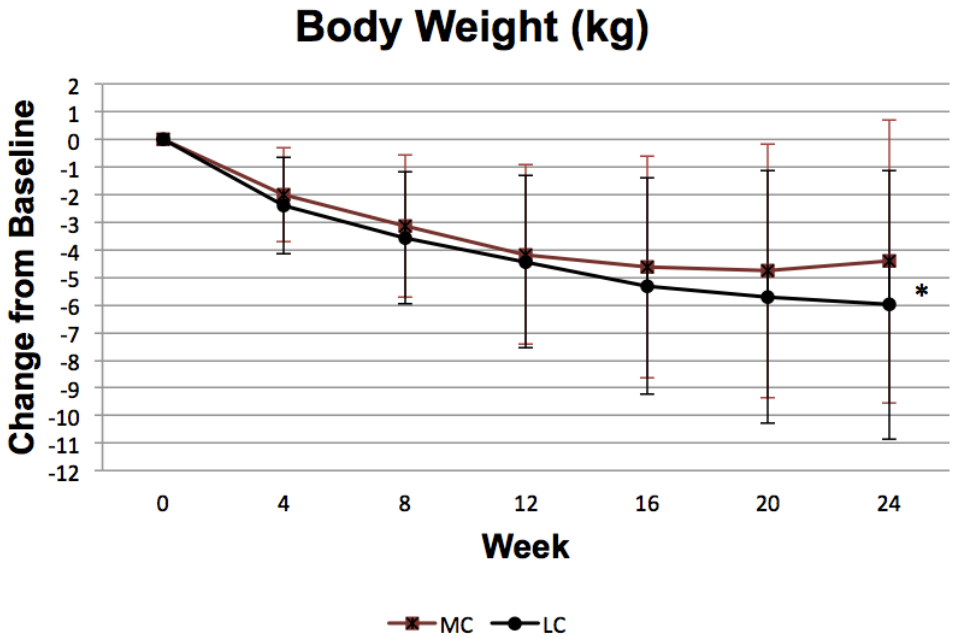

Figure 3: Delta change in body weight observed between diet groups Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

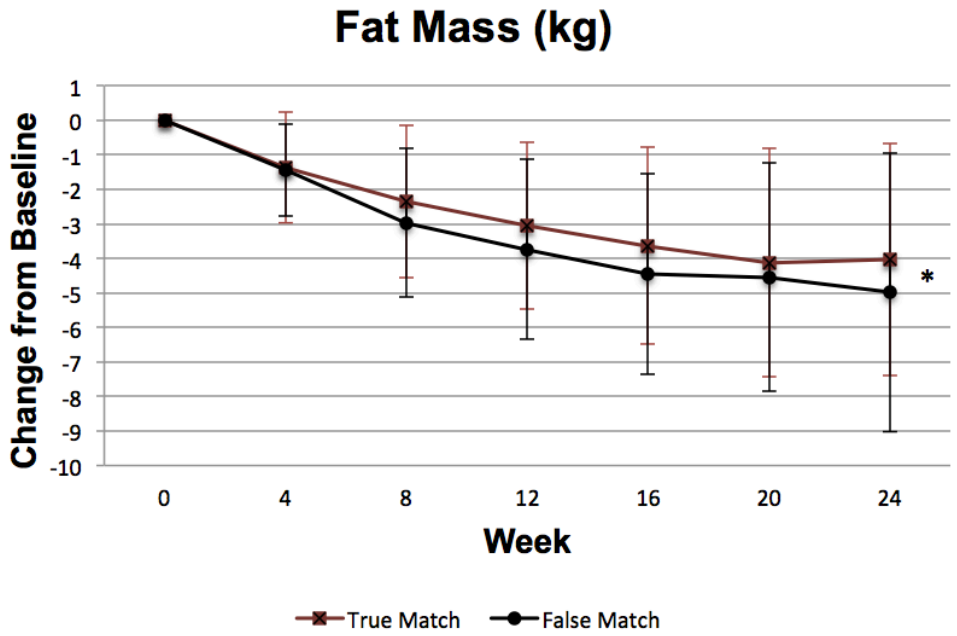

Figure 4: Delta change in fat mass observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

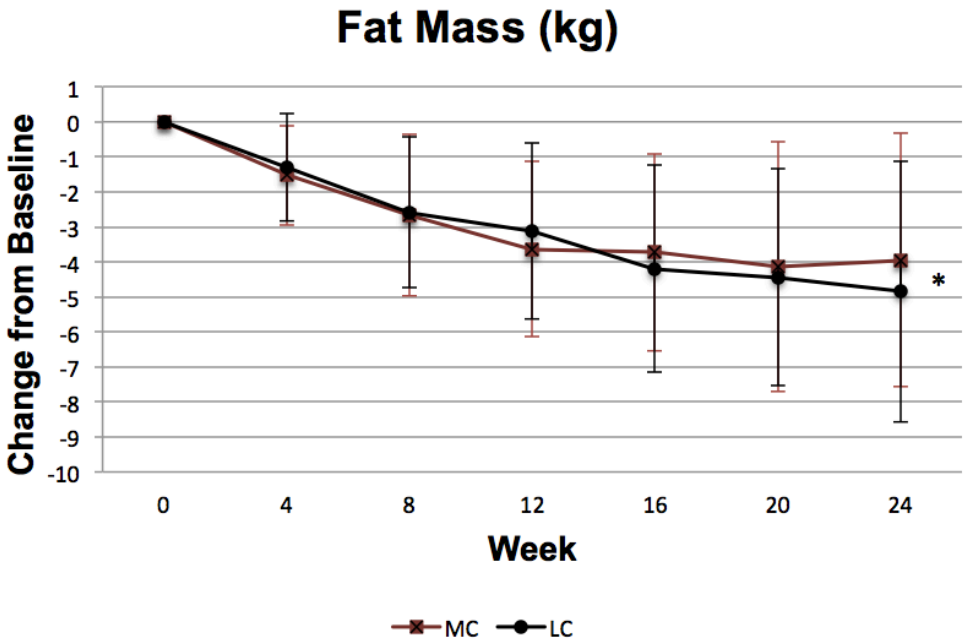

Figure 5: Delta change in fat mass observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

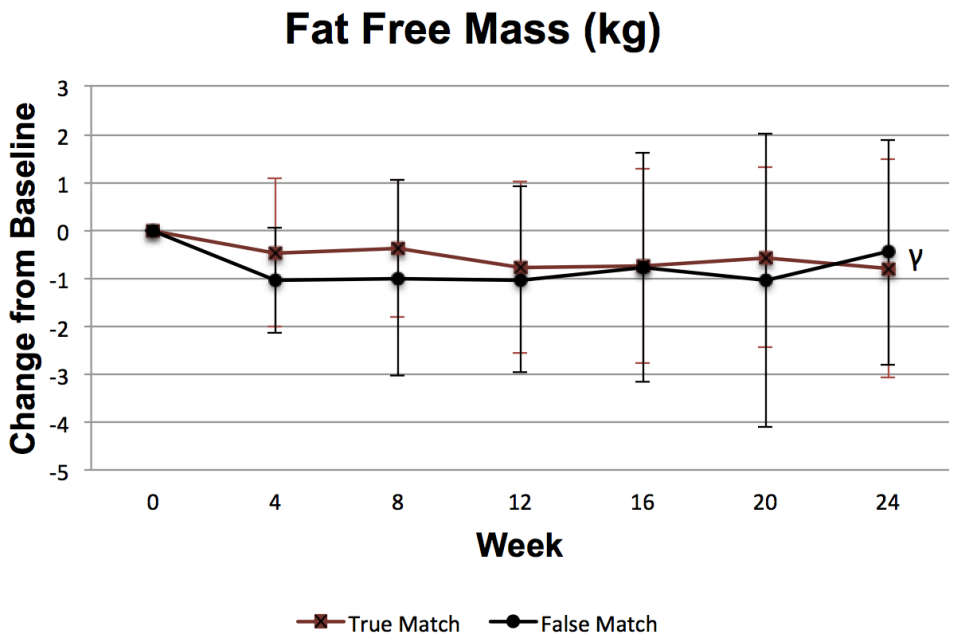

Figure 6: Delta change in fat free mass observed between genotype. Values presented as mean ± SD, n = 51, T: n= 29, F: n = 22. γ trend in genotype effect $p > 0.05$ and $p < 0.1$

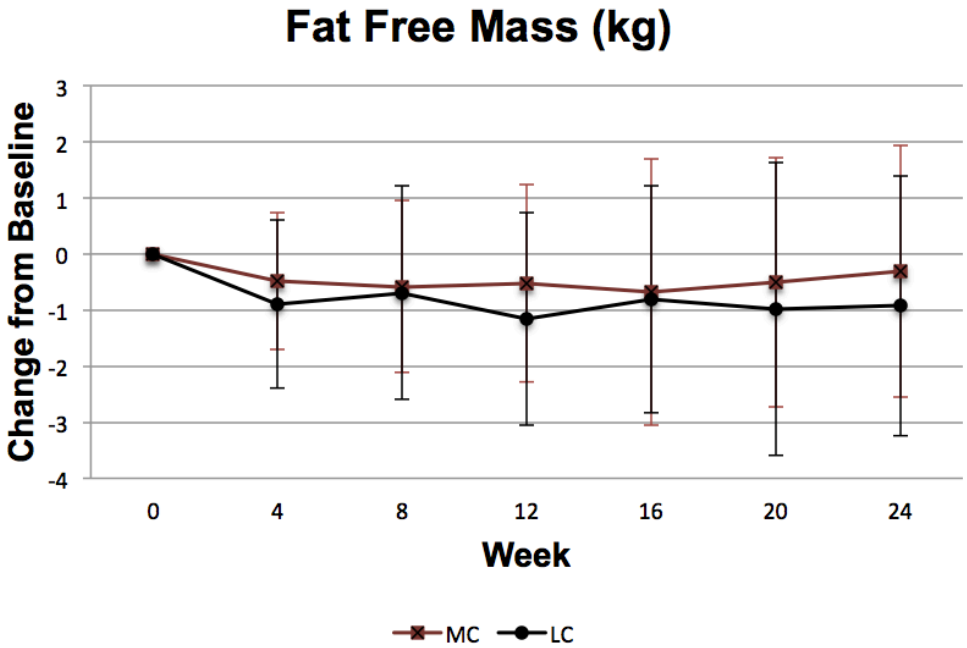

Figure 7: Delta change in fat free mass observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28

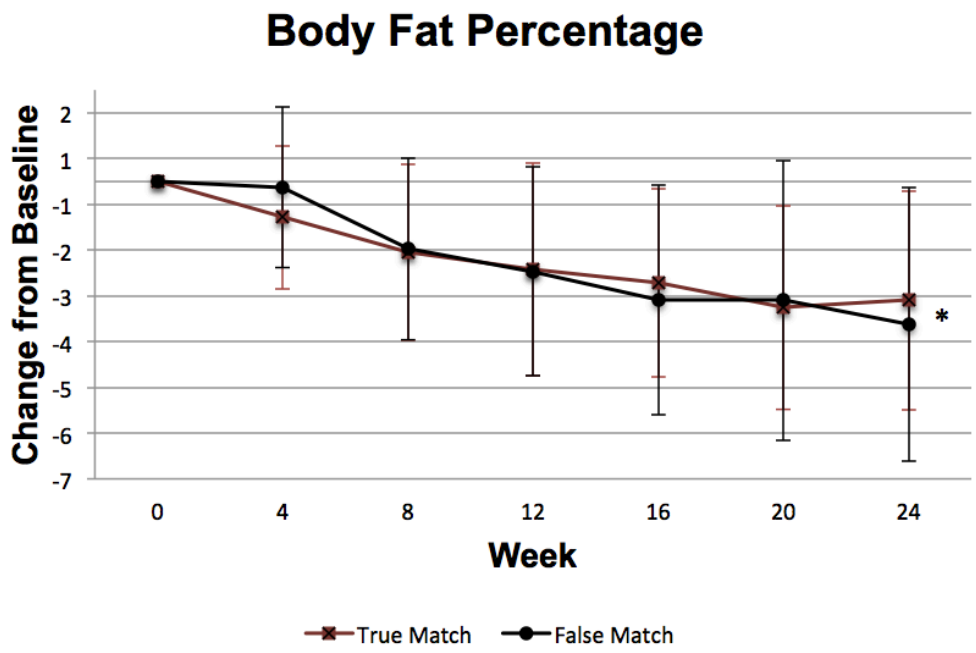

Figure 8: Delta change in body fat percentage observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

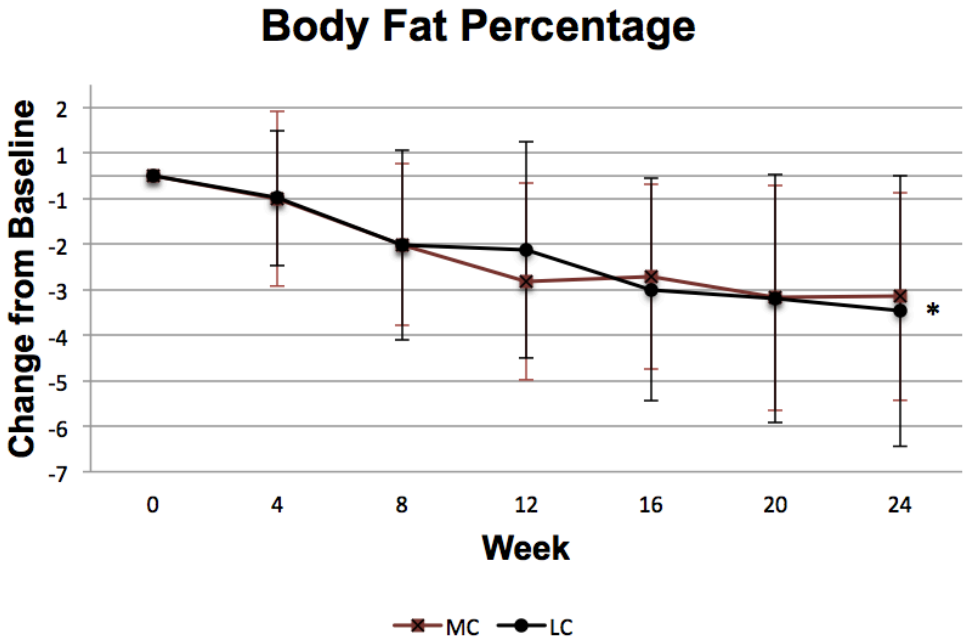

Figure 9: Delta change in body fat percentage observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

Visceral Adipose Tissue

Overall, a Wilks' Lambda effect of time ($p<0.001$) with no significant time x genotype ($p=0.14$), time x diet ($p=0.26$), or time x genotype x diet ($p=0.51$) interaction was observed for visceral adipose tissue mass, area, and volume. Univariate analyses revealed significant time effects for visceral adipose tissue mass, area, and volume, where all measures decreased linearly from baseline to completion for all participants (mass: -155.9±240.9 grams, $p<0.001$; area: -32.3±49.9 cm^2, $p<0.001$; volume: -168.5±260.4 cm^3, $p<0.001$). There were no significant time interactions, genotype or diet effects, or genotype x diet interactions. Table 14 represents visceral adipose tissue mass, area, and volume observed for each group throughout the study. Since we did not observed statistical significant interactions favoring true matches for visceral adipose tissue, we reject H_2.

Table 14: Visceral adipose tissue (VAT) mass, area, and volume observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
VAT Mass (g)	T-MC	884.4±354	812.8±398	743.8±256	792.9±339	770.8±347	770.0±301	725.6±260	785.7±91	T<0.001
	T-LC	846.7±397	766.0±304	732.0±285	746.9±307	708.4±313	681.3±286	701.8±285	740.4±100	G=0.33
	F-MC	922.6±382	925.7±436	835.3±373	762.7±309	831.4±363.8	823.6±318	814.7±360	845.1±137	D=0.99
	F-LC	982.7±491	1044±571	884.8±491	846.7±482	827.4±473	860.3±492	797.7±391	892.0±94	G×D=0.67
	T	867.5±367	791.8±353	738.5±265	772.3±320	742.8±328	730.2±292	714.9±267	763.1±68	T×G=0.20
	F	963.5±451	1006.5±524	869.0±448	820.0±428	828.7±432	848.6±436	803.1±373	868.6±83	T×D=0.76
	MC	896.0±354	847.1±403	771.6±291	783.7±323	789.2±345	786.3±300	752.7±289	815.4±82	T×G×D=0.76
	LC	919.5±447	915.0±479	813.8±409	800.4±406	772.1±404	777.2±412	753.1±343	816.2±69	
	Time	908.9±404	884.4±444	794.8±358*	792.9±367*	779.8±375*	781.3±362*	753.0±316*		
VAT Area (cm^2)	T-MC	183.4±74	168.6±82	154.2±53	163.5±70	159.8±72	159.7±62	150.5±54	162.8±19	T<0.001
	T-LC	175.6±82	158.8±63	152.0±59	155.1±64	147.0±65	141.3±59	145.6±59	153.6±21	G=0.33
	F-MC	191.3±79	192.0±91	173.1±77	158.1±64	172.4±75	173.7±65	169.0±75	175.7±28	D=1.00
	F-LC	203.8±102	216.6±118	183.4±102	175.7±100	171.5±98	178.5±102	165.4±81	185.0±19	G×D=0.68
	T	179.9±76.3	164.2±73.3	153.2±55.0	159.7±66.4	154.1±67.9	151.5±60.7	148.3±55.4	158.2±14	T×G=0.20
	F	199.8±93.5	208.8±108.8	180.1±92.9	170.1±88.8	171.8±89.6	177.0±90.3	166.5±77.3	180.3±17	T×D=0.71
	MC	185.8±74	175.8±84	160.0±60	161.8±67	163.8±71	164.0±62	156.1±60	169.2±17	T×G×D=0.77
	LC	190.7±93	189.8±100	168.8±85	166.1±84.2	160.1±84	161.2±86	156.2±71	169.3±14	
	Time	188.5±84	183.5±92	164.8±74*	164.2±76*	161.7±78*	162.5±75*	156.2±66*		
VAT Volume (cm^3)	T-MC	956.2±383	878.6±430	841.6±369	852.5±367	833.3±376	832.4±325	784.6±281	854.2±99	T<0.001
	T-LC	914.6±430	828.0±329	791.3±308	807.5±332	765.7±338	736.7±309	758.8±308	800.4±110	G=0.34
	F-MC	997.4±413	1000.9±472	903.1±403	824.7±334	898.7±393	905.7±340	880.4±390	915.9±149	D=0.98
	F-LC	1062.3±531	1129.0±617	956.5±531	915.4±521	894.3±511	930.1±532	862.3±422	964.3±102	G×D=0.66
	T	937.6±398	855.9±382	819.0±338	832.3±346	803.0±355	789.5±316	773.0±288	827.3±74	T×G=0.22
	F	1041.6±487	1088.2±567	939.5±485	886.5±463	895.7±468	922.3±471	868.0±403	940.1±90	T×D=0.74
	MC	968.7±383	915.8±436	860.3±371	844.0±350	853.2±373	854.7±324	813.7±312	885.0±89	T×G×D=0.78
	LC	993.7±484	989.3±519	879.8±442	865.3±439	834.6±437	840.3±446	814.2±371	882.3±75	
	Time	982.5±437	956.1±480	871.0±408*	855.7±398*	843.0±405*	846.8±392*	814.0±342*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$

Fat Deposition

Regarding android fat deposition, an overall Wilks' Lambda effect of time was exhibited (p=0.00) with no significant interactions for time x genotype (p=0.38), time x diet (p=0.93), or time x genotype x diet (p=0.37). Univariate analyses revealed significant effect of time for android total mass, fat mass, fat free mass, and fat percentage. A significant linear relationship was observed for total mass, fat mass, and fat percentage, such that all participants exhibited a reduction in these variables from baseline to completion (total mass: -747±863grams, p=0.00; fat mass: -532±528 grams, p=0.00; body fat percentage: -2.9±3.2 %, p=0.00). A significant cubic relationship was observed for fat free mass where fat free mass decreased from baseline to three months, then increased slightly from 3-5 months and decreased from 5-6 months (baseline-3-months: -205±385 grams, 3-5-months: +45±268 grams, 5-6-months: -56±336 grams p=0.003, p_c=0.02). From baseline to completion, participants experienced a reduction in android fat free mass (-215±452 grams).

No significant time interactions were observed; however a trend in time x genotype x diet interaction with moderate effect for total mass was observed. From baseline to completion F-LC experienced the greatest reduction in android total mass (-1004±872 grams), followed by T-MC (-732±919 gram), T-LC (-593±801 grams) and F-MC (-517±875 grams) (p=0.09, η^2_p=0.045, d=0.73). Post-hoc power analyses revealed a required sample size of 411 with a difference of 509 grams android total mass to detect statistical significance between groups. Additionally, a trend in time x genotype x diet with moderate effect for android fat free mass was observed such that upon completion,

F-MC exhibited greatest retention in fat free mass (-68±435 grams), followed by T-LC (-182±460 grams), T-MC (-234±459 grams), and F-LC (-294±473 grams) (p=0.08, η^2_p=0.043, d=0.71). Post-hoc power analyses revealed a required sample size of 797 with a difference of 45.9 grams android fat free mass to detect statistical significance between groups.

Moreover, a significant genotype effect was revealed for android total mass such that false matches presented with larger total mass at each time point and experienced a greater reduction in total mass upon completion of the study (F -849.1±882.8, T -669.7±855.4 grams, p=0.05). A significant genotype effect was also exhibited for fat free mass. While false matches contained greater fat free mass at each time point, true matches exhibited better retention of android fat free mass from baseline to completion (T -210.5±451.7, F -222.0±463.8 grams, p=0.04). Along with this, a trend in genotype with a strong effect was observed for fat mass where false matches once more presented with larger fat mass at each time point and exhibited a greater reduction in fat mass upon completion (F -627±583, T -459±480 grams, p=0.07, η^2_p=0.071, d=0.89). Post-hoc power analyses revealed a required sample size of 753 with a difference of 646 grams android fat mass to detect statistical significance between groups. Table 15 represents android total mass, fat mass, fat free mass, and fat percentage in each group throughout the study. Figures 10-17 represent changes in android total mass, fat mass, fat free mass, and fat percentage between genotype and diet groups at each time point throughout the study.

Table 15: Android total mass, fat mass, fat free mass, fat percentage observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Android Total Mass (g)	T-MC	7,019±1,714	6,664±1,565$^{\wedge}$	6,600±1,415$^{\wedge}$	6,498±1,541$^{\wedge}$	6,378±1,399$^{\wedge}$	6,389±1,308$^{\wedge}$	6,287±1,382$^{\wedge}$	6,548±550	T=0.00
	T-LC	7,250±2,347	6,777±1,995$^{\wedge}$	6,875±2,204$^{\wedge}$	6,719±2,047$^{\wedge}$	6,749±2,085$^{\wedge b}$	6,782±2,132$^{\wedge b}$	6,658±2,120$^{\wedge b}$	6,830±611	G=0.05
	F-MC	8,357±1,781	7,982±1,837$^{\wedge bc}$	7,713±1,729$^{\wedge bc}$	7,657±2,287$^{\wedge bc}$	7,738±1,876$^{\wedge bc}$	8,033±2,270$^{\wedge bc}$	7,840±1,931$^{\wedge bc}$	7,903±832	D=0.74
	F-LC	8,708±3,276	8,415±3,261^{bcd}	8,131±2,955$^{\wedge bcd}$	7,846±2,796$^{\wedge bc}$	7,857±2,852$^{\wedge bc}$	7,776±2,750$^{\wedge bcd}$	7,704±2,863$^{\wedge bc}$	8,062±568	G×D=0.93
	T	7,123±1,987	6,715±1,738	6,723±1,781	6,597±1,756	6,544±1,717	6,565±1,704	6,453±1,728	6,689±411	T×G=0.42
	F	8,596±2,844	8,277±2,846	7,998±2,592	7,786±2,591	7,819±2,536	7,858±2,555	7,747±2,556	7,983±504$^{\Gamma}$	T×D=0.58
	MC	7,426±1,807	7,065±1,725	6,938±1,567	6,850±1,829	6,792±1,644	6,890±1,781	6,759±1,689	7,225±499	T×G×D=0.09
	LC	8,031±2,926	7,654±2,824	7,547±2,663	7,323±2,499	7,342±2,543	7,314±2,489	7,218±2,555	7,446±417	
	Time	7,758±2,480	7,389±2,388*	7,273±2,237*	7,110±2,213*	7,094±2,181*	7,123±2,188*	7,011±2,199*		
Android Fat Mass (g)	T-MC	3,215±929	2,989±868$^{\wedge}$	2,935±821$^{\wedge}$	2,815±898$^{\wedge}$	2,800±846$^{\wedge}$	2,575±985$^{\wedge}$	2,717±788$^{\wedge}$	2,863±353	T=0.00
	T-LC	3,346±1,466	3,099±1,288$^{\wedge b}$	3,111±1,420$^{\wedge b}$	3,011±1,338$^{\wedge b}$	2,930±1,306$^{\wedge b}$	2,953±1,357$^{\wedge b}$	2,935±1,375$^{\wedge b}$	3,055±392	G=007
	F-MC	3,946±1,173	3,832±1,249^{bc}	3,619±1,140$^{\wedge bc}$	3,467±1,433$^{\wedge bc}$	3,458±1,154$^{\wedge bc}$	3,680±1,432$^{\wedge bc}$	3,496±1,238$^{\wedge bc}$	3,643±534	D=0.63
	F-LC	4,288±2,024	4,128±2,061$^{\wedge bcd}$	3,937±1,961$^{\wedge bcd}$	3,721±1,866$^{\wedge bcd}$	3,699±1,969$^{\wedge bcd}$	3,623±1,932$^{\wedge}$	3,579±1,886$^{\wedge}$	3,854±365	G×D=0.98
	T	3,274±1,178	3,038±1,057	3,014±1,110	2,903±1,099	2,858±1,058	2,744±1,160	2,815±1,075	2,959±264	T×G=0.26
	F	4,180±1,775	4,034±1,816	3,836±1,720	3,640±1,709	3,622±1,726	3,641±1,754	3,553±1,677	3,748±324$^{\gamma}$	T×D=0.88
	MC	3,438±1,040	3,246±1,047	3,143±958	3,013±1,097	3,000±973	2,911±1,221	2,954±988	3,253±320	T×G×D=0.15
	LC	3,851±1,819	3,650±1,792	3,553±1,751	3,392±1,652	3,342±1,709	3,312±1,694	3,280±1,671	3,454±268	
	Time	3,665±1,518	3,468±1,503*	3,368±1,450*	3,221±1,428*	3,188±1,422*	3,131±1,499*	3,133±1,401*		
Android Fat Free Mass (kg)	T-MC	3,803±846	3,675±749	3,664±665	3,683±717	3,578±595	3,649±598	3,569±644	3,660±209	T=0.003
	T-LC	3,904±955	3,678±789	3,764±835	3,708±755	3,818±826	3,829±826	3,722±800	3,775±232	G=0.04
	F-MC	4,411±723	4,150±651	4,094±656	4,189±882	4,281±767	4,354±931	4,343±714	4,260±316	D=0.90
	F-LC	4,420±1,301	4,287±1,230	4,194±1,065	4,125±985	4,158±939	4,132±886	4,125±1,072	4,206±216	G×D=0.73
	T	3,848±882	3,677±753	3,709±733	3,694±721	3,686±705	3,730±702	3,638±709	3,718±156$^{\Gamma}$	T×G=0.67
	F	4,417±1,130	4,243±1,065	4,162±939	4,145±933	4,197±871	4,203±884	4,195±961	4,233±191	T×D=0.71
	MC	3,988±844	3,820±740	3,795±678	3,837±787	3,792±715	3,864±768	3,805±745	3,960±189	T×G×D=0.08
	LC	4,180±1,163	4,004±1,076	3,994±972	3,931±895	4,000±889	3,991±857	3,938±961	3,990±158	
	Time	4,094±1,026	3,921±935*	3,904±850*	3,889±841*	3,906±814*	3,934±812*	3,878±864*		
Android Fat (%)	T-MC	45.4±3.9	44.3±4.2	43.9±4.9	42.5±5.4	43.1±4.8	42.3±4.7	42.6±4.3	43.4±1.5	T=0.00
	T-LC	44.9±5.4	44.4±5.8	43.6±6.1	43.3±5.9	41.9±6.1	41.9±6.8	42.5±6.3	43.2±1.6	G=0.29
	F-MC	46.5±5.8	47.1±6.1	46.1±5.8	43.6±6.2	43.8±5.5	43.1±7.9	43.6±5.6	44.8±2.2	D=0.87
	F-LC	47.8±5.5	47.0±6.8	46.3±7.3	45.3±7.4	44.5±8.4	44.0±8.6	44.2±7.9	45.6±1.5	G×D=0.78
	T	45.2±4.6	44.4±4.8	43.8±5.4	42.9±5.6	42.6±5.4	42.1±5.6	42.5±5.2	43.3±1.1	T×G=0.52
	F	47.3±5.5	47.0±6.4	46.2±6.7	44.8±6.9	44.3±7.5	43.7±8.0	44.0±7.1	45.2±1.3	T×D=0.61
	MC	45.7±4.5	45.1±4.8	44.5±5.1	42.9±5.6	43.3±5.0	42.5±5.3	42.9±4.6	44.1±1.3	T×G×D=0.79
	LC	46.4±5.6	45.8±6.4	45.0±6.8	44.4±6.7	43.3±7.4	43.0±7.7	43.4±7.1	44.4±1.1	
	Time	46.1±5.1	45.5±5.7	44.8±6.1*	43.7±6.2*	43.3±6.3*	42.8±6.7*	43.2±6.1*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, Γ significant genotype effect $p < 0.05$, γ trend in genotype effect $p > 0.05$ and $p < 0.1$, ^ significant difference compared to baseline (Tukey LSD). Letter superscripts indicate significance ($p < 0.05$) from Tukey LSD post hoc analyses: [b]significant difference from T-MC, [c]significant difference from T-LC, [d]significant difference from F-MC, [e]significant difference from F-LC.

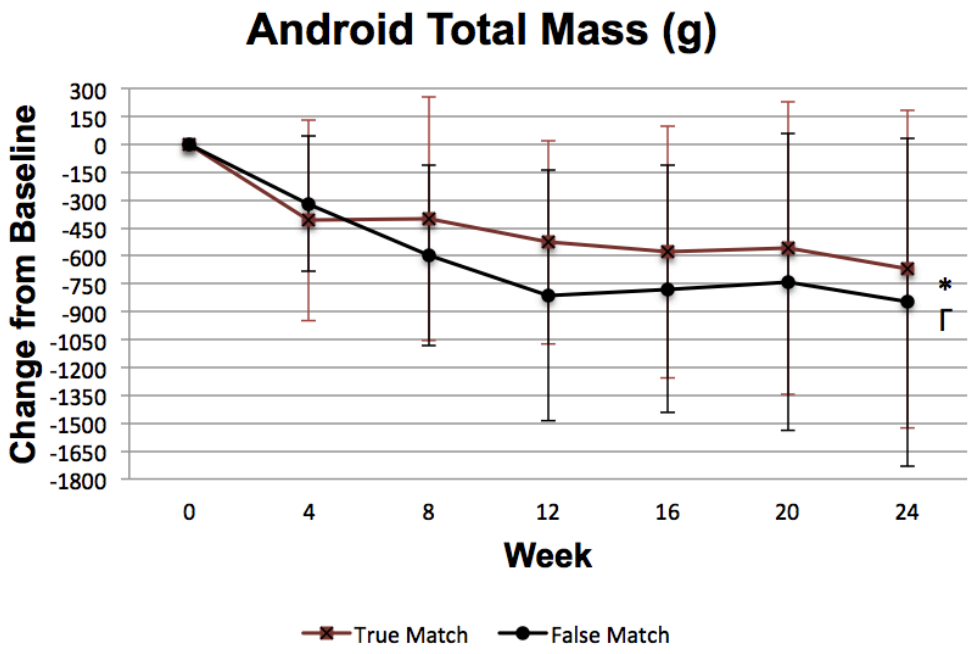

Figure 10: Delta change in android total mass observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$), Γ genotype effect ($p < 0.05$)

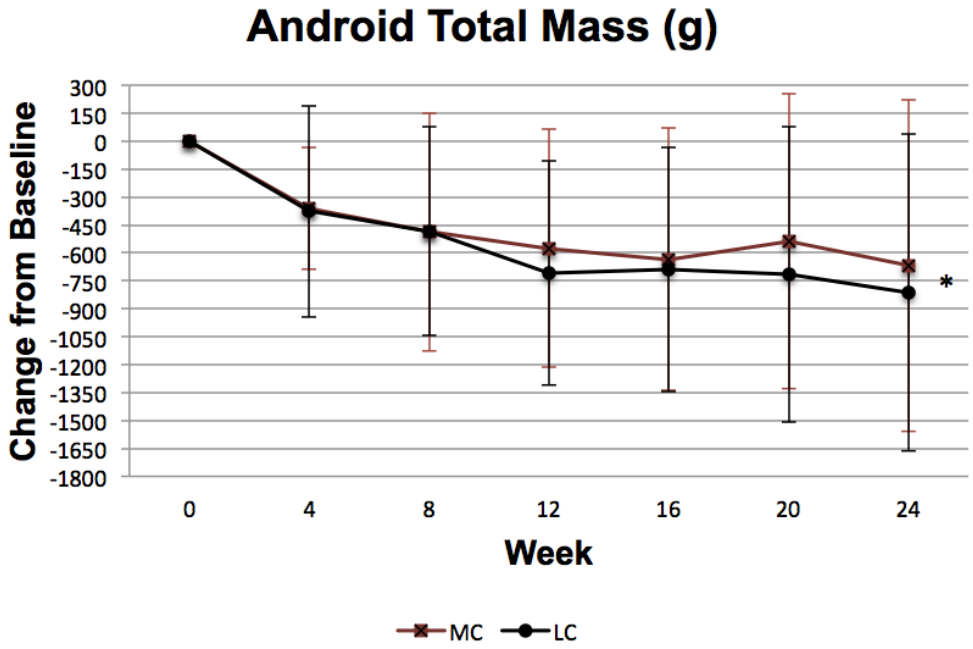

Figure 11: Delta change in android total mass observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

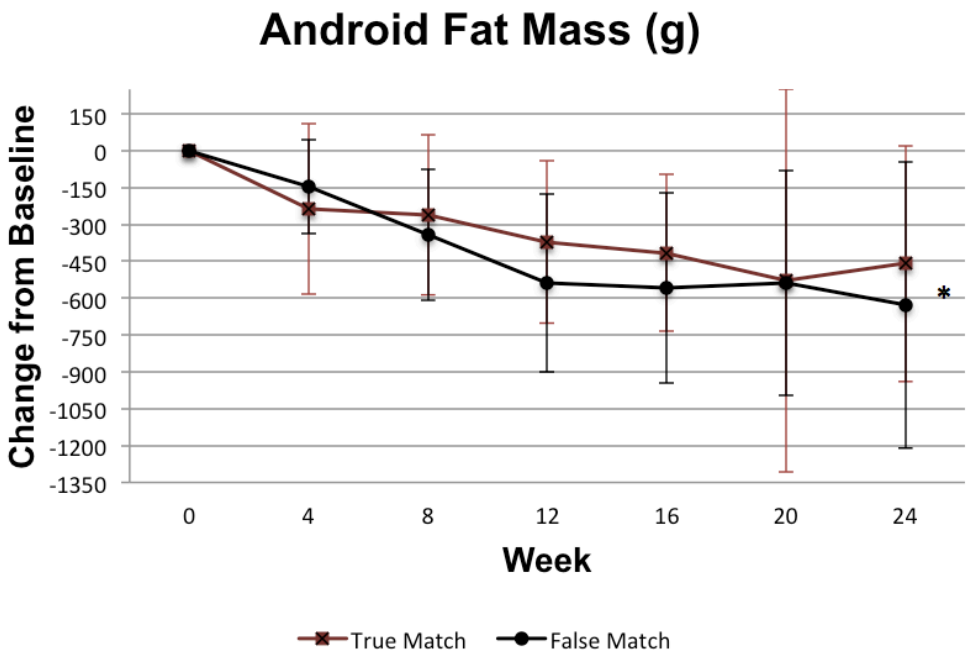

Figure 12: Delta change in android fat mass observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

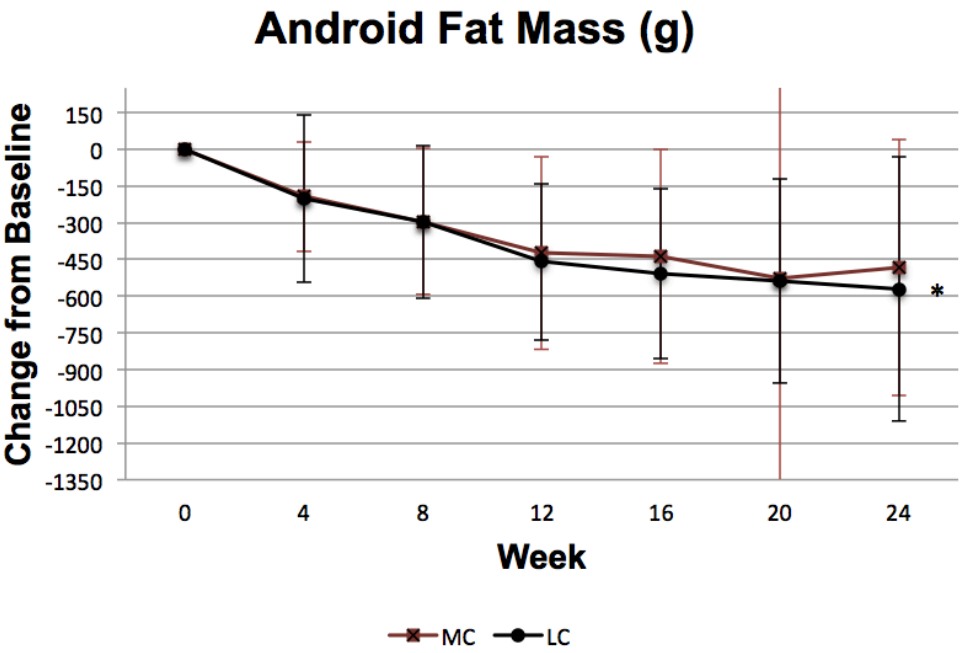

Figure 13: Delta change in android fat mass observed between diet. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$).

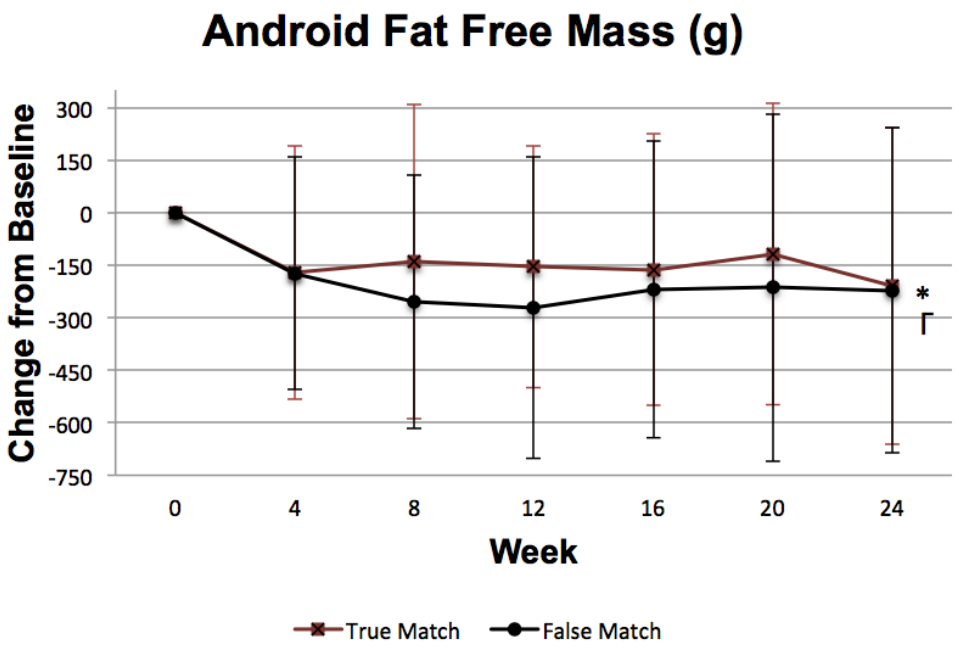

Figure 14: Delta change in android fat free mass observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$), Γ genotype effect ($p < 0.05$)

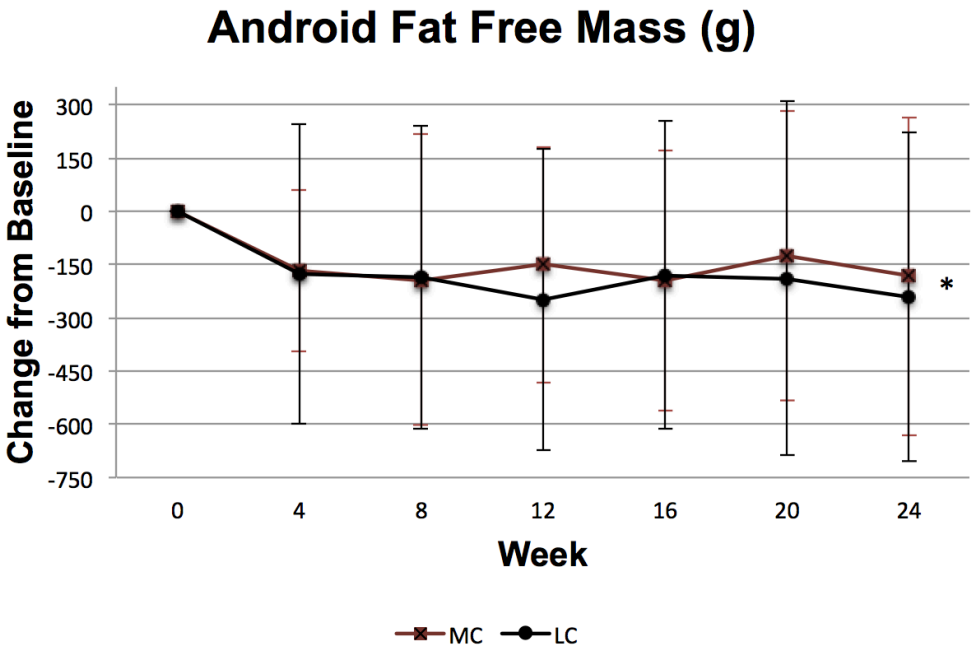

Figure 15: Delta change in android fat free mass observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

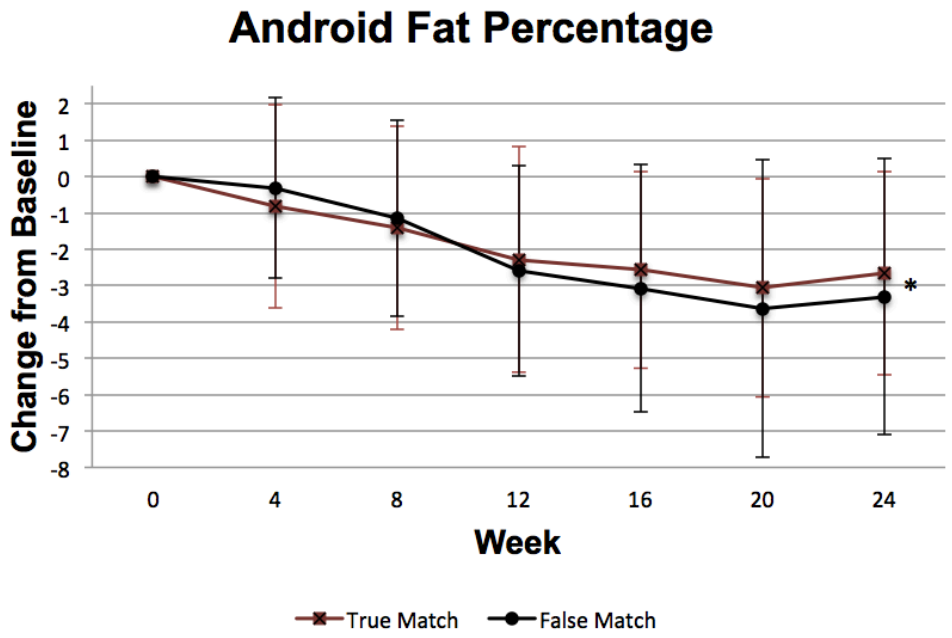

Figure 16: Delta change in android fat percentage observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

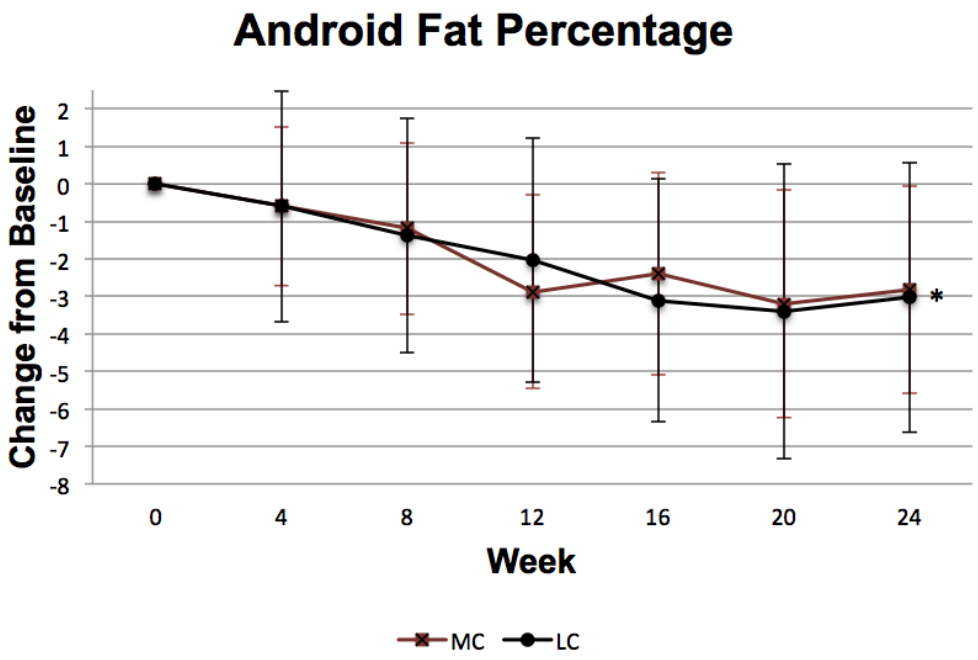

Figure 17: Delta change in android fat percentage observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$

In addition to android fat deposition, gynoid fat deposition was also measured.. An overall Wilks' Lambda effect of time was exhibited (p=0.00) with no significant interaction for time x genotype (p=0.31), time x diet (p=0.31), or time x genotype x diet (p=0.24). Univariate analyses revealed significant effect of time for gynoid total mass, fat mass, and fat percentage, where all participants demonstrated a reduction in these variables from baseline to completion (total mass: -865±1010 grams, p=0.00; fat mass: -831±886 gram, p=0.00; fat percentage: -2.5±2.3 %, p=0.00). A significant time x genotype x diet interaction was revealed for gynoid total mass such that from baseline to completion F-LC experienced the greatest loss in gynoid total mass (-1012.1±1025.8 grams) followed by T-MC (-899.9±1132.0 grams), T-LC (-850.7±793.7 grams), and F-MC (-507.6±1170.5 grams) (p=0.04). No other significant time interactions were observed.

Furthermore, a trend in genotype with a strong effect was exhibited for total mass, where true matches presented with less gynoid total mass at each time point and experienced a greater reduction in total mass upon completion (T -878±978, F -852±1073 grams, p=0.09, η^2_p=0.062, d=0.83). Post-hoc power analyses revealed a required sample size of 13,468 with a difference of 427.4 grams gynoid total mass to detect statistical significance between groups. Figure 18 represents change in gynoid total mass between genotype. A trend in genotype with strong effect was also observed for fat free mass, where false presented with greater gynoid fat free mass at each time point in comparison to true and experienced better retention in fat free mass upon completion (F +3.0±665, T -199±534 grams, pp=0.09, η^2_p=0.061, d=0.82). Post-hoc

power analyses revealed a required sample size of 15,681 with a difference of 3,432 grams gynoid fat free mass to detect statistical significance between groups. No other trends or significant effects were revealed for genotype, diet, or genotype x diet interaction. Table 16 represents gynoid total mass, fat mass, fat free mass, and fat percentage in each group throughout the study. Figures 19-25 represent changes in gynoid total mass, fat mass, fat free mass, and fat percentage between genotype and diet groups at each time point throughout the study. Since statistically significant interactions in favor of true matches was not observed for fat deposition, we reject H_3.

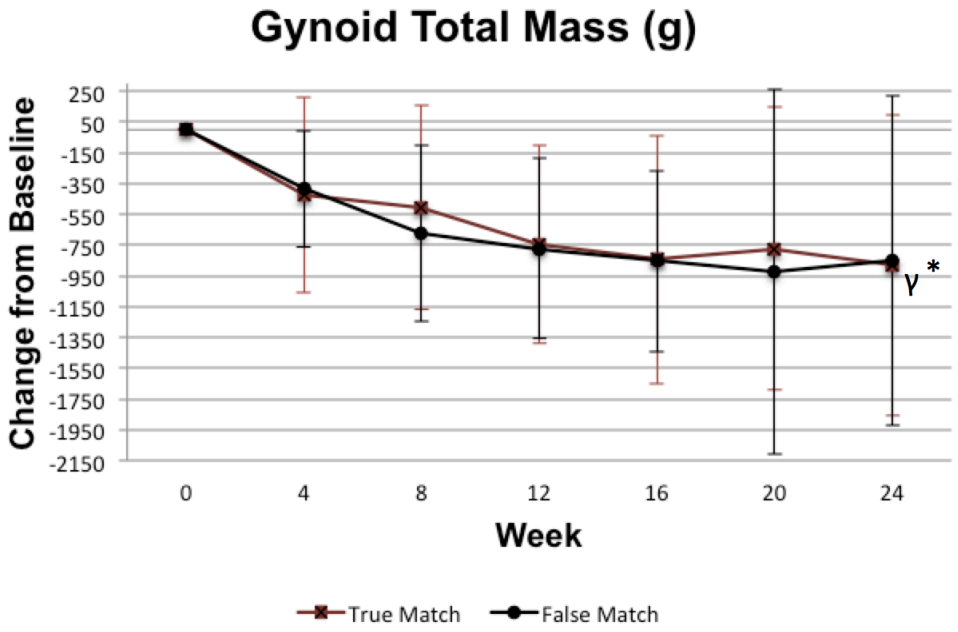

Figure 18: Delta change in gynoid total mass observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$) γ trend in genotype effect $p > 0.05$ and $p < 0.1$

Table 16: Gynoid total mass, fat mass, fat free mass, and fat percentage observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Gynoid Total Mass (g)	T-MC	14,524±2,683	14,208±2,552$^{\wedge}$	13,976±2,452$^{\wedge}$	13,719±2,503$^{\wedge}$	13,555±2,423$^{\wedge}$	13,711±2,457$^{\wedge}$	13,624±2,647$^{\wedge}$	13,902±844	T=0.00
	T-LC	15,062±3,640	14,505±3,403$^{\wedge b}$	14,614±3,794$^{\wedge b}$	14,394±35,45$^{\wedge b}$	14,373±3,571$^{\wedge b}$	14,339±3,59$^{\wedge b}$	14,211±3,503$^{\wedge b}$	14,500±936	G=0.09
	F-MC	16,639±2,487	16,120±2,235$^{\wedge bc}$	15,645±2,288$^{\wedge bc}$	15,805±2,546$^{\wedge bc}$	16,052±2,813$^{\wedge bc}$	16,324±3,313$^{\wedge bc}$	16,132±2,529$^{\wedge bc}$	16,102±1276	D=0.88
	F-LC	16,486±4,402	16,163±4,342$^{\wedge bc}$	15,958±4,390$^{\wedge bcd}$	15,742±4,222$^{\wedge bc}$	15,508±4,244$^{\wedge bcd}$	15,278±3,975$^{\wedge bcd}$	15,473±4,285$^{\wedge bcd}$	15,801±872	G×D=0.65
	T	14,765±3,100	14,341±2,911	14,262±3,120	14,022±2,976	13,922±2,964	13,992±2,976	13,887±3,017	14,201±630$^{\gamma}$	T×G=0.65
	F	16,534±3,833	16,149±3,741	15,859±3,791	15,762±3,707	15,681±3,786	15,611±3,731	15,683±3,764	15,951±773	T×D=0.12
	MC	15,168±2,754	14,790±2,572	14,484±2,539	14,354±2,646	14,315±2,746	14,506±2,936	14,387±2,813	15,002±765	T×G×D=0.04
	LC	15,824±4,057	15,393±3,954	15,334±4,106	15,117±3,911	14,981±3,918	14,841±3,762	14,887±3,922	15,150±640	
	Time	15,528±3,512	15,121±3,382*	14,951±3,482*	14,773±3,390*	14,681±3,423*	14,691±3,386*	14,662±3,443*		
Gynoid Fat Mass (g)	T-MC	6,500±1,643	6,236±1,545	6,024±1,555	5,794±1,605	5,766±1,544	5,763±1,560	5,823±1,592	5,986±533	T=0.00
	T-LC	6,882±2,218	6,536±1,996	6,426±2,182	6,404±2,181	6,251±2,062	6,219±2,136	6,183±2,065	6,414±591	G=0.14
	F-MC	7,649±1,370	7,301±1,214	6,939±1,187	6,927±1,399	7,099±1,657	7,131±1,708	7,054±1,501	7,157±805	D=0.76
	F-LC	7,826±2,814	7,572±2,827	7,310±2,885	7,149±2,749	6,687±3,284	6,670±2,611	6,605±3,179	7,117±550	G×D=0.71
	T	6,671±1,895	6,371±1,735	6,204±1,838	6,067±1,874	5,983±1,777	5,967±1,820	5,985±1,794	6,200±398	T×G=0.82
	F	7,770±2,413	7,486±2,401	7,192±2,446	7,078±2,368	6,818±2,830	6,817±2,330	6,748±2,726	7,137±488	T×D=0.15
	MC	6,849±1,626	6,560±1,511	6,302±1,489	6,139±1,605	6,172±1,663	6,179±1,694	6,197±1,637	6,572±483	T×G×D=0.12
	LC	7,388±2,554	7,091±2,488	6,899±2,575	6,803±2,485	6,484±2,744	6,461±23,70	6,409±2,680	6,766±404	
	Time	7,145±2,181	6,852±2,102*	6,630±2,156*	6,503±2,340*	6,343±2,304*	6,334±2,077*	8,387±1,479*		
Gynoid Fat Free Mass (kg)	T-MC	8,037±1,185	7,975±1,218	7,952±1,208	7,925±1,221	7,789±1,062	7,948±1,135	7,801±1,175	7,918±352	T=0.50
	T-LC	8,179±1,668	8,046±1,497	8,265±1,680	7,990±1,535	8,122±1,693	8,119±1,595	8,027±1,570	8,107±390	G=0.09
	F-MC	8,989±1,206	8,818±1,198	8,706±1,216	8,878±1,188	8,953±1,284	8,908±1,258	9,077±1,093	8,904±532	D=0.87
	F-LC	8,659±1,692	8,590±1,626	8,648±1,702	8,594±1,622	8,497±1,619	8,408±1,237	8,623±1,705	8,574±363	G×D=0.54
	T	8,101±1,396	8,007±1,325	8,093±1,420	7,955±1,345	7,939±1,365	8,025±1,337	7,902±1,345	8,013±263	T×G=0.18
	F	8,764±1,533	8,663±1,478	8,667±1,534	8,684±1,475	8,642±1,505	8,567±1,329	8,767±1,526	8,739±322$^{\gamma}$	T×D=0.44
	MC	8,327±1,247	8,232±1,249	8,182±1,234	8,215±1,266	8,144±1,232	8,240±1,230	8,190±1,276	8,411±319	T×G×D=0.40
	LC	8,437±1,667	8,338±1,563	8,470±1,672	8,314±1,583	8,323±1,634	8,274±1,460	8,346±1,642	8,341±267	
	Time	8,387±1,479	8,290±1,417	8,340±1,483	8,269±1,435	8,242±1,455	8,259±1,348	8,275±1,476		
Gynoid Fat (%)	T-MC	44.2±4.5	43.4±4.8	42.6±5.3	41.7±6.0	42.0±5.4	41.4±5.4	42.2±4.7	42.5±1.2	T=0.00
	T-LC	45.2±5.1	44.6±4.3	43.4±4.5	43.8±5.0	42.9±4.9	42.7±4.6	42.9±4.5	43.6±1.3	G=0.36
	F-MC	45.8±2.4	44.1±3.8	44.3±2.6	43.6±2.2	43.9±3.2	43.5±3.3	43.4±2.9	44.1±1.8	D=0.55
	F-LC	46.6±4.5	45.8±4.8	44.7±5.5	44.3±5.2	44.1±5.5	43.7±6.0	43.2±5.2	44.6±1.2	G×D=0.83
	T	44.6±4.7	43.9±4.5	42.9±4.9	42.6±5.6	42.4±5.1	42.0±5.0	42.5±4.5	43.1±0.9	T×G=0.77
	F	46.3±3.9	45.3±4.5	44.5±4.7	44.1±4.4	44.0±4.8	43.6±5.2	43.3±4.5	44.4±1.1	T×D=0.35
	MC	44.7±4.0	43.6±4.4	43.1±4.7	42.3±5.2	42.6±4.8	42.1±4.9	42.5±4.2	43.3±1.1	T×G×D=0.75
	LC	45.9±4.7	45.2±4.6	44.1±5.0	44.1±5.0	43.5±5.2	43.2±5.3	43.1±4.8	44.1±0.9	
	Time	45.4±4.4	44.5±4.5*	43.6±4.8*	43.3±5.1*	43.1±5.0*	42.7±5.1*	42.8±4.5*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *siginificant time effect from baseline $p < 0.05$, γ trend in genotype effect $p > 0.05$ and $p < 0.1$, ^ significant difference compared to baseline (Tukey LSD). Letter superscripts indicate significance ($p < 0.05$) from Tukey LSD post hoc analyses: [b]significant difference from T-MC, [c]significant difference from T-LC, [d]significant difference from F-MC, [e]significant difference from F-LC.

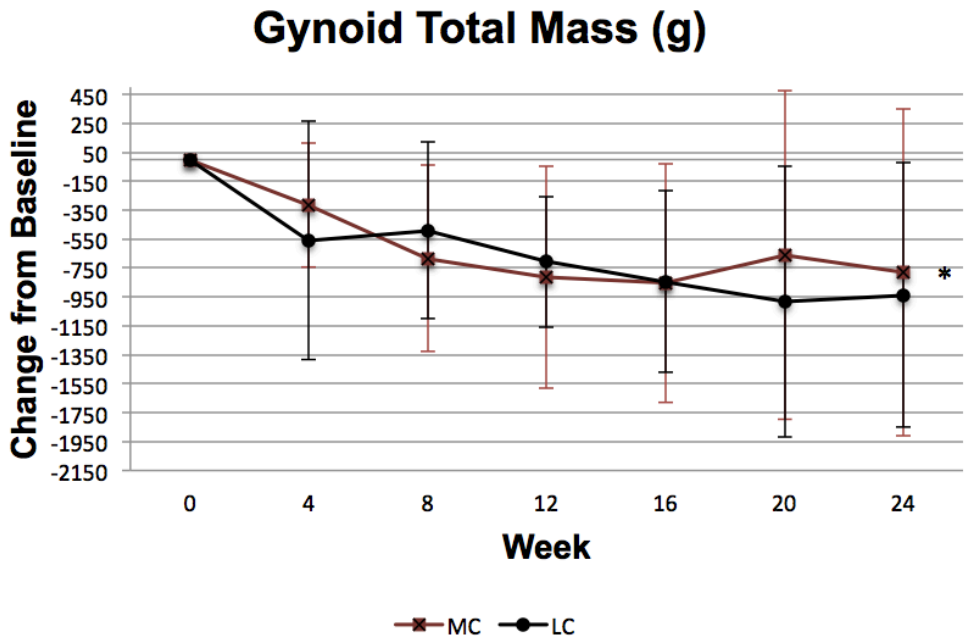

Figure 19: Delta change in gynoid total mass observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

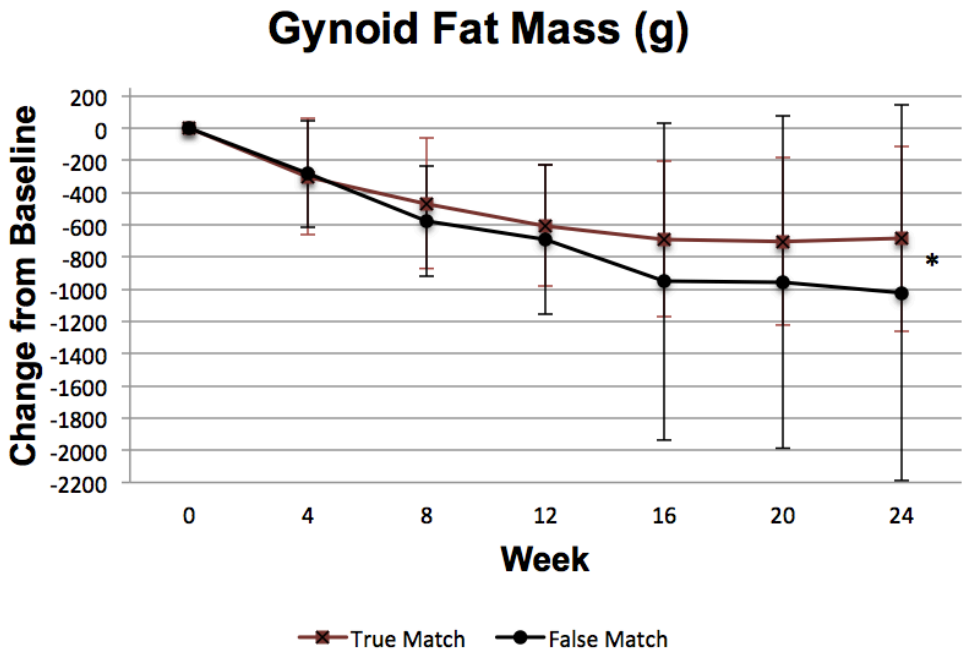

Figure 20: Delta change in gynoid fat mass observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

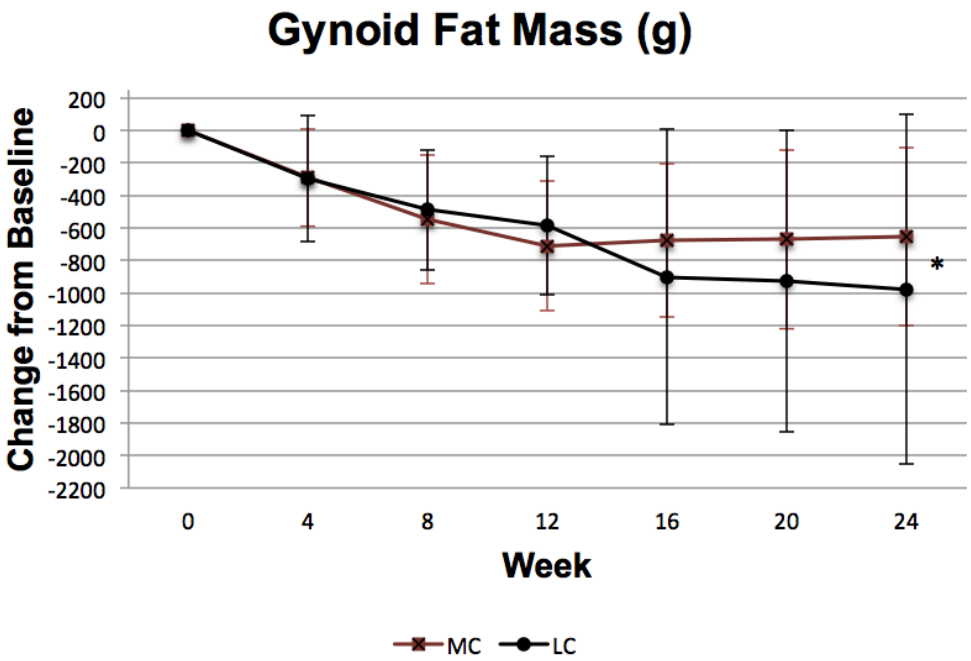

Figure 21: Delta change in gynoid fat mass observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

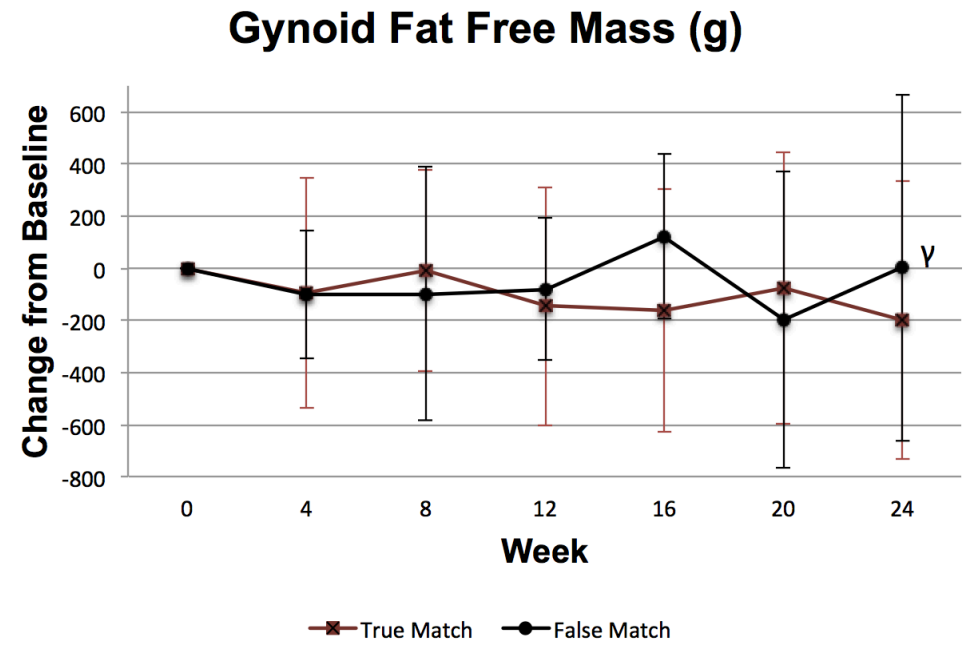

Figure 22: Delta change in gynoid fat free mass observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22. γ trend in genotype effect $p > 0.05$ and $p < 0.1$

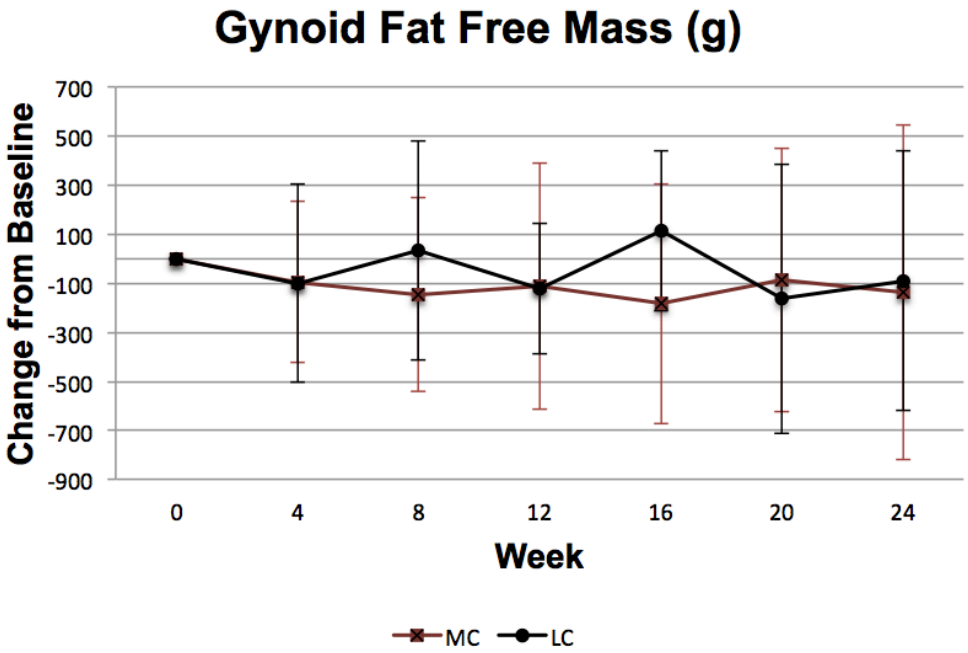

Figure 23: Delta change in gynoid fat free mass observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28

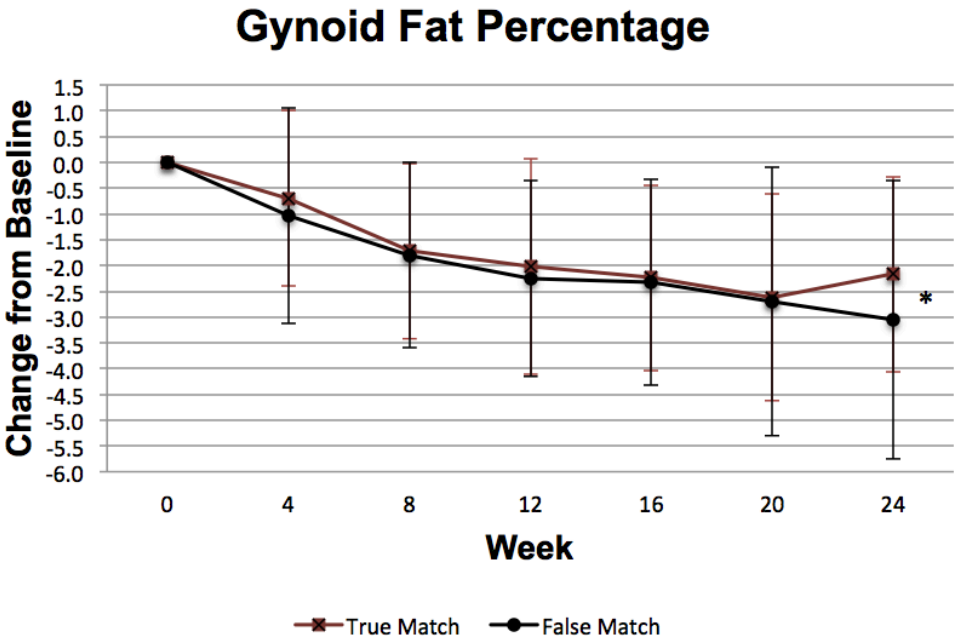

Figure 24: Delta change in gynoid fat percentage observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

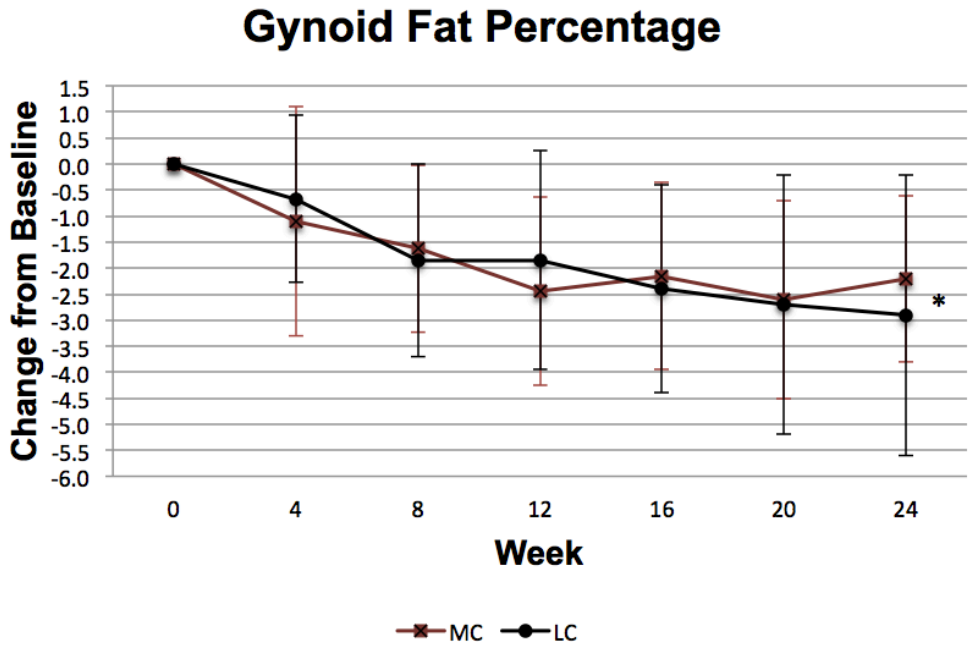

Figure 25: Delta change in gynoid fat percentage observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

Waist and Hip Circumference

An overall Wilks' Lambda effect of time (p=0.00) was observed with no significant interaction for time x genotype (0.89), time x diet (p=0.37), and time x genotype x diet (p=0.53). Univariate analyses revealed a significant effect of time for waist circumference and hip circumference, where all participants demonstrated a reduction in variables upon completion of the study (waist -5.2±5.7 cm, p=0.00; hip -5.0±4.0 cm, p=0.00). A trend in waist to hip ratio with moderate effect size (p=0.09, η^2_p=0.040, d=0.61) was also observed containing a trend in cubic relationship (p_c=0.06). Aside from time effects, no significant time interactions were observed. Moreover, for hip circumference a trend in genotype with a strong effect was revealed where true matches presented with smaller hip circumference at each time point in comparison to

false and experienced a greater reduction in hip circumference from baseline to completion (T -5.1±5.5, F -4.9±3.7 cm, p=0.07, η^2_p=0.070, d=0.88). No other significant effects or trends in genotype, diet, or genotype x diet interaction were observed. Table 17 represents waist circumference, hip circumference, and waist to hip ratio for each group throughout the study. Since we did not observe statistically significant interactions in favor of true matches for anthropometric variables we reject H_4.

BMI and Resting Energy Expenditure

An overall effect of time was observed (Wilks' Lambda p=0.00) with no significant interaction for time x genotype (p=0.49), time x diet (p=0.71), and time x genotype x diet (p=0.81). Findings regarding changes in body weight are described earlier. Univariate analyses revealed a significant effect of time among all variables with no significant time interactions. All participants experienced a significant reduction in BMI and increase in absolute and relative resting energy expenditure (REE) (BMI -1.7±2.6 kg/m^2, p=0.00; absolute REE +63±247 kcal/d, p=0.02; relative REE +1.8±2.9 kcal/kg/d, p=0.00). In addition, a significant effect of genotype for absolute REE was observed such that false matches presented with larger REE at each time point in comparison to true and exhibited a greater increase in REE upon completion (T +54.8±256.2, F +74.0±239 kcal/d, p=0.03). No other significant genotype, diet, or genotype x diet interaction was observed. Table 18 represents changes in weight, BMI, and absolute and relative energy expenditure in each group throughout the study. Based on these findings we reject H_5 since we did not observed statistically significant interactions in favor of true matches for resting energy expenditure.

Table 17: Waist circumference, hip circumference, and waist/hip ratio observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Waist (cm)	T-MC	95.9±12.3	92.9±9.9	92.0±11.4	89.5±9.7	90.0±8.8	90.2±10.4	90.1±10.9	91.5±3.2	T=0.00
	T-LC	93.6±12.8	91.0±13.5	91.4±13.2	91.9±13.2	90.7±13.1	90.0±11.9	89.2±10.3	91.1±3.6	G=0.26
	F-MC	98.7±13.2	97.8±14.0	95.9±13.5	93.5±12.3	95.1±11.9	96.4±14.1	94.0±12.2	95.9±4.9	D=0.90
	F-LC	98.9±15.7	95.8±14.6	96.7±17.3	95.3±16.3	92.8±14.6	94.6±16.0	93.5±16.7	95.4±3.3	G×D=0.98
	T	94.9±12.3	92.1±11.5	91.7±12.0	90.6±11.2	90.3±10.8	90.2±10.9	89.7±10.5	91.3±2.4	T×G=0.79
	F	98.9±14.6	96.4±14.1	96.5±15.9	94.7±14.8	93.5±13.6	95.1±15.1	93.7±15.1	95.6±2.9	T×D=0.11
	MC	96.7±12.3	94.4±11.2	93.2±11.9	90.7±10.4	91.5±9.9	92.1±11.6	91.3±11.2	93.7±2.9	T×G×D=0.42
	LC	96.5±14.4	93.5±14.0	94.3±15.5	93.7±14.7	91.8±13.7	92.5±14.2	91.5±14.1	93.2±2.4	
	Time	96.6±13.4	93.9±12.7*	93.8±13.9*	92.3±12.9*	91.7±12.0*	92.3±13.0*	91.4±12.7*		
Hip (cm)	T-MC	118.6±12.4	117.5±9.6	115.8±11.0	114.0±9.3	113.1±8.8	113.4±10.6	113.6±10.7	115.1±3.7	T=0.00
	T-LC	119.4±15.6	118.3±16.0	116.7±15.7	117.5±15.7	116.6±14.6	115.3±14.0	114.3±13.9	116.9±4.1	G=0.07
	F-MC	126.3±11.9	126.6±11.7	124.9±10.6	123.2±11.7	123.8±12.8	123.5±12.5	122.7±10.2	124.4±5.6	D=0.88
	F-LC	128.2±20.8	125.1±20.0	125.0±19.3	122.9±19.6	122.3±20.0	122.4±19.5	122.7±20.9	124.1±3.9	G×D=0.82
	T	119.0±13.6	117.8±12.6	116.2±13.1	115.6±12.4	114.7±11.7	114.2±12.1	113.9±12.0	116.0±2.8γ	T×G=0.81
	F	127.6±18.2	125.6±17.5	125.0±16.8	123.0±17.2	122.8±17.7	122.8±17.3	122.7±18.0	124.3±3.4	T×D=0.59
	MC	120.9±12.5	120.2±10.9	118.6±11.5	116.8±10.7	116.4±11.0	116.5±11.9	116.4±11.2	119.8±3.4	T×G×D=0.16
	LC	124.1±18.8	121.9±18.3	121.1±17.9	120.4±17.8	119.7±17.6	119.1±17.2	118.8±18.2	120.5±2.8	
	Time	122.7±16.2	121.2±15.3*	120.0±15.3*	118.8±15.0*	118.2±15.0*	117.9±15.0*	117.7±15.3*		
Waist/Hip Ratio (cm)	T-MC	0.81±0.04	0.79±0.04	0.79±0.04	0.79±0.05	0.79±0.03	0.79±0.04	0.79±0.05	0.79±0.01	T=0.09
	T-LC	0.78±0.05	0.77±0.05	0.78±0.05	0.78±0.03	0.78±0.05	0.78±0.04	0.78±0.04	0.78±0.01	G=0.21
	F-MC	0.78±0.07	0.77±0.06	0.77±0.07	0.76±0.07	0.77±0.06	0.78±0.07	0.77±0.07	0.77±0.02	D=0.60
	F-LC	0.77±0.05	0.77±0.06	0.77±0.06	0.78±0.06	0.76±0.05	0.77±0.05	0.76±0.05	0.77±0.01	G×D=0.62
	T	0.80±0.05	0.78±0.05	0.79±0.04	0.78±0.04	0.79±0.04	0.79±0.04	0.79±0.04	0.79±0.01	T×G=0.76
	F	0.78±0.06	0.77±0.06	0.77±0.06	0.77±0.06	0.76±0.05	0.77±0.05	0.76±0.06	0.77±0.01	T×D=0.22
	MC	0.80±0.05	0.78±0.05	0.78±0.05	0.78±0.06	0.79±0.04	0.79±0.05	0.78±0.05	0.78±0.01	T×G×D=0.96
	LC	0.78±0.05	0.77±0.05	0.78±0.06	0.78±0.05	0.77±0.05	0.78±0.05	0.77±0.05	0.77±0.01	
	Time	0.79±0.05	0.78±0.05*	0.78±0.05*	0.78±0.05*	0.78±0.05*	0.78±0.05*	0.78±0.05*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, γ trend in genotype effect $p > 0.05$ and $p < 0.1$, τ trend in time effect from baseline $p > 0.05$ and $p < 0.1$

Table 18: Weight, BMI, and absolute and relative resting energy expenditure observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Body Weight (kg)	T-MC	88.0±15.6	86.0±14.6	85.1±14.5	83.7±14.0	83.2±13.8	83.0±13.9	83.2±14.4	84.6±5.2	T=0.00
	T-LC	91.4±24.6	89.3±24.2	88.6±24.1	87.9±23.8	86.8±23.3	86.6±23.1	86.1±22.6	88.1±5.8	G=0.10
	F-MC	101±15.4	99.0±15.5	97.4±16.0	97.2±15.8	96.9±16.0	97.0±15.1	97.6±15.4	98.1±7.9	D=0.97
	F-LC	99.5±26.7	96.8±25.9	95.3±25.4	94.3±25.4	93.6±25.0	93.1±24.9	93.0±25.9	95.1±5.4	G×D=0.60
	T	89.5±19.8	87.5±19.2	86.7±19.1	85.6±18.8	84.8±18.4	84.6±18.3	84.5±18.2	86.4±3.9	T×G=0.57
	F	100.1±23.4	97.5±22.7	96.0±22.4	95.2±22.4	94.6±22.2	94.3±22.0	94.4±22.8	96.6±4.8$^{\gamma}$	T×D=0.32
	MC	92.0±16.4	90.0±15.8	88.9±15.7	87.8±15.6	87.4±15.5	87.3±15.4	87.6±15.8	91.3±4.7	T×G×D=0.43
	LC	95.8±25.6	93.3±25.0	92.2±24.6	91.3±24.4	90.4±24.0	90.1±23.9	89.8±24.2	91.6±3.9	
	Time	94.1±21.8	91.8±21.2*	90.7±20.9*	89.7±20.8*	89.1±20.5*	88.8±20.4*	88.8±20.7*		
BMI (kg/m^2)	T-MC	33.6±8.0	33.7±6.4	33.4±6.2	32.8±6.0	32.6±5.8	32.5±5.8	32.6±5.9	33.0±1.8	T=0.00
	T-LC	34.9±7.9	34.1±7.8	33.8±7.7	33.6±7.6	33.2±7.6	33.1±7.5	32.9±7.4	33.7±2.0	G=0.34
	F-MC	36.9±7.0	36.1±6.9	35.5±6.9	35.4±6.8	35.3±6.8	35.3±6.4	35.5±6.5	35.7±2.8	D=0.98
	F-LC	36.7±8.8	35.8±8.5	35.2±8.4	34.8±8.5	34.6±8.4	34.5±8.5	34.4±8.9	35.1±1.9	G×D=0.78
	T	34.2±7.8	33.9±6.9	33.6±6.8	33.2±6.6	32.9±6.5	32.8±6.5	32.7±6.4	33.3±1.4	T×G=0.46
	F	36.8±8.1	35.9±7.9	35.3±7.8	35.0±7.9	34.8±7.8	34.7±7.7	34.8±8.1	35.4±1.7	T×D=0.42
	MC	34.6±7.7	34.4±6.5	34.0±6.4	33.6±6.2	33.4±6.1	33.3±6.0	33.5±6.1	34.4±1.7	T×G×D=0.67
	LC	35.9±8.3	35.0±8.1	34.6±8.0	34.3±8.0	34.0±7.9	33.8±7.9	33.7±8.1	34.4±1.4	
	Time	35.3±8.0	34.8±7.3*	34.3±7.2*	34.0±7.2*	33.7±7.1*	33.6±7.1*	33.6±7.2*		
REE (kcal/d)	T-MC	1,385±280	1,312±262	1,351±285	1,437±190	1,460±238	1,465±300	1,468±254	1,411±57	T=0.02
	T-LC	1,411±356	1,363±272	1,276±260	1,411±288	1,390±246	1,438±194	1,433±266	1,389±63	G=0.03
	F-MC	1,523±319	1,585±308	1,608±261	1,619±255	1,691±274	1,651±180	1,533±129	1,601±86	D=0.34
	F-LC	1,415±297	1,495±342	1,482±299	1,499±256	1,527±226	1,513±272	1,519±265	1,493±59	G×D=0.53
	T	1,397±311	1,335±263	1,318±272	1,426±235	1,428±240	1,453±254	1,452±255	1,400±43	T×G=0.11
	F	1,449±301	1,524±327	1,522±288	1,538±256	1,579±248	1,557±251	1,523±227	1,547±52$^{\Gamma}$	T×D=0.62
	MC	1,427±292	1,395±298	1,429±297	1,493±222	1,530±266	1,521±279	1,487±222	1,506±52	T×G×D=0.86
	LC	1,413±320	1,434±313	1,386±295	1,458±270	1,463±241	1,478±238	1,479±264	1,441±43	
	Time	1,420±305	1,416±304	1,406±294	1,474±248	1,493±252*	1,498±256*	1,483±244		
REE (kcal/kg/d)	T-MC	15.9±2.5	15.3±2.3	16.0±2.7	17.3±1.8	17.6±1.7	17.6±2.1	17.8±2.1	16.8±0.4	T=0.00
	T-LC	15.6±2.7	15.7±3.2	14.9±3.3	16.4±2.3	16.4±2.2	17.2±2.4	17.2±3.4	16.2±0.5	G=0.71
	F-MC	15.3±3.2	16.0±1.5	16.6±1.7	16.7±1.8	17.5±1.1	17.1±1.0	15.9±2.1	16.4±0.7	D=0.41
	F-LC	14.5±2.2	15.7±2.2	16.0±2.8	16.4±2.3	17.0±3.4	16.6±1.6	16.8±2.5	16.1±0.5	G×D=0.79
	T	15.8±2.5	15.5±2.7	15.5±3.0	16.9±2.0	17.1±2.0	17.4±2.2	17.5±2.7	16.5±0.3	T×G=0.13
	F	14.8±2.5	15.8±2.0	16.2±2.5	16.5±2.1	17.2±2.8	16.8±1.4	16.6±2.4	16.3±0.4	T×D=0.70
	MC	15.7±2.7	15.5±2.1	16.2±2.4	17.2±1.7	17.6±1.5	17.5±1.8	17.2±2.2	16.6±0.4	T×G×D=0.76
	LC	15.0±2.4	15.7±2.7	15.5±3.0	16.4±2.3	16.7±2.9	16.9±2.0	17.0±2.9	16.2±0.3	
	Time	15.3±2.5	15.6±2.4	15.8±2.8	16.7±2.1*	17.1±2.4*	17.1±1.9*	17.1±2.6*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, Γ significant genotype effect $p < 0.05$, γ trend in genotype effect $p > 0.05$ and $p < 0.1$

Fitness

Peak Aerobic Capacity (VO_2)

Multivariate analyses revealed significant time effect (Wilks' Lambda p=0.00) with no significant interaction for time x genotype (p=0.87), time x diet (p=0.76), and time x genotype x diet (p=0.17). Univariate analyses revealed a significant time effect for absolute and relative VO_2, and time to exhaustion (TTE). All participants exhibited an increase in all variables from baseline to completion (absolute VO_2 +0.2±0.2 L/min, p=0.00; relative VO_2 +3.7±3.2 ml/kg/min, p=0.00; TTE +1.1±0.7 minutes, p=0.00). Further a trend in time x genotype x diet interaction with a large effect size was exhibited for absolute VO_2 (p=0.08 η^2_p=0.056, d=0.82). The trend was linear in nature and overall favored F-MC (+5.7±5.7), followed by T-LC (+4.1±3.2), T-MC (+3.4±2.0), and F-LC (+2.9±2.7 L/min). The same relationship was demonstrated for relative VO_2 (p=0.07, η^2_p=0.058, d=0.84). No other significant time interactions, genotype or diet effects, and genotype x diet interaction were observed. Table 19 represents absolute and relative peak aerobic capacity, and time to exhaustion in each group throughout the study. Figures 26-31 represent absolute and relative peak aerobic capacity and time to exhaustion for genotype and diet groups throughout the study. All in all we accept H_{o6} since we did not observe statistically significant interactions favoring true matches for cardiorespiratory fitness.

Table 19: Absolute and relative peak aerobic capacity and time to exhaustion observed between groups

Variable	Group	Baseline	12 Weeks	24 Weeks	Group (SEM)	P-value
VO_2max (L/min)	T-MC	1.98±0.33	2.14±0.36^	2.15±0.34^	2.09±0.08	T = 0.00
	T-LC	1.89±0.36	2.06±0.38^	2.11±0.36^	2.03±0.09	G = 0.79
	F-MC	1.97±0.19	2.18±0.27^c	2.25±0.32^bc	2.14±0.12	D = 0.38
	F-LC	1.96±0.28	2.06±0.36^d	2.06±0.33^bcd	2.03±0.08	G×D = 0.81
	T	1.94±0.34	2.10±0.36	2.10±0.35	2.06±0.06	T×G = 0.97
	F	1.96±0.25	2.10±0.34	2.10±0.34	2.08±0.07	T×D = 0.39
	MC	1.98±0.29	2.15±0.33	2.18±0.33	2.11±0.07	T×G×D = 0.08
	LC	1.93±0.31	2.06±0.36	2.09±0.34	2.03±0.06	
	Time	1.95±0.30	2.10±0.35*	2.13±0.34*		
VO_2max (ml/kg/min)	T-MC	22.9±4.2	25.9±4.6^	26.3±4.3^	25.0±1.2	T = 0.00
	T-LC	21.6±0.47	24.5±5.5^	25.6±5.4^	23.9±1.3	G = 0.18
	F-MC	19.8±3.2	22.9±4.2^bc	25.5±6.4^	22.7±1.8	D = 0.59
	F-LC	20.6±4.5	22.9±5.5^bc	23.5±6.0^bcd	22.3±1.2	G×D = 0.79
	T	22.3±4.4	25.3±4.9	26.0±4.8	24.5±0.9	T×G = 0.54
	F	20.4±4.0	22.9±5.0	24.1±6.0	22.5±1.1	T×D = 0.37
	MC	22.0±4.1	25.0±4.6	26.0±4.9	23.8±1.1	T×G×D = 0.07
	LC	21.1±4.5	23.7±5.4	24.5±5.7	23.1±0.9	
	Time	21.5±4.3	24.3±5.1*	25.2±5.4*		
Time to Exhaustion (min)	T-MC	7.9±1.9	8.8±1.6	9.1±1.5	8.6±0.4	T = 0.00
	T-LC	8.0±1.3	8.8±1.4	9.1±1.4	8.7±0.4	G = 0.30
	F-MC	7.5±1.0	8.5±1.2	8.8±1.4	8.3±0.6	D = 0.90
	F-LC	7.5±1.6	8.2±1.6	8.5±1.6	8.1±0.4	G×D = 0.75
	T	8.0±1.7	8.8±1.5	9.1±1.4	8.6±0.3	T×G = 0.96
	F	7.5±1.4	8.3±1.5	8.6±1.5	8.2±0.3	T×D = 0.42
	MC	7.8±1.7	8.7±1.4	9.0±1.4	8.4±0.3	T×G×D = 0.86
	LC	7.8±1.5	8.5±1.5	8.8±1.5	8.4±0.3	
	Time	7.8±1.6	8.6±1.5*	8.9±1.5*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, ^ significant difference compared to baseline (Tukey LSD). Letter superscripts indicate significance ($p < 0.05$) from Tukey LSD post hoc analyses: [b]significant difference from T-MC, [c]significant difference from T-LC, [d]significant difference from F-MC, [e]significant difference from F-LC

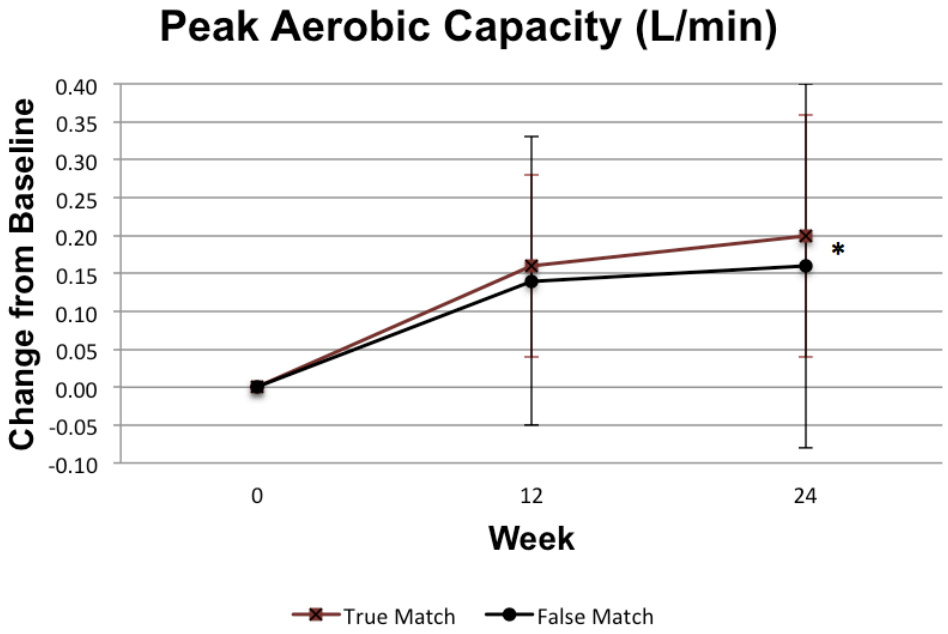

Figure 26: Delta change in absolute peak aerobic capacity observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

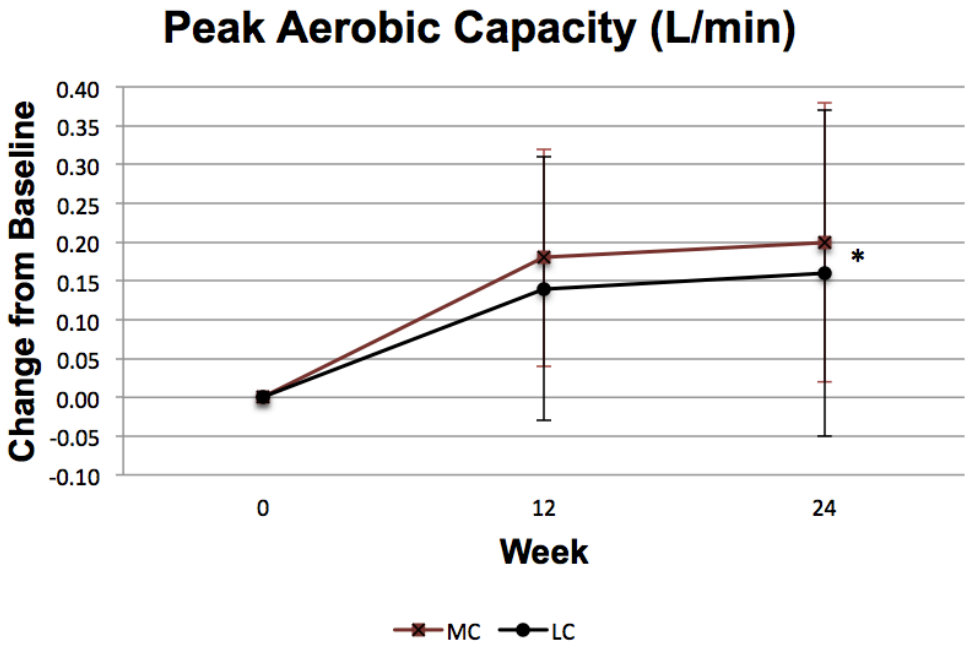

Figure 27: Delta change in absolute peak aerobic capacity observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

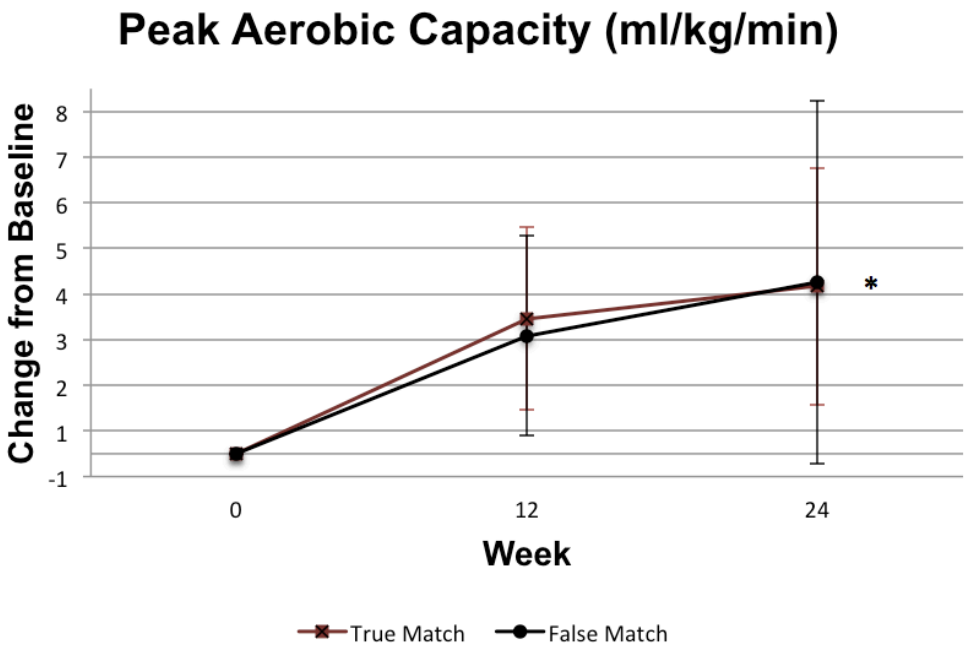

Figure 28: Delta change in relative peak aerobic capacity observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

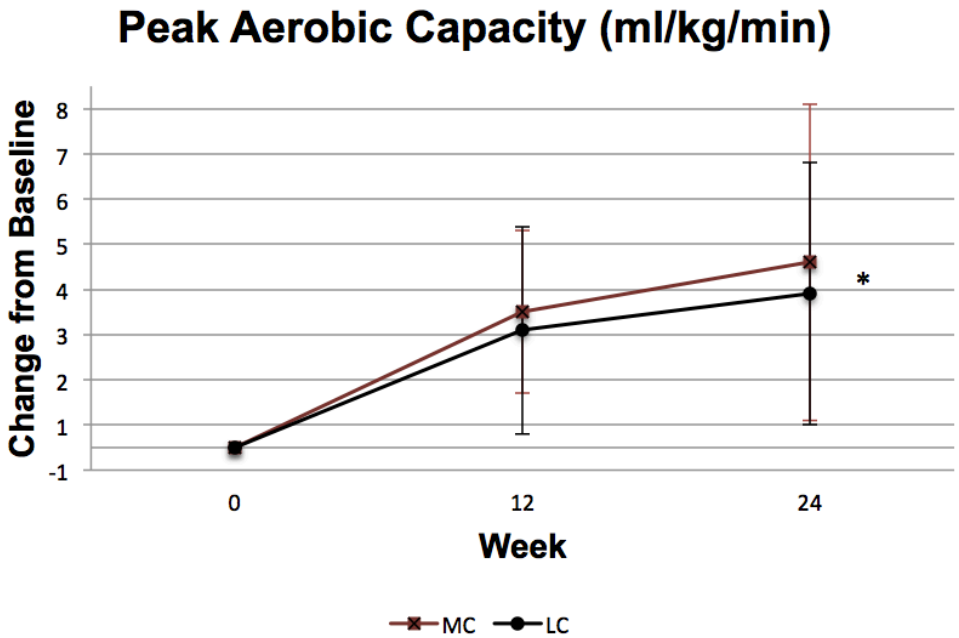

Figure 29: Delta change in relative peak aerobic capacity observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

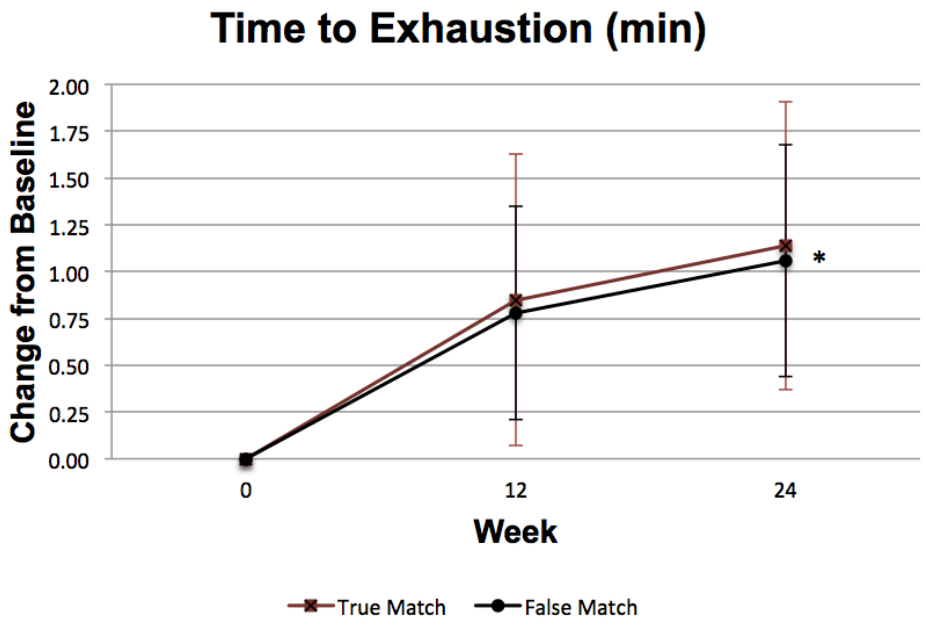

Figure 30: Delta change in time to exhaustion observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

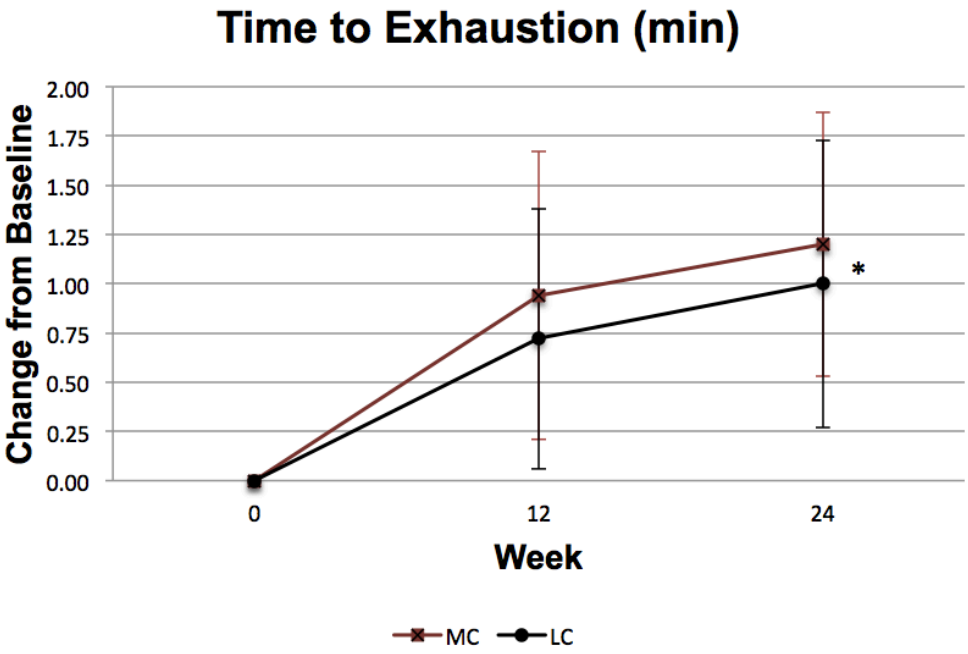

Figure 31: Delta change in time to exhaustion observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

Upper and Lower Body Muscular Strength and Endurance

An overall Wilks' Lambda time effect was observed (p=0.00) with no significant interaction for time x genotype (p=0.83), time x diet (p=0.35), and time x genotype x diet (p=0.96). Univariate analyses revealed significant time effect for lower and upper body muscular strength (p=0.00), with no significant time effect for lower or upper body muscular endurance (p=0.44 and p=0.16 respectively). From baseline to completion, all participants experienced an increase in lower and upper body muscular strength (lower: +51.1±56.7 kg, p=0.00; upper +5.7±3.9 kg, p=0.00). Further, a significant time x diet interaction was observed for lower body muscular strength where individuals in MC demonstrated greater improvements throughout the study in comparison to LC (baseline-3 months: MC +46.4±55.7, LC +24.6±28.2, baseline-6 months: MC +72.4±68.6, LC +33.5±37.6 kg, p=0.4). No other significant time interactions were observed. A significant diet effect was exhibited for lower body muscular strength such that MC demonstrated greater strength at each time point along with a greater increase in strength upon completion (p=0.04). No other significant diet or genotype effects, or diet x genotype interactions were observed. Table 20 represents upper and lower body strength and endurance observed in each group from baseline to completion. Figures 32-35 represents changes in lower and upper body strength for genotype and diet groups at each time point measured. Since we did not observe statistically significant interactions favoring true matches for upper or lower body muscular strength and endurance, we accept H_{o7} and H_{o8} respectively.

Table 20: Upper and lower body strength and endurance observed between groups

Variable	Group	Baseline	12 Weeks	24 Weeks	Group (SEM)	P-value
Leg Press 1RM (kg)	T-MC	228.7±98.9	278.7±114.3	304.5±132.8	270.6±20.6	T = 0.00
	T-LC	191.3±51.0	219.8±54.8	238.5±62.8	216.5±22.8	G = 0.75
	F-MC	226.3±66.3	264.6±87.4	290.9±92.7	260.6±31.1	D = 0.04
	F-LC	196.4±57.2	217.6±72.7	218.0±76.8	210.7±21.3	G×D = 0.93
	T	211.9±81.9	252.3±95.8	274.9±110.7	243.6±15.4	T×G = 0.36
	F	205.9±60.3	232.5±78.8	241.2±87.1	235.6±18.8	T×D = 0.04
	MC	228.0±88.7	274.4±105.0^	300.4±120.0^	265.6±18.7Ð	T×G×D = 0.69
	LC	194.0±53.5	218.6 ±63.8^a	227.5 ±70.1^a	231.6±15.6	
	Time	209.3±72.8	243.8±88.5*	260.4±101.7*		
Leg Press Endurance (reps)	T-MC	17±8	17±9	15±8	15±1.2	T = 0.44
	T-LC	14±5	12±5	11±3	13±1.4	G = 0.30
	F-MC	13±2	11±4	12±5	12±1.8	D = 0.57
	F-LC	12±7	13±6	14±6	13±1.3	G×D = 0.19
	T	15±6	14±7	13±6	14±0.9	T×G = 0.38
	F	12±6	12±5	13±6	12±1.1	T×D = 0.88
	MC	15±7	14±8	14±7	14±1.1	T×G×D = 0.72
	LC	13±6	13±5	12±5	13±0.9	
	Time	14±6	13±7	13±6		
Bench Press 1RM (kg)	T-MC	36.5±8.2	39.5±9.5	42.6±8.9	39.5±1.9	T = 0.00
	T-LC	33.7±6.3	36.2±5.3	40.2±7.2	36.7±2.1	G = 0.51
	F-MC	35.7±7.4	39.3±8.2	41.6±7.4	38.9±2.9	D = 0.12
	F-LC	32.1±8.1	34.2±7.8	36.8±8.7	34.4±2.0	G×D = 0.72
	T	35.3±7.4	38.0±7.9	41.5±8.1	38.1±1.4	T×G = 0.44
	F	33.3±7.9	35.8±8.1	38.3±8.4	36.6±1.8	T×D = 0.58
	MC	36.3±7.8	39.4±8.9	42.3±8.3	39.2±1.7	T×G×D = 0.71
	LC	32.9±7.3	35.1±6.7	38.4±8.0	35.6±1.5	
	Time	34.4±7.6	37.1±8.0*	40.2±8.3*		
Bench Press Endurance (reps)	T-MC	8±2	8±3	7±3	8±0.5	T = 0.16
	T-LC	9±3	8±3	7±3	8±0.6	G = 0.74
	F-MC	9±3	7±2	7±2	8±0.8	D = 0.76
	F-LC	8±4	8±4	8±3	8±0.5	G×D = 0.97
	T	9±3	8±3	7±3	8±0.4	T×G = 0.79
	F	8±3	8±3	8±3	8±0.5	T×D = 0.58
	MC	9±2	8±3	7±3	8±0.5	T×G×D = 0.41
	LC	8±3	8±3	8±3	8±0.4	
	Time	8±3	8±3	7±3		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, Ð signifciant diet effect $p < 0.05$, ^ significant difference compared to baseline (Tukey LSD), [a]significant difference from MC $p < 0.05$ (Tukey LSD post hoc).

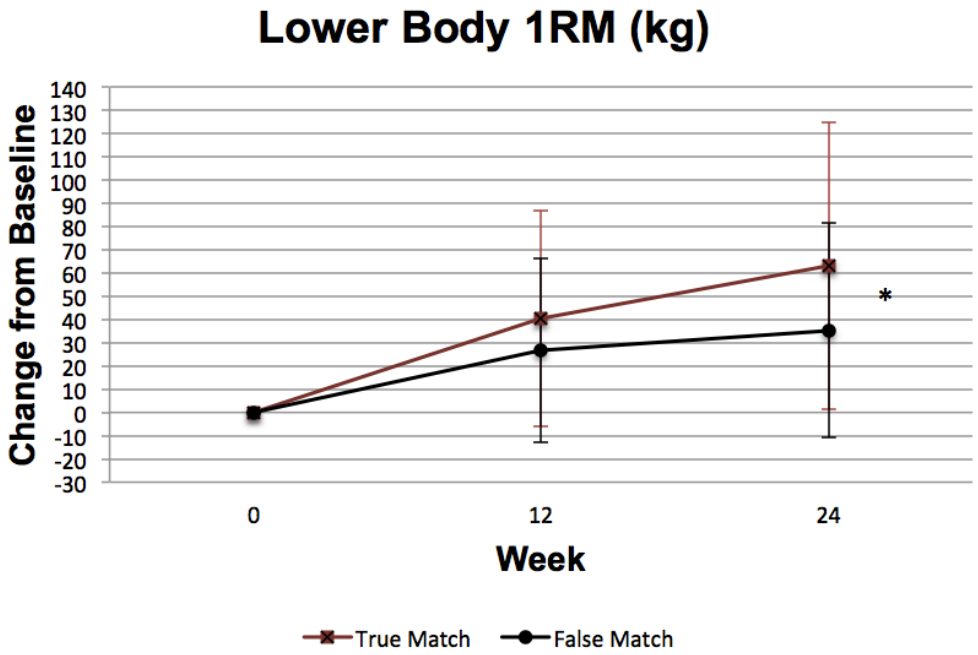

Figure 32: Delta change in lower body muscular strength observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

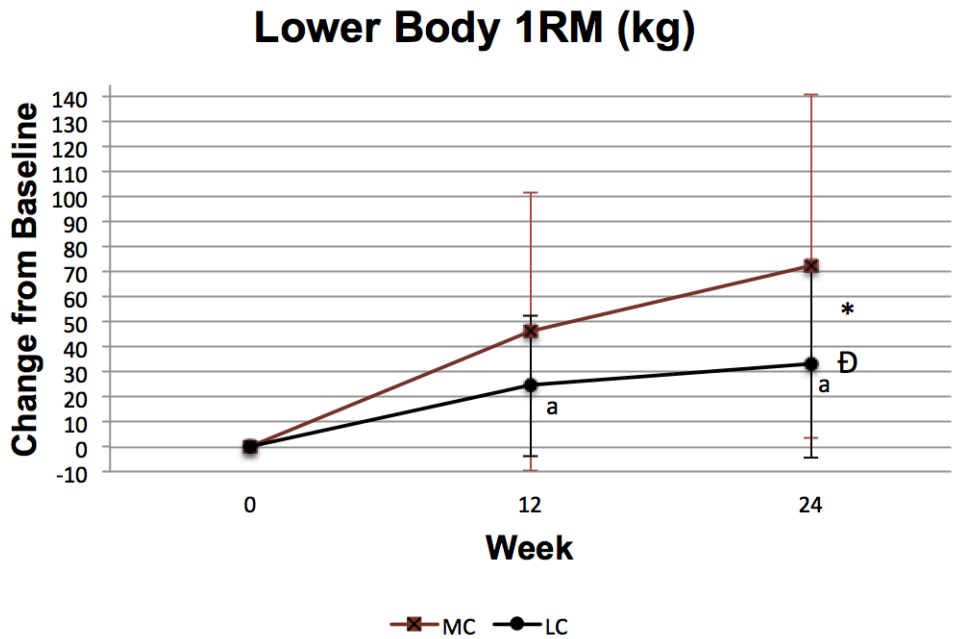

Figure 33: Delta change in lower body muscular strength observed between diet. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$), Đ diet effect ($p < 0.05$), [a]significant difference from MC $p < 0.05$ (Tukey LSD post hoc).

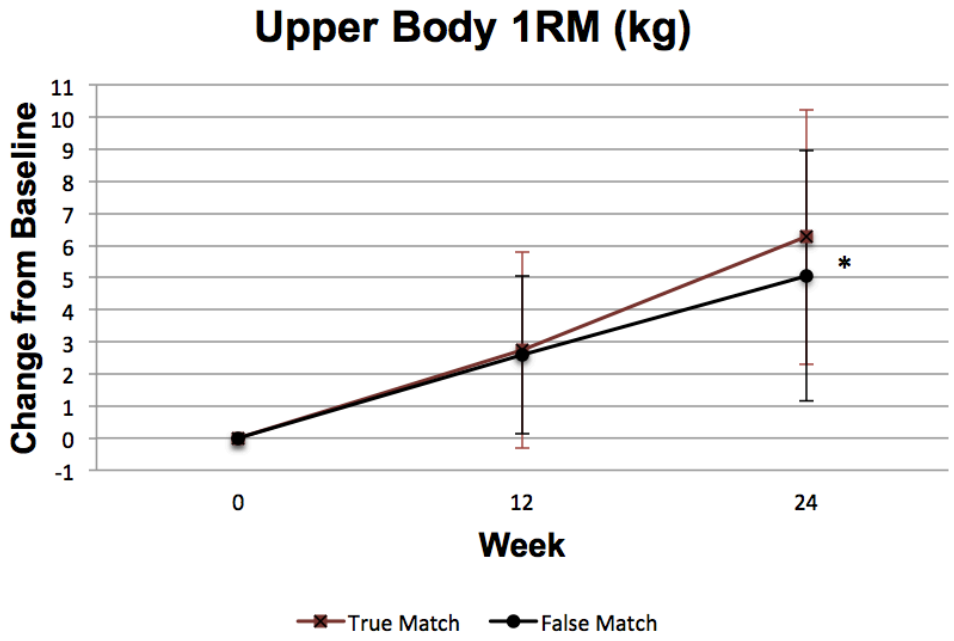

Figure 34: Delta change in upper body muscular strength observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, F: n = 22, * time effect ($p < 0.05$)

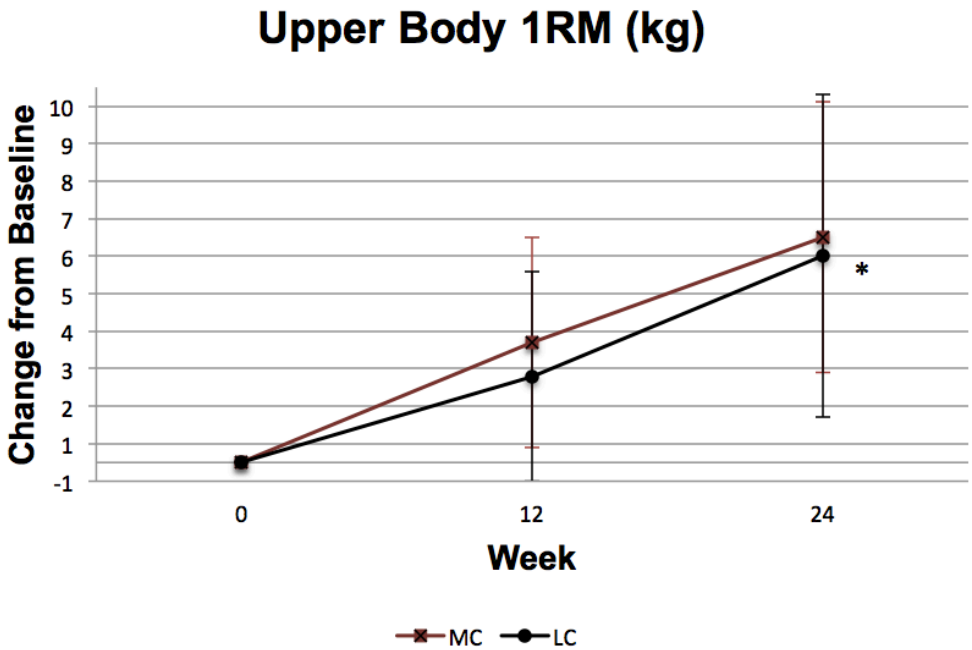

Figure 35: Delta change in upper body muscular strength observed between diet. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$)

Biochemical Markers

Blood Lipid Profile

A significant effect of time was observed (Wilks' Lambda p=0.00) along with a significant time x diet interaction (p=0.001) and no significant time x genotype (p=0.39) or time x genotype x diet interaction (p=0.36). Univariate analyses revealed significant time effect with a quadratic relationship for total cholesterol (p=0.00, p_q=0.00), HDL cholesterol (p=0.00, p_q=0.00), LDL cholesterol (p=0.00, p_q=0.00), and triglycerides (p=0.00, p_q=0.02). However all participants experienced favorable changes for blood lipids by 6-months (total cholesterol -7.2±36.0 mg/dL, HDL +4.6±13.3 mg/dL, LDL -2.5±29.3 mg/dL, Triglycerides -20.9±57.9 mg/dL). A significant time x diet interaction was observed for total cholesterol, HDL, LDL, and triglycerides such that MC demonstrated significant reductions from baseline to completion and greater reductions in comparison to LC for total cholesterol (MC: -25.2±31.3, LC: +7.7±33.1 mg/dL, p=0.001), LDL (MC: -13.6±28.6, LC: +6.7±26.9 mg/dL, p=0.01), and triglycerides (MC: -37.1±65.7, LC: -7.6 ± 47.7 mg/dL, p=0.00). LC demonstrated a greater increase in HDL upon completion in comparison to MC (MC: -0.6±12.2, LC: +8.9±12.8 mg/dL, p=0.01). Further a significant time x genotype interaction was observed for triglycerides, such that from baseline to completion false matches experienced a significant reduction in triglycerides and greater reduction in comparison to true matches (T -9.9±62.3, F -35.5±49.1 mg/dL, p=0.05). There were no other time interactions among variables.

In addition, significant diet effect was experienced in total cholesterol (p=0.00), LDL (p=0.00), and triglycerides (p=0.00), where MC presented with larger blood lipids

at each time point in comparison to LC. A trend in genotype x diet interaction with a large effect was observed for total cholesterol such that by week 12 T-MC and F-MC presented with cholesterol that was significant different from T-LC and F-LC ($p=0.06$, $\eta^2_p=0.074$, $d=0.94$). Further, T-MC and F-MC demonstrated greater reductions in total cholesterol upon completion (T-MC -26.0±32.1, F-MC -23.5±32.0, F-LC +7.0±31.8, T-LC +8.5±35.8 mg/dL). Similarly, a significant genotype x diet interaction was observed for LDL cholesterol. By week 12 T-MC and F-MC presented with LDL that was significantly different from T-LC and F-LC. From baseline to completion, T-MC exhibited the greatest reduction in LDL (-15.8±26.7 mg/dL) followed by F-MC (-8.6±34.2), F-LC (+3.7±28.1 mg/dL), and T-LC (+10.1±26.3 mg/dL) ($p=0.02$). No other significant genotype x diet interactions, or genotype or diet effects was observed among variables. Table 21 represents fasting blood lipids in each group at each time point measured. Figures 36-39 represent changes in total cholesterol, LDL, HDL, and triglycerides by diet group for each time point measured throughout the study. Figure 40 represents changes in triglycerides for genotype. Since statistically significant interactions favoring true matches were not observed for any measured blood lipids, we reject H_9.

Table 21: Fasting blood lipids observed between groups

Variable	Group	Baseline	12 Weeks	24 Weeks	Group (SEM)	P-value
Total Cholesterol (mg/dL)	T-MC	253.5±54.3	282.1±55.5^{ce}	227.5±42.4	254.4±9.8$^{\delta}$	T = 0.00
	T-LC	176.9±31.1	194.5±42.6	185.4±40.4	185.6±10.8	G = 0.91
	F-MC	225.6±46.3	264.6±67.6^{c}	202.1±37.5	230.8±14.8$^{\delta}$	D = 0.00
	F-LC	200.0±40.7	213.0±39.7	206.9±46.3	206.7±10.1	G×D = 0.06
	T	219.1±59.1	242.8±66.3	208.6±46.0	220.0±7.3	T×G = 0.95
	F	208.2±43.2	229.4±54.4	205.4±42.9	218.7±9.0	T×D=0.001
	MC	245.0±52.6	276.8±58.4$^{\wedge}$	219.8±41.9$^{\wedge}$	242.6±8.9^{Đ}	T×G×D = 0.79
	LC	189.3±37.8	204.4 ±41.4$^{\wedge a}$	197.0±44.2^{a}	196.1±7.4	
	Time	214.4±52.6	237.1±61.2*	207.2±44.3$^{\tau}$		
HDL (mg/dL)	T-MC	56.7±17.4	68.7±18.2	56.8±15.3	60.7±4.2	T = 0.00
	T-LC	50.3±18.0	57.8±14.6	56.4±13.7	54.8±4.6	G = 0.40
	F-MC	62.2±22.7	71.0±24.0	60.2±22.7	64.5±6.3	D = 0.27
	F-LC	51.4±14.7	64.0±19.7	62.8±20.6	59.4±4.3	G×D = 0.94
	T	53.8±17.6	63.8±17.3	56.6±14.4	57.8±3.1	T×G = 0.88
	F	54.8±17.8	66.2±20.8	61.9±20.8	61.9±3.8	T×D = 0.01
	MC	58.4±18.8	69.4±19.6$^{\wedge}$	57.8±17.4$^{\wedge}$	62.6±3.8	T×G×D = 0.42
	LC	50.9±16.0	61.1 ±17.5$^{\wedge a}$	59.8±17.7$^{\wedge}$	57.1±3.2	
	Time	54.3±17.6	64.8±18.7*	58.9±17.5*		
LDL (mg/dL)	T-MC	162.2±42.7	184.1±46.4^{c}	146.5±38.0	164.2±7.9$^{\Upsilon}$	T = 0.00
	T-LC	99.5±24.4	113.0±25.2	109.6±31.1	107.4±8.7	G = 0.73
	F-MC	133.2±31.5	155.7±49.2^{c}	124.6±44.6	137.9±11.9$^{\Upsilon}$	D = 0.00
	F-LC	122.6±30.1	133.2±31.5	126.4±33.0	127.4±8.1	G×D = 0.02
	T	134.1±47.3	152.2±52.2	129.9±39.2	135.8±5.9	T×G = 0.98
	F	126.0±30.2	140.4±38.3	125.8±36.0	132.6±7.2	T×D = 0.01
	MC	153.4±41.2	175.4±48.0$^{\wedge}$	139.8±40.4$^{\wedge}$	151.1±7.1^{Đ}	T×G×D = 0.72
	LC	111.9±29.5	123.8 ±30.1$^{\wedge a}$	118.6±32.7^{a}	117.4±6.0	
	Time	130.6±40.7	147.1±46.6*	128.2±37.5		
Triglycerides (mg/dL)	T-MC	179.2±86.9	188.6±81.5	147.6±54.4	171.8±13.3	T = 0.001
	T-LC	102.6±32.1	97.9±35.5	119.3±60.0	106.6±14.7	G = 0.69
	F-MC	183.2±80.9	221.0±115.3	133.4±60.5	179.3±20.1	D = 0.00
	F-LC	129.5±45.4	104.6±36.6	100.9±33.0	111.7±13.7	G×D = 0.94
	T	144.9±77.4	147.9±78.8	134.9±57.7	139.2±9.9	T×G = 0.05
	F	146.6±62.4	141.7±88.2	111.2±44.8$^{\wedge f}$	145.4±12.1	T×D = 0.00
	MC	180.4±83.3	198.4±91.6$^{\wedge}$	143.3±55.3^	175.5 ±12.0^{Đ}	T×G×D = 0.31
	LC	117.0±41.4	101.5 ±35.6$^{\wedge a}$	109.4±47.4^{a}	109.1±10.1	
	Time	145.6±70.6	145.2±82.2	124.7±53.4*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, τ trend in time effect from baseline $p > 0.05$ and $p < 0.1$ (univariate), Đ signifciant diet effect $p < 0.05$, ϒ significant genotype x diet interaction $p < 0.05$ (Tukey LSD), δ trend in genotype x diet interaction $p > 0.05$ and $p < 0.1$ (Tukey LSD), ^ significant difference compared to baseline (Tukey LSD). Letter superscripts indicate significance ($p < 0.05$) from Tukey LSD post hoc analyses: [a]significant difference from MC, [b]significant difference from T-MC, [c]significant difference from T-LC, [d]significant difference from F-MC, [e]significant difference from F-LC, [f]significant difference from T.

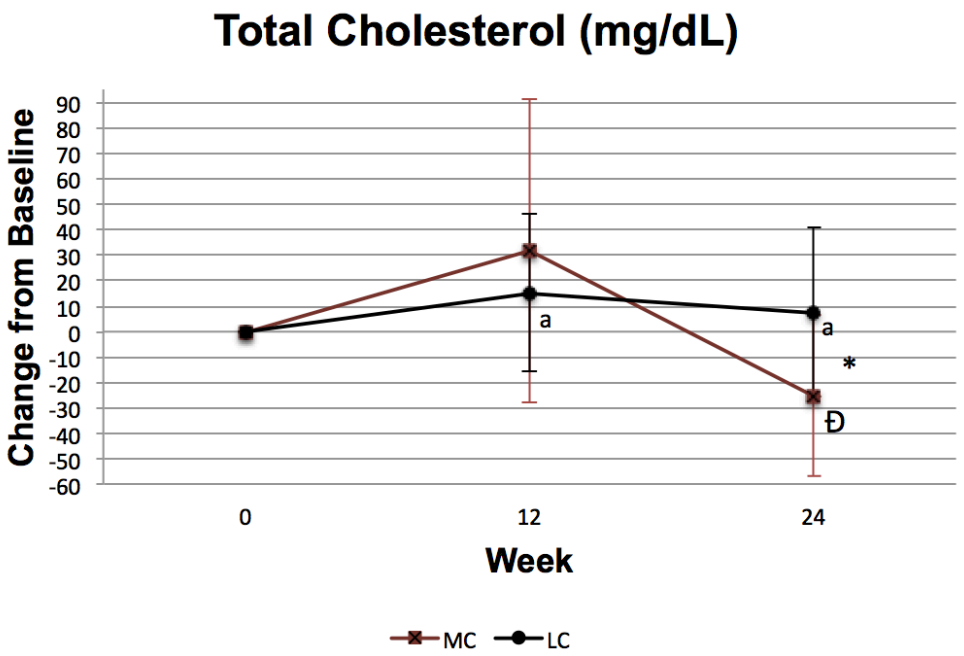

Figure 36: Delta change in total cholesterol observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$), Ð diet effect ($p < 0.05$), [a]significant difference from MC ($p < 0.05$, Tukey LSD post hoc).

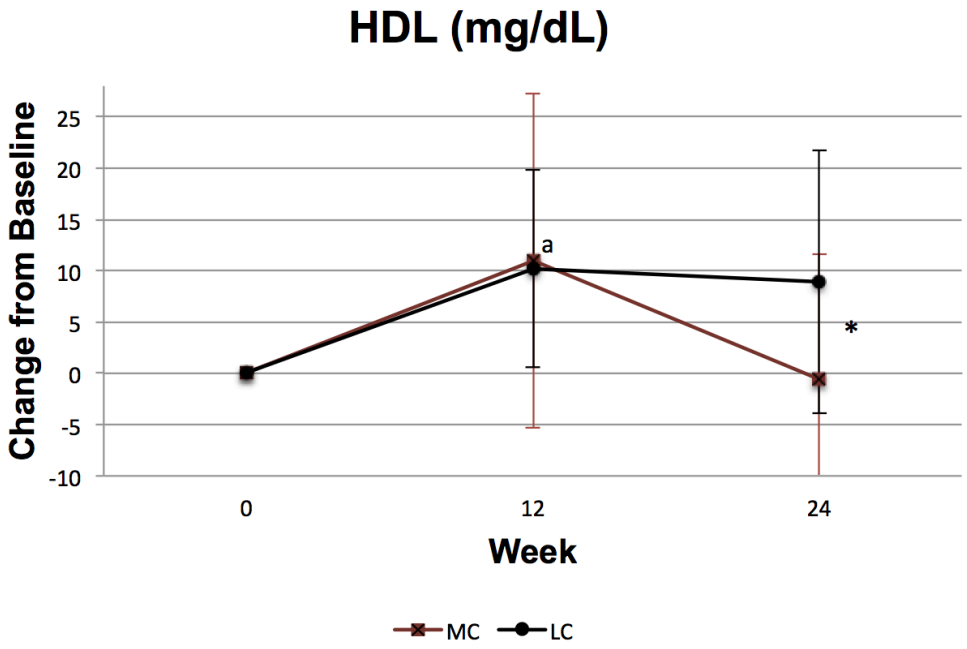

Figure 37: Delta change in HDL observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28, * time effect ($p < 0.05$), [a]significant difference from MC ($p < 0.05$, Tukey LSD post hoc).

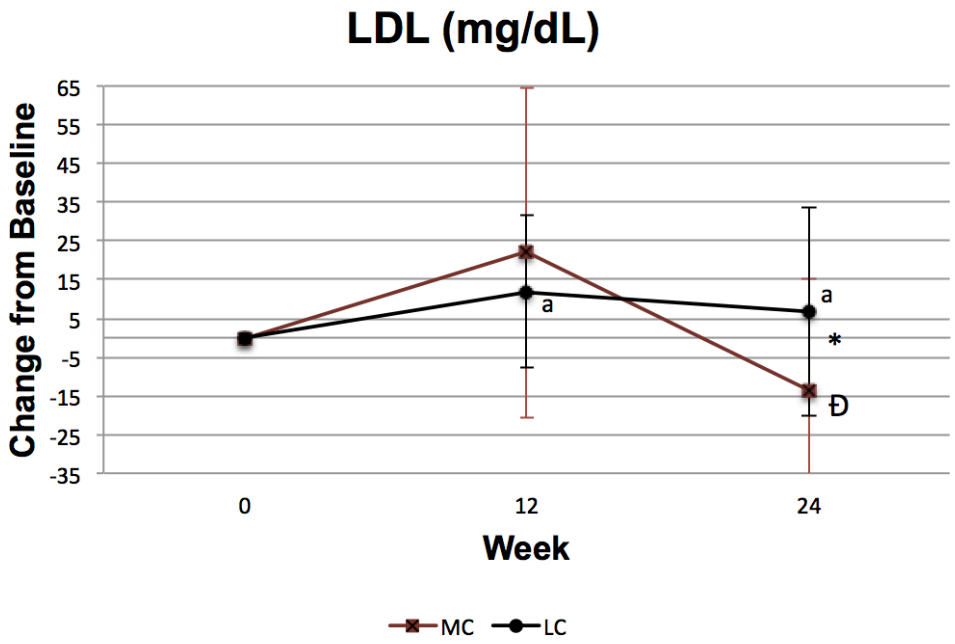

Figure 38: Delta change in LDL observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28* time effect ($p < 0.05$), Đ diet effect ($p < 0.05$), [a]significant difference from MC (Tukey LSD post hoc).

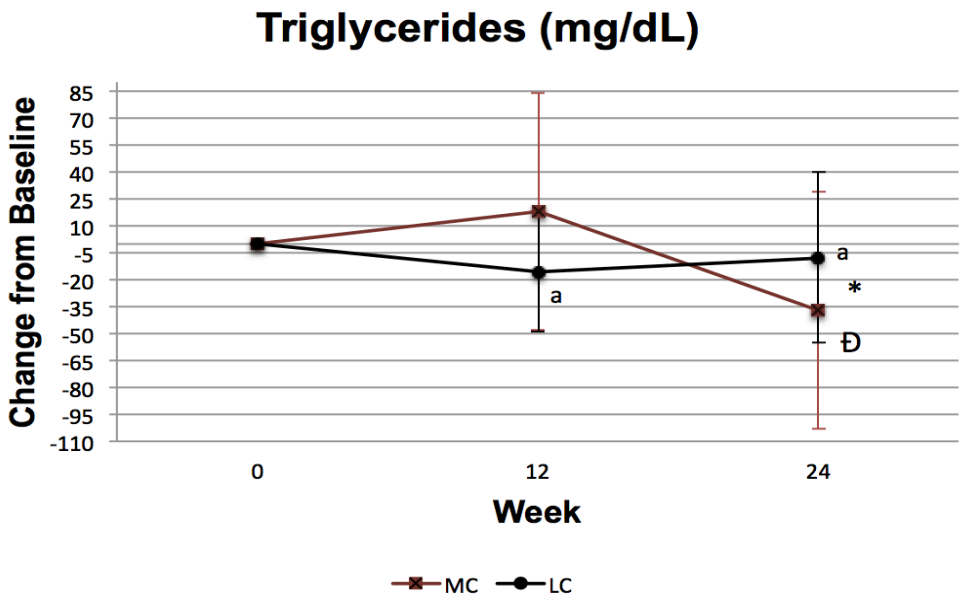

Figure 39: Delta change in triglycerides observed between diet groups. Values presented as mean ± SD, n = 51, MC: n = 23, LC: n = 28* time effect ($p < 0.05$), Đ diet effect ($p < 0.05$), [a]significant difference from MC ($p < 0.05$, Tukey LSD post hoc).

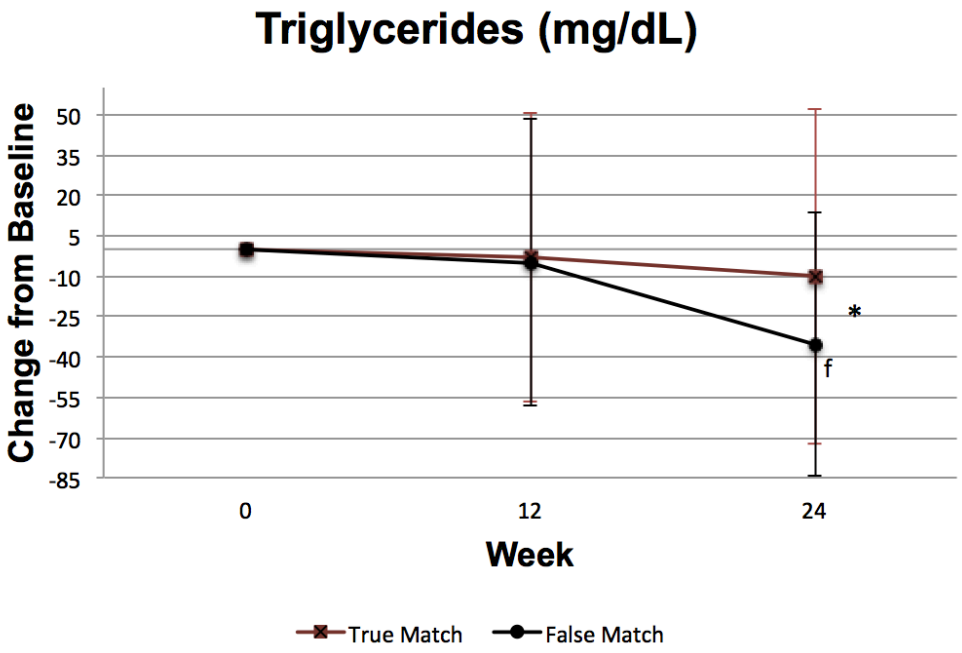

Figure 40: Delta change in triglycerides observed between genotype. Values presented as mean ± SD, n = 51, T: n = 29, LC: n = 22, * time effect ($p < 0.05$), [f]significant difference from T ($p < 0.05$, Tukey LSD post hoc).

Markers Related to Insulin Resistance

Multivariate analyses did not reveal any significant effects for time (p=0.31), time x genotype (p=0.26), time x diet (p=0.60), time x genotype x diet (p=0.18). Univariate analyses revealed a trend in time with a moderate effect between time and fasting insulin, such that all participants experienced a clinically insignificant increase in fasting insulin levels from baseline to completion (+1.1±5.2 μIU/mL, p=0.08, η^2_p=0.062, d=0.77). No other time effects or interactions were observed among variables.

A significant genotype effect was observed for insulin such that false matches presented with larger fasting insulin values at all time points in relation to true matches (p=0.04). However, true matches experienced a slight, yet clinically insignificant,

increase in change of fasting insulin from baseline to completion (T +1.9±5.3, F +0.2±5.1 μIU/mL). Additionally, a significant genotype effect was observed for glucose/insulin ratio, where false matches experienced an increase in glucose/insulin ratio from baseline to completion while true matches experienced the opposite (F+0.4±4.1, T-1.5±3.8, p=0.03). Similarly, a trend in genotype with a large effect was observed for HOMA-IR where false matches experienced a reduction in HOMA-IR and true matches experienced an increase (F-0.06±1.3, T0.5±1.2, p=0.06, η^2_p=0.075, d=0.92). Finally a diet effect was observed, such that LC presented with greater fasting blood glucose at baseline and completion in comparison to MC (p=0.001). There were no other genotype effects, diet effects, or genotype x diet interactions observed. Table 22 represents glucose, insulin, glucose/insulin ratio, and HOMA-IR in each group from baseline to completion. Since statistically significant interactions favoring true matches were not observed for markers related to insulin resistance, we accept H_{o10}.

Table 22: Markers related to insulin resistance observed between groups

Variable	Group	Baseline	24 Weeks	Group (SEM)	P-value
Glucose (mg/dL)	T-MC	85.0±7.3	90.0±9.3	87.0±1.6	T = 0.57
	T-LC	95.6±8.2	95.0±9.8	92.2±1.8	G = 0.54
	F-MC	86.4±6.6	85.5±8.6	87.0±2.5	D = 0.001
	F-LC	93.9±10.6	94.3±11.3	91.9±1.7	G×D = 0.93
	T	89.7±9.3	92.2±9.7	91.3±1.4	T×G = 0.48
	F	91.5±10.0	91.5±11.1	90.0±1.7	T×D = 0.54
	MC	85.4±7.0	88.6±9.1	87.0±1.5	T×G×D = 0.31
	LC	94.7±9.4	94.6±10.4	92.1±1.2^{Đ}	
	Time	90.5±9.6	91.9±10.2		
Insulin (µIU/mL)	T-MC	11.2±7.5	12.2±5.7	11.7±1.6	T = 0.08
	T-LC	12.0±5.0	15.0 ±7.2	13.5±1.8	G = 0.04
	F-MC	17.0±8.5	19.2 ±5.5	18.1±2.5	D = 0.80
	F-LC	15.8±8.1	15.0 ±7.6	15.4±1.7	G×D = 0.25
	T	11.6±6.4	13.5±6.4	12.6±1.2	T×G = 0.40
	F	16.2±8.0	16.3±7.2	16.7±1.5^{Γ}	T×D = 0.75
	MC	13.0±8.1	14.3±6.4	14.9±1.5	T×G×D = 0.11
	LC	14.0±7.0	15.0±7.3	14.4±1.2	
	Time	13.5±7.4	14.7±6.8^{τ}		
Glucose/Insulin Ratio	T-MC	10.5±5.2	9.2±4.9	9.9±0.9	T = 0.15
	T-LC	9.4±3.9	7.5±3.0	8.5±1.0	G = 0.03
	F-MC	6.5±3.8	4.9±1.9	5.7±1.4	D = 0.78
	F-LC	7.1±2.6	8.4±5.3	7.7±1.0	G×D = 0.13
	T	10.0±4.6	8.5±4.2	9.2±0.7	T×G = 0.24
	F	6.9±2.9	7.3±4.7	6.7±0.9^{Γ}	T×D = 0.30
	MC	9.3±5.1	7.9±4.7	7.8±0.8	T×G×D = 0.12
	LC	7.5±3.0	8.0±4.3	8.1±0.7	
	Time	8.5±4.2	8.0±4.4		
HOMA-IR	T-MC	2.3±1.5	2.7±1.2	2.5±0.4	T = 0.12
	T-LC	2.8±1.2	3.6±1.9	3.2±0.4	G = 0.06
	F-MC	3.6±1.7	4.0±1.0	3.8±0.6	D = 0.55
	F-LC	3.8±2.1	3.5±1.7	3.6±0.4	G×D = 0.32
	T	2.6±1.4	3.1±1.6	2.9±0.3	T×G = 0.22
	F	3.7±2.0	3.6±1.5	3.7±0.3^{γ}	T×D = 0.72
	MC	2.7±1.6	3.1±1.3	3.1±0.3	T×G×D = 0.16
	LC	3.3±1.8	3.5±1.8	3.4±0.3	
	Time	3.1±1.6	3.3±1.6		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. Γ significant genotype effect $p < 0.05$, τ trend in time from baseline $p > 0.05$ and $p < 0.1$, γ trend in genotype effect $p > 0.05$ and $p < 0.1$

Psychosocial Evaluation

Self-Esteem and Social Physical Anxiety

Regarding self-esteem as measured by the Rosenberg self-esteem scale, multivariate analyses revealed a significant time effect for self esteem scores ($p=0.001$) with no significant interaction for time x genotype ($p=0.82$), time x diet ($p=0.91$), or time x genotype x diet ($p=0.19$). Univariate analyses revealed a significant time effect such that all participants reported increased self-esteem from baseline to completion ($+1.8\pm3.0$; $p=0.00$). No significant time interactions were observed. Moreover a trend in diet with moderate effect was observed such that individuals in LC reported higher self-esteem scores at all time points. A change in reported self-esteem score increased greater in LC versus MC from baseline to completion (MC: $+1.6\pm3.5$, LC: $+2.0\pm2.6$; $p=0.10$, $\eta^2_p=0.056$, $d=0.79$). No significant genotype effect or genotype x diet interaction was observed.

Furthermore, for anxiety as measured by the social physical anxiety scale, multivariate analyses revealed a significant time effect for social physical anxiety scores ($p=0.00$) along with a significant time x genotype x diet interaction ($p=0.03$), and no significant interaction for time x genotype ($p=0.66$), and time x diet ($p=0.89$). Univariate analyses also revealed a significant time effect, such that from baseline to completion all participants exhibited reduced ratings of social anxiety regarding physique (-3.1 ± 5.6; $p=0.00$). A significant time x genotype x diet interaction was observed with a significant cubic relationship ($p=0.03$, $p_c=0.00$) such that anxiety scores fluctuated between diets and genotypes throughout the duration of the study; however overall F-MC experienced

the greatest reduction in social anxiety (-4.3±5.8), followed by T-LC (-3.6±5.5), T-MC (-2.7±6.0), F-LC (-2.4±5.6). There were no other time effects, time interactions, genotype or diet effect, or genotype x diet interaction observed. Table 23 represents self-esteem and social physical anxiety score in each group throughout the study.

Eating Satisfaction Survey

Among the six domains within the eating satisfaction survey, appetite, hunger, satisfaction from food, feeling of fullness, amount of energy, and overall quality of diet, multivariate analyses revealed significant Wilks' Lambda time effect (p=0.00) and time x diet interaction (p=0.05), with no significant time x genotype (p=0.23) or time x genotype x diet interaction (p=0.77). Univariate analyses revealed significant time effects for appetite, hunger, amount of energy, and overall diet quality. The time effect for appetite demonstrated a significant quadratic relationship revealing a significant decline in appetite for all participants from baseline to 3-months followed by a steady increase from 3-6- months, but still an overall decline in appetite upon completion (baseline-3-months: -0.5±1.4, baseline-6-months: -0.1±1.3; p=0.01, p_q=0.00). The time effect for hunger exhibited a significant cubic relationship (p=0.03, p_c=0.01) such that hunger rating fluctuated throughout the course of the study, with a trend towards significance from baseline after one month of intervention and a significant difference from baseline after two months for all participants. Further, energy demonstrated a significant linear relationship such that all participants reported increased energy levels throughout the duration of the study (baseline to 6-months: +1.6±1.8; p=0.00). Finally,

Table 23: Self-esteem and social physical anxiety scores observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Self-esteem Score	T-MC	30.0±4.3	30.3±4.4	28.8±4.4	31.2±4.0	31.3±3.9	31.8±4.2	31.7±3.6	30.7±0.9	T=0.001
	T-LC	31.2±4.7	31.7±4.9	29.8±5.6	31.3±5.0	32.5±4.1	31.9±4.9	33.3±4.3	31.7±1.1	G=0.27
	F-MC	30.4±3.3	30.6±4.2	31.1±3.2	30.7±5.0	32.0±4.3	30.9±3.2	31.7±4.3	31.1±1.4	D=0.10
	F-LC	33.2±4.5	32.8±5.4	32.1±5.0	34.8±3.9	34.5±4.5	34.3±4.6	35.0±3.6	33.8±1.0	G×D=0.43
	T	30.5±4.4	30.9±4.6	29.2±4.9	31.2±4.4	31.8±4.0	31.9±4.0	32.4±4.0	31.2±0.7	T×G=0.62
	F	32.3±4.3	32.1±.0	31.8±4.5	33.5±4.6	33.7±4.5	33.2±4.4	34.0±4.1	32.4±0.9	T×D=0.84
	MC	30.1±4.0	30.3±4.2	29.5±4.2	31.0±4.2	31.5±4.0	31.5±3.9	31.7±3.7	30.9±0.9	T×G×D=0.44
	LC	32.3±4.6	32.3±5.1	31.0±5.3	33.2±4.7	33.6±4.4	33.2±4.8	34.3±4.0	32.7±0.7[đ]	
	Time	31.3±4.4	31.4±4.8	30.3±4.9	32.2±4.6[τ]	32.6±4.3[*]	32.5±4.5[τ]	33.1±4.0[*]		
Anxiety Score	T-MC	40.1±7.7	38.9±6.5[^]	38.8±5.7[^]	36.9±7.5[^]	35.9±7.7[^]	36.6±7.7[^]	37.4±7.8[^]	30.7±0.9	T=0.00
	T-LC	42.5±7.7	39.6±7.4[^]	39.1±8.0[^]	40.7 ±9.7[^b]	41.0 ±9.2[^b]	38.3 ±7.3[^b]	38.8 ±8.3[^b]	31.7±1.1	G=0.45
	F-MC	41.7±8.5	37.0 ±9.6[^bc]	36.9 ±10.6[^bc]	37.9 ±9.6[^c]	40.7±12.1[b]	37.1 ±10.6[^b]	37.4 ±10.3[^c]	31.1±1.4	D=0.99
	F-LC	37.7±7.5	37.1±6.2[bc]	36.4±7.3[bc]	35.2 ±6.9[^bcd]	36.4 ±7.4[^bcd]	34.7 ±7.2[^bcd]	35.3 ±6.9[^bcd]	33.8±1.0	G×D=0.30
	T	30.5±4.4	30.9±4.6	29.2±4.9	31.2±4.4	31.8±4.0	31.9±4.0	32.4±4.0	31.2±0.7	T×G=0.58
	F	32.3±4.3	32.1±5.0	31.8±4.5	33.5±4.6	33.7±4.5	33.2±4.4	34.0±4.1	32.4±0.9	T×D=0.90
	MC	40.6±7.8	38.3±7.4	38.2±7.3	37.2±8.0	37.4±9.2	36.7±8.5	37.4±8.4	30.9±0.9	T×G×D=0.03
	LC	39.9±7.8	38.3±6.8	37.6±7.6	37.8±8.6	38.5±8.4	36.4±7.3	36.9±7.6	32.7±0.7	
	Time	31.3±4.4	31.4±4.8[*]	30.3±4.9[*]	32.2±4.6[*]	32.7±4.3[*]	32.5±4.5[*]	33.1±4.0[*]		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, τ trend in time effect from baseline $p > 0.05$ and $p < 0.1$ (univariate), đ trend in diet effect $p > 0.05$ and $p < 0.1$, ^ significant difference compared to baseline (Tukey LSD). Letter superscripts indicate significance ($p < 0.05$) from Tukey LSD post hoc analyses: [b]significant difference from T-MC, [c]significant difference from T-LC, [d]significant difference from F-MC, [e]significant difference from F-LC.

overall diet quality exhibited a significant linear relationship such that all participants reported an increase in diet quality from baseline to six months (+1.7±2.1; p=0.00).

Along with observed time effects, a trend for time x genotype with a moderate effect was observed for feeling of fullness and demonstrated a significant quadratic relationship. False matches experienced a greater decline in feeling of fullness from baseline to 3-months (T -0.03±1.7, F -0.6±0.6), and smaller increase in ratings from 3-6 months (T +0.10±1.4, F +0.09±1.4). Overall false matches experienced a decline in feeling of fullness from baseline to completion while ratings for true matches was relatively unchanged upon completion in comparison to baseline levels (T +0.07±1.8, F -0.5±1.9; p_q=0.04, p=0.09, η^2_p=0.039, d=0.67). Additionally a trend in time x diet with moderate effect for feeling of fullness was observed that exhibited a significant cubic relationship indicating fluctuation over time in fullness ratings within diet groups; however, overall from baseline to completion, MC exhibited an increase in fullness (MC +0.61±1.8, LC -0.86±1.6; p_c=0.02, p=0.08, η^2_p=0.041, d=0.68).

Further, a significant time x diet interaction was also observed for overall quality of diet with a significant quadratic relationship. MC demonstrated a greater increase in diet quality from baseline to 3-month (MC +2.7±1.8, LC +0.9±2.2) with a slight decline in quality ratings from 3-6 months, while LC quality ratings increased from 3-6 months (MC -0.30±1.3, LC +0.25±1.7; p=0.03, p_q=0.01). Along with this, no diet or genotype effects were observed, nor was a significant genotype x diet interaction evident. Table 24 represents eating satisfaction ratings among the six domains in each group throughout the study.

Table 24: Eating satisfaction observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Appetite	T-MC	6.5±1.2	5.4±1.1	5.4±1.3	5.5±1.1	6.1±1.1	6.1±1.7	6.3±1.5	5.9±0.2	T=0.01
	T-LC	6.3±1.2	5.5±1.5	5.1±1.3	6.1±1.9	5.5±2.0	6.1±2.1	6.4±1.4	5.8±0.3	G=0.12
	F-MC	5.9±1.2	6.1±0.9	5.6±1.5	5.3±1.0	6.0±1.3	5.6±1.4	5.6±1.5	5.7±0.4	D=0.28
	F-LC	5.5±1.1	5.1±1.3	4.5±1.4	5.2±0.9	5.3±1.4	5.1±1.4	5.4±1.2	5.2±0.2	G×D=0.38
	T	6.4±1.2	5.5±1.3	5.2±1.2	5.8±1.5	5.8±1.6	6.1±1.8	6.3±1.4	5.9±0.2	T×G=0.28
	F	5.6±1.1	5.4±1.3	4.9±1.5	5.2±0.9	5.6±1.4	5.3±1.4	5.5±1.3	5.4±0.2	T×D=0.39
	MC	6.3±1.2	5.7±1.1	5.4±1.3	5.4±1.0	6.1±1.1	5.9±1.6	6.1±1.5	5.8±0.2	T×G×D=0.86
	LC	5.9±1.2	5.3±1.4	4.8±1.3	5.6±1.5	5.4±1.7	5.6±1.8	5.9±1.4	5.5±0.2	
	Time	6.1±1.2	5.5±1.3*	5.1±1.4*	5.5±1.3*	5.7±1.5	5.7±1.7	6.0±1.4		
Hunger	T-MC	5.7±1.6	5.1±1.7	5.3±1.6	5.1±1.8	5.9±1.3	6.0±1.8	6.1±1.9	5.6±0.3	T=0.03
	T-LC	5.1±1.8	4.8±1.7	4.2±1.6	5.5±2.0	5.1±2.1	5.5±1.9	5.4±1.6	5.1±0.3	G=0.49
	F-MC	5.4±1.1	5.1±1.1	5.4±1.7	5.4±1.5	5.4±1.3	5.3±1.0	5.1±1.9	5.3±0.4	D=0.16
	F-LC	5.3±1.0	4.9±1.0	4.1±1.6	4.6±1.3	4.9±1.3	5.1±1.5	5.0±1.1	4.8±0.3	G×D=0.97
	T	5.4±1.7	4.9±1.6	4.8±1.7	5.2±1.8	5.5±1.7	5.8±1.8	5.8±1.8	5.3±0.2	T×G=0.59
	F	5.3±1.0	5.0±1.0	4.6±1.7	5.5±1.7	5.1±1.3	5.1±1.4	5.1±1.3	5.1±0.3	T×D=0.40
	MC	5.6±1.4	5.1±1.5	5.4±1.6	5.2±1.7	5.7±1.3	5.8±1.6	5.8±1.9	5.5±0.3	T×G×D=0.51
	LC	5.2±1.4	4.8±1.3	4.2±1.6	5.0±1.7	5.0±1.7	5.3±1.7	5.2±1.3	5.0±0.2	
	Time	5.4±1.4	4.9±1.4τ	4.7±1.7*	5.1±1.7	5.3±1.5	5.5±1.6	5.5±1.6		
Satisfaction from Food	T-MC	5.6±1.9	6.4±1.1	6.6±1.0	5.9±1.5	6.4±1.3	6.5±0.8	6.4±1.3	6.3±0.3	T=0.17
	T-LC	6.1±1.4	7.0±1.2	6.8±1.1	6.5±1.8	6.5±1.9	6.1±2.2	6.2±2.2	6.4±0.3	G=0.60
	F-MC	5.7±1.0	7.0±1.6	6.3±1.0	6.4±1.5	6.1±1.7	6.1±1.2	7.0±0.6	6.4±0.4	D=0.73
	F-LC	6.5±1.0	5.8±1.5	5.6±1.1	6.1±1.2	5.8±1.2	6.0±1.2	6.3±1.1	6.0±0.3	G×D=0.37
	T	5.8±1.6	6.7±1.2	6.7±1.0	6.1±1.7	6.4±1.6	6.3±1.6	6.3±1.7	6.4±0.2	T×G=0.16
	F	6.3±1.0	6.2±1.6	5.8±1.1	6.2±1.3	5.9±1.3	6.1±1.2	6.5±1.0	6.2±0.2	T×D=0.20
	MC	5.7±1.6	6.6±1.3	6.5±1.0	6.1±1.5	6.3±1.4	6.4±0.9	6.6±1.1	6.3±0.2	T×G×D=0.23
	LC	6.3±1.2	6.4±1.5	6.1±1.2	6.3±1.5	6.1±1.6	6.0±1.7	6.3±1.6	6.2±0.2	
	Time	6.0±1.4	6.5±1.4	6.3±1.1	6.2±1.5	6.2±1.5	6.2±1.4	6.4±1.4		
Feeling of fullness	T-MC	5.9±1.8	6.3±1.2	6.4±1.2	6.3±1.5	6.3±1.1	6.2±1.6	6.6±1.5	6.3±0.2	T=0.50
	T-LC	6.9±1.3	7.1±1.0	6.6±0.9	6.4±1.3	7.0±1.4	6.2±2.0	6.2±1.6	6.6±0.3	G=0.58
	F-MC	6.7±1.4	7.3±1.4	6.1±1.1	6.4±1.3	6.0±1.8	6.9±1.6	7.0±1.5	6.6±0.4	D=0.60
	F-LC	7.5±1.5	6.2±1.3	6.5±1.2	6.7±1.3	6.2±1.2	6.6±1.4	6.5±1.4	6.6±0.3	G×D=0.50
	T	6.3±1.7	6.6±1.2^	6.5±1.1	6.3±1.4^	6.6±1.2^	6.2±1.7	6.4±1.5	6.5±0.2	T×G=0.09
	F	7.2±1.4	6.6±1.4^	6.4±1.1^	6.6±1.3^f	6.1±1.4^f	6.7±1.4^f	6.7±1.4^f	6.6±0.2	T×D=0.08
	MC	6.1±1.7	6.6±1.3^	6.4±1.2^	6.3±1.4	6.2±1.3	6.4±1.6^	6.7±1.5	6.5±0.2	T×G×D=0.27
	LC	7.2±1.4	6.6±1.2^	6.5±1.0^	6.5±1.3^	6.6±1.3^f	6.4±1.6^	6.4±1.5	6.6±0.2	
	Time	6.7±1.6	6.6±1.3	6.5±1.1	6.4±1.3	6.4±1.3	6.4±1.6	6.5±1.5		
Amount of Energy	T-MC	4.9±1.6	6.6±1.5	6.6±1.7	6.3±1.8	6.5±1.4	6.4±1.8	6.8±1.6	6.3±0.3	T=0.00
	T-LC	5.0±1.9	6.9±1.1	6.5±1.2	6.6±1.3	7.2±0.8	5.9±1.5	6.6±2.0	6.4±0.3	G=0.89
	F-MC	5.4±1.1	6.9±1.7	6.6±1.6	6.1±1.8	6.6±1.8	6.3±0.8	7.3±1.8	6.4±0.4	D=0.94
	F-LC	5.3±1.2	6.7±1.3	6.9±1.3	6.6±0.9	6.3±1.0	6.3±1.3	6.4±1.0	6.3±0.3	G×D=0.78
	T	5.0±1.7	6.8±1.3	6.6±1.5	6.5±1.5	6.8±1.2	6.2±1.6	6.7±1.7	6.3±0.2	T×G=0.70
	F	5.3±1.2	6.7±1.4	6.8±1.4	6.5±1.2	6.4±1.3	6.3±1.1	6.7±1.3	6.4±0.2	T×D=0.47
	MC	5.1±1.5	6.7±1.5	6.6±1.6	6.3±1.7	6.5±1.5	6.4±1.5	7.0±1.7	6.4±0.2	T×G×D=0.58
	LC	5.1±1.5	6.8±1.2	6.7±1.2	6.6±1.1	6.7±1.0	6.1±1.4	6.5±1.5	6.4±0.2	
	Time	5.1±1.5	6.8±1.3*	6.7±1.4*	6.5±1.4*	6.6±1.2*	6.2±1.4*	6.7±1.6*		
Overall Quality of Diet	T-MC	4.0±1.9	6.3±1.5	6.2±1.5	6.6±0.8	6.8±1.2	6.2±1.2	6.5±1.2	6.1±0.2	T=0.00
	T-LC	4.7±1.9	6.7±1.3	5.4±2.0	5.2±1.6	6.5±1.2	5.9±1.9	5.9±1.6	5.8±0.2	G=0.87
	F-MC	3.9±1.1	7.0±1.2	6.6±1.0	6.7±1.0	6.3±1.4	6.3±0.8	5.9±1.6	6.1±0.3	D=0.25
	F-LC	4.8±1.1	6.3±1.2	5.9±1.4	6.1±1.5	6.1±1.0	5.9±1.6	5.9±1.5	5.8±0.2	G×D=0.87
	T	4.3±1.9	6.5±1.4	5.8±1.8	5.9±1.4	6.7±1.2	6.1±1.6	6.2±1.4	5.9±0.2	T×G=0.42
	F	4.5±1.1	6.5±1.2	6.1±1.3	6.3±1.4	6.2±1.1	6.0±1.3	5.9±1.5	6.0±0.2	T×D=0.03
	MC	4.0±1.7	6.5±1.4^	6.3±1.3^	6.6±0.8^	6.7±1.3^	6.2±1.1^	6.3±1.3^	6.1±0.2	T×G×D=0.64
	LC	4.8±1.5	6.5±1.2^	5.6±1.7^a	5.6±1.6^a	6.3±1.1^a	5.9±1.7^	5.9±1.5^a	5.8±0.2	
	Time	4.4±1.6	6.5±1.3*	5.9±1.6*	6.1±1.4*	6.5±1.2*	6.0±1.5*	6.1±1.4*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$, τ trend in time effect from baseline $p > 0.05$ and $p < 0.1$ (univariate), ^ significant difference compared to baseline (Tukey LSD). Letter superscripts indicate significance ($p < 0.05$) from Tukey LSD post hoc analyses: [a]significant difference from MC, [f]significant difference from T.

Body Image

The five domains within the body image questionnaire include appearance evaluation, appearance orientation, body area satisfaction, overweight preoccupation, and self-classification of weight. Multivariate analyses revealed significant Wilks' Lambda effect of time ($p=0.00$) with no significant interaction for time x genotype ($p=0.32$), time x diet ($p=0.59$), or time x genotype x diet ($p=0.58$). Univariate analyses revealed a significant time effect for appearance evaluation and body area satisfaction such that all participants reported an increase in rating of appearance and satisfaction with most areas of the body from baseline to completion of the study (appearance: $+0.5\pm0.6$; $p=0.01$; body area satisfaction: $+0.36\pm0.45$; $p=0.00$). In addition a significant time effect was observed for overweight preoccupation suggesting that from baseline to completion, all participants exhibited an increase in rating for fat anxiety, weight vigilance, dieting, and eating restraint ($+0.4\pm0.7$; $p=0.00$). Further a significant time effect and time x genotype interaction was observed for self-classification of weight. The time effect demonstrated a reduction in rating of overweight perception from baseline to completion for all participants (-0.4 ± 0.7; $p=0.00$). The time x genotype interaction demonstrated a greater reduction in rating of overweight perception from baseline to completion in favor of the false matches (F -0.5 ± 0.7, T -0.2 ± 0.7; $p=0.04$). There were no other time effects, time interactions, genotype effect, diet effects, or genotype x diet interactions observed. Table 25 represents body image ratings among the five domains within the questionnaires. Overall, since no statistically significant interactions favoring true matches were observed for the psychosocial evaluation, we accept H_{o11}.

Table 25: Body image observed between groups

Variable	Group	Baseline	4 Weeks	8 Weeks	12 Weeks	16 Weeks	20 Weeks	24 Weeks	Group (SEM)	P-value
Appearance Evaluation	T-MC	2.3±0.7	2.7±0.5	2.7±0.7	2.7±0.7	2.9 ±0.8	2.9±0.7	2.9±0.7	2.7±0.2	T=0.00
	T-LC	2.5±0.6	2.6±0.6	2.7±0.6	2.6±0.6	2.8±0.9	2.7±0.9	2.8±0.8	2.7±0.2	G=0.68
	F-MC	2.4±0.5	2.8±0.8	2.8±0.9	2.8±1.0	2.8±0.9	2.9±0.7	3.1±0.5	2.8±0.3	D=0.86
	F-LC	2.5±0.9	2.6±0.8	2.7±0.8	2.8±0.8	2.9±0.7	2.9±0.8	2.8±0.7	2.8±0.2	G×D=0.98
	T	2.4 ±0.7	2.6 ±0.5	2.6±0.7	2.7±0.7	2.8±0.8	2.8±0.8	2.9±0.7	2.7±0.1	T×G=0.97
	F	2.5 ±0.8	2.7 ±0.8	2.7±0.8	2.8±0.8	2.9±0.8	2.9±0.7	2.9±0.6	2.8±0.2	T×D=0.28
	MC	2.3±0.7	2.7±0.6	2.7±0.8	2.7±0.8	2.9±0.8	2.9±0.7	3.0±0.6	2.8±0.2	T×G×D=0.59
	LC	2.5±0.7	2.6±0.7	2.7±0.7	2.7±0.7	2.8±0.8	2.8±0.8	2.8±0.7	2.7±0.1	
	Time	2.4±0.7	2.7±0.6*	2.7±0.7*	2.7±0.7*	2.8±0.8*	2.9±0.8*	2.9±0.7*		
Appearance Orientation	T-MC	3.4±0.6	3.4±0.4	3.5±0.5	3.4±0.5	3.4±0.5	3.4±0.5	3.4±0.4	3.4±0.1	T=0.62
	T-LC	3.4±0.5	3.2±0.7	3.2±0.7	3.2±0.6	3.3±0.8	3.2±0.7	3.3±0.6	3.3±0.1	G=0.98
	F-MC	3.3±0.4	3.3±0.4	3.3±0.5	3.3±0.6	3.2±0.5	3.3±0.3	3.1±0.3	3.2±0.2	D=0.92
	F-LC	3.4±0.7	3.4±0.5	3.4±0.6	3.4±0.6	3.4±0.6	3.4±0.6	3.3±0.7	3.4±0.1	G×D=0.34
	T	3.4±0.5	3.3±0.5	3.3±0.6	3.3±0.5	3.3±0.6	3.3±0.6	3.3±0.5	3.3±0.1	T×G=0.78
	F	3.4±0.6	3.3±0.4	3.4±0.6	3.4±0.6	3.3±0.6	3.4±0.5	3.3±0.6	3.3±0.1	T×D=0.67
	MC	3.3±0.5	3.3±0.4	3.4±0.5	3.3±0.5	3.3±0.5	3.4±0.5	3.3±0.4	3.3±0.1	T×G×D=0.56
	LC	3.4±0.6	3.3±0.6	3.3±0.6	3.3±0.6	3.4±0.7	3.3±0.6	3.3±0.7	3.3±0.1	
	Time	3.4±0.6	3.3±0.5	3.3±0.6	3.3±0.5	3.3±0.6	3.3±0.5	3.3±0.6		
Body Area Satisfaction	T-MC	2.6±0.5	2.9±0.4	2.8±0.5	3.0±0.5	3.0±0.6	3.0±0.5	3.0±0.6	2.9±0.1	T=0.00
	T-LC	2.5±0.5	2.6±0.6	2.7±0.5	2.8±0.5	2.8±0.7	2.8±0.7	2.8±0.8	2.7±0.1	G=0.56
	F-MC	2.7±0.5	3.0±0.4	2.9±0.4	2.9±0.5	2.9±0.5	3.0±0.5	3.1±0.3	2.9±0.2	D=0.41
	F-LC	2.6±0.5	2.8±0.6	2.9±0.6	2.8±0.6	2.9±0.6	3.1±0.6	3.0±0.6	2.9±0.1	G×D=0.73
	T	2.6±0.5	2.8±0.5	2.8±0.5	2.9±0.5	2.9±0.6	2.9±0.6	2.9±0.7	2.8±0.1	T×G=0.30
	F	2.6±0.5	2.9±0.6	2.9±0.5	2.9±0.6	2.9±0.6	3.1±0.6	3.0±0.5	2.9±0.1	T×D=0.81
	MC	2.6±0.5	2.9±0.4	2.9±0.5	3.0±0.5	3.0±0.6	3.0±0.5	3.0±0.5	2.9±0.1	T×G×D=0.60
	LC	2.6±0.5	2.8±0.6	2.8±0.5	2.8±0.6	2.9±0.7	2.9±0.7	2.9±0.7	2.8±0.1	
	Time	2.6±0.5	2.8±0.5*	2.8±0.5*	2.9±0.5*	2.9±0.6*	3.0±0.6*	3.0±0.6*		
Overweight Preoccupation	T-MC	2.8±0.6	3.3±0.5	3.4±0.5	3.4±0.4	3.4±0.5	3.3±0.6	3.3±0.5	3.3±0.1	T=0.00
	T-LC	3.0±1.0	3.7±0.7	3.6±0.7	3.3±0.8	3.3±0.8	3.4±0.8	3.3±0.8	3.4±0.2	G=0.21
	F-MC	2.7±0.4	3.0±0.6	3.0±0.4	3.2±0.4	3.1±0.4	3.0±0.4	3.1±0.4	3.0±0.2	D=0.37
	F-LC	2.8±0.8	3.3±0.6	3.3±0.6	3.4±0.6	3.3±0.6	3.2±0.7	3.2±0.8	3.2±0.1	G×D=0.75
	T	2.9±0.8	3.5±0.6	3.4±0.6	3.4±0.6	3.3±0.6	3.3±0.7	3.3±0.6	3.3±0.1	T×G=0.49
	F	2.8±0.7	3.2±0.6	3.2±0.6	3.3±0.5	3.2±0.6	3.1±0.6	3.1±0.7	3.1±0.1	T×D=0.37
	MC	2.8±0.6	3.2±0.5	3.3±0.5	3.3±0.4	3.3±0.5	3.2±0.5	3.2±0.5	3.1±0.1	T×G×D=0.51
	LC	2.9±0.9	3.5±0.7	3.4±0.7	3.3±0.7	3.3±0.7	3.3±0.7	3.2±0.8	3.3±0.1	
	Time	2.8±0.7*	3.4±0.6*	3.3±0.6*	3.3±0.6*	3.3±0.6*	3.2±0.6*	3.2±0.7*		
Self Classification of Weight	T-MC	4.25±0.9	4.0±0.9	4.1±0.7	3.9±0.9	4.0±0.7	3.9±0.9	3.9±0.7	4.0±0.2	T=0.00
	T-LC	4.23±1.0	4.3±0.9	4.1±1.0	4.2±0.7	4.2±0.6	4.2±0.6	4.1±0.9	4.2±0.2	G=0.36
	F-MC	4.6±0.6	4.6±0.6	4.4±0.6	4.5±0.7	3.8±1.2	4.3±0.7	3.8±1.2	4.3±0.2	D=0.59
	F-LC	4.6±0.4	4.4±0.5	4.3±0.5	4.3±0.5	4.1±0.5	4.1±0.5	4.2±0.6	4.3±0.2	G×D=0.66
	T	4.2±0.9	4.2±0.9	4.1±0.8^	4.0±0.8^	4.1±0.7^	4.0±0.8^	4.0±0.8^	4.1±0.1	T×G=0.04
	F	4.6±0.5	4.5±0.6^f	4.4±0.5^f	4.4±0.6^f	4.0±0.8^f	4.2±0.6^f	4.1±0.8^f	4.3±0.1	T×D=0.38
	MC	4.3±0.8	4.2±0.9	4.2±0.7	4.1±0.9	4.0±0.9	4.0±0.9	3.9±0.9	4.1±0.1	T×G×D=0.11
	LC	4.4±0.8	4.4±0.7	4.2±0.8	4.3±0.6	4.2±0.5	4.1±0.6	4.2±0.7	4.2±0.1	
	Time	4.4±0.8	4.3±0.8τ	4.2±0.7	4.2±0.7*	4.1±0.7*	4.1±0.7*	4.0±0.8*		

Data presented as Mean±SD. Significance level $p < 0.05$. Mean (n = 51), T = true match (n = 29), F = false match (n = 22), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T-MC (n = 16), T-LC (n = 13), F-MC (n = 7), F-LC (n = 15). T = time effect, G = genotype match to diet effect, D = diet effect, G×D = genotype match to diet x diet effect, T×G = time x genotype match to diet effect, T×D = time x diet effect, T×G×D = time x diet x genotype match to diet effect. *significant time effect from baseline $p < 0.05$. τ trend in time effect from baseline $p > 0.05$ and $p < 0.1$ (univariate), ^ significant difference compared to baseline (Tukey LSD), [f]significant difference from T $p < 0.05$ (Tukey LSD post hoc).

Summary of Significance and Trends

A multitude of significance and trends have been demonstrated within this investigation regarding genotype effects, diet effects, time x genotype interactions, time x diet interaction, and time x genotype x diet interactions. Tables 26 and 27 provide a comprehensive overview of relevant findings related to psychosocial health and physical health.

Table 26: Significant findings and trends related to psychosocial health

Variable	Effect or Interaction	P-value	Effect Size (cohens d)	Interpretation
Self-Esteem	Diet	0.10	0.79	Moderate effect Favor LC
Eating Satisfaction-Feeling of Fullness	Time x Diet	0.08	0.68	Moderate effect Favor MC
	Time x Genotype	0.09	0.67	Moderate effect Favor true match
Eating Satisfaction-Diet Quality	Time x Diet	0.03*	0.78	Moderate effect Favor MC
Social Physical Anxiety	Time x Genotype x Diet	0.03*	1.9	Large effect FMC, TLC,TMC, FLC[#]
Body Image-Weight Classification	Time x Genotype	0.04*	0.77	Moderate effect Favor false match

Mean (n = 51), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T = True match (n = 29), F = False match (n = 22), TMC (n = 16), TLC (n = 13), FMC (n = 7), FLC (n = 15), *indicates statistical significance, $p < 0.05$, # time x genotype x diet interaction interpretation includes genotype and diet combination listed from most favorable to least favorable health outcome.

Table 27: Significant findings and trends related to physical health

Variable	Effect or Interaction	P-value	Effect Size (cohens d)	Interpretation
Body Weight	Genotype	0.10	0.78	Moderate effect Favor false match
Fat Free Mass	Genotype	0.09	0.83	Large effect Favor false match
Android- Total Mass	Genotype	0.05*	0.94	Large effect Favor false match
	Time x Genotype x Diet	0.09	0.73	Moderate effect FLC, TMC, TLC, FMC#
Android- Fat Free Mass	Genotype	0.04*	0.98	Large effect Favor true match
	Time x Genotype x Diet	0.08	0.71	Moderate effect FMC, TLC, TMC, FLC#
Android- Fat Mass	Genotype	0.07	0.89	Large effect Favor false match
Gynoid- Total Mass	Time x Genotype x Diet	0.04*	0.93	Large effect FLC, TMC, TLC, FMC#
	Genotype	0.09	0.83	Large effect Favor true match
Gynoid- Fat Free Mass	Genotype	0.09	0.82	Large effect Favor false match
Hip Circumference	Genotype	0.07	0.88	Large effect Favor true match
Absolute EE	Genotype	0.03*	1.03	Large effect Favor false match
Absolute VO_2	Time x Genotype x Diet	0.08	0.82	Large effect FMC, TLC, TMC, FLC#
Relative VO_2	Time x Genotype x Diet	0.07	0.84	Large effect FMC, TLC, TMC, FLC#
Lower Body Strength	Diet	0.04*	1.01	Large effect Favor MC
	Time x Diet	0.04*	1.01	Large effect Favor MC
Total Cholesterol	Diet	0.00*	1.89	Large effect Favor MC
	Time x Diet	0.001*	1.45	Large effect Favor MC
	Genotype x Diet	0.06	0.94	Large effect TMC, FMC, FLC, TLC#
HDL	Time x Diet	0.01*	1.11	Large effect Favor LC
LDL	Diet	0.001*	1.70	Large effect Favor MC
	Time x Diet	0.01*	1.14	Large effect Favor MC
	Genotype x Diet	0.02*	1.20	Large effect TMC, FMC, FLC, TLC#
Triglycerides	Diet	0.00*	1.99	Large effect Favor MC
	Time x Diet	0.00*	1.57	Large effect Favor MC
	Time x Genotype	0.05*	0.84	Large effect Favor false match
Glucose	Diet	0.01*	1.24	Large effect Favor LC
Insulin	Genotype	0.04*	1.02	Large effect Favor false match
Glucose/Insulin Ratio	Genotype	0.03*	1.04	Large effect Favor false match
HOMA-IR	Genotype	0.06	0.92	Large effect Favor false match

Mean (n = 51), MC = moderate CHO (n = 23), LC = low CHO (n = 28), T = True match (n = 29), F = False match (n = 22), TMC (n = 16), TLC (n = 13), FMC (n = 7), FLC (n = 15), *indicates statistical significance, $p < 0.05$, # time x genotype x diet interaction interpretation includes genotype and diet combination listed from most favorable to least favorable health outcome.

CHAPTER V

SUMMARY AND CONCLUSIONS

Summary

The concept of genetic profiling within the arena of weight management is in its infancy. Of the few studies that have applied genetic profiling to weight loss[7-9], available results from Dopler-Nelson and colleagues[9] study demonstrated a 2-3 fold greater reduction in BW in true matches versus false matches ($p=0.02$), along with greater reductions in waist circumference ($p=0.01$) and triglycerides ($p=0.007$), and an increase in HDL ($p=0.01$). These clear-cut findings with the simple genetic profile used warranted further investigation. Since their study was retrospective, we aimed to use the same genetic profile in a prospective study. Therefore, the purpose of our 6-month weight loss intervention was to determine if prospectively matching individuals to a dietary intervention that aligned with their genotype (true match) would demonstrate greater improvements in health outcomes in comparison to individuals matched to a diet that did not align with their genotype (false match).

While Dopler-Nelson and colleagues[9] used commercialized diet programs, we used the Curves International diet and exercise program as previous research from our lab has demonstrated advantageous health outcomes with this program in comparison to other commercialized weight management programs.[26,112-116] Additionally, based on our review of the weight loss interventions that have assessed each candidate gene within the tested genetic profile, evidence suggests inclusion of an exercise component within

weight loss interventions utilizing these candidate genes for profiling.[117] Thus, we tested the Curves Complete diet, which was a moderate CHO, adequate fat, moderate protein diet (30% kcal CHO, 25% kcal fat, 45% kcal protein; MC), in comparison to a lower CHO, adequate fat, moderate protein diet (20% kcal CHO, 35% kcal fat, 45% kcal protein; LC). All participants engaged in the Curves Exercise program, a circuit-style resistance-training program completed four days per week, and were encouraged to complete 10,000 steps per day three days per week to increase lifestyle activity. We hypothesized that true matches would experience greater improvements in measured health variables upon completion of the study in comparison to false matches. Overall we found the opposite of our hypothesized outcomes.

Compliance to Diet, Exercise, and Lifestyle Activity Prescription

Among all participants, significant time effects were observed for total energy intake (-520±498 kcal/d, p=0.00) supporting adherence to the caloric restriction. Total CHO intake was reduced in both diet groups and conformed to the classifications of a moderate CHO diet and low CHO diet. Fat intake was also reduced and complied with the classification of a diet adequate in fat. While fat intake in MC was higher than the prescription, intake was still lower than the prescription for LC and actual intake of fat in LC. Individuals in LC met their dietary prescription for fat. Protein intake increased in both groups and while lower than the 45% prescription, intake was still high enough for the diet to be considered moderate in protein.

Additionally, exercise compliance among all participants was acceptable, averaging 86±11% completion of the prescribed workouts. Reported vigorous MET

minutes also increased over time for all participants (+618±1198 min/wk, p=0.00). Lifestyle activity increased for all participants as evidenced by the time effect for reported leisure-time MET minutes (+854±1399 min/wk; p=0.002). Taken together, these findings support the notion of compliance among participants within the diet and exercise prescription, and encouraged increase in lifestyle activity.

Anthropometrics, Body Composition, Resting Energy Expenditure

Upon completion of the 6-month intervention, all participants experienced weight loss success, -5.3±5.0 kg BW. The amount of weight loss observed in the present investigation aligns with previous research conducted in our lab testing a similar diet and exercise regimen (-3.1±3.7[26], -6.1±3.2[115], -5.1±4.2[116] kg BW). True matches lost 5.0±5.0 kg BW and false matches lost 5.6±5.0 kg BW. These findings contrast the reductions observed in Dopler-Nelson and colleagues[9] investigation, where at six-months true matches lost approximately 6-7 kg BW and false matches lost about 2-3 kg BW. Additionally, while all participants in the present investigation experienced a reduction in waist circumference from baseline to completion (-5.2±5.7 cm), significant differences or trends in genotype were not observed, which contrasts Dopler-Nelson and colleagues[9] findings of a significant difference for change in waist circumference favoring true matches.

The discrepancy in results between studies may be attributed to the degree of CHO and fat restriction within the prescribed diets per genotype. In Dopler-Nelson and colleagues[9] study CHO and fat prescription per genotype was restricted to a much greater degree than restriction in the present study. For example, true matches to low

CHO diet may have followed the Atkins diet (20 g CHO/d x 2-3 months then ≤ 50 g CHO/d) whereas true matches to low fat may have followed the Ornish diet (≤ 10% kcal fat/d). In the present investigation, true matches to low CHO were assigned to LC (20% kcal CHO/d or 60 g CHO/d x 1 week then 75 g CHO/d x 2-24 weeks) while true matches to low fat were assigned to MC (25% kcal fat or 39 g fat/d x 1 week then 42 g fat/d x 2-24 weeks).

Additionally, the present investigation included a supervised, structured exercise program, whereas participation in unsupervised daily physical activity was encouraged in Dopler-Nelson and colleagues[9] study. Further, the exercise program in the present investigation included circuit-style resistance training exercises, whereas the encouraged exercise in Dopler-Nelson and colleagues[9] investigation may have been exclusively aerobic, resistance, or a combination of both pending on the diet group participants were matched to (i.e. LEARN, Ornish, Atkins, Zone). Therefore, the inclusion of a structured exercise program consisting of circuit-style resistance training may contribute to findings favoring false matches in the present investigation.

Along with anthropometric measurements, we also assessed changes in body composition, fat deposition, and visceral adipose tissue (VAT). This is the first investigation to date to assess changes in these variables with the tested genetic profile. The observed significant differences and trends with moderate-large effect sizes favoring false matches have great implications towards disease prevention. While all participants experienced a significant quadratic effect for fat free mass (0-3-months: -0.9±1.8 kg, 3-6-months: +0.2±1.7 kg, p_q=0.01), upon completion of the study a trend in genotype with

a large effect was observed favoring false matches such that false matches retained on average 0.4 more kg fat free mass (F -0.4±2.3, T -0.8±2.3 kg). Additionally, a trend in genotype with a large effect was observed for gynoid fat free mass where false matches gained gynoid fat free mass upon completion (+3.0±665 grams) and true matches lost mass (-199±534 grams). Coordinately, although false matches lost more body weight, the better retention in fat free mass may likely contribute to the significant genotype effect for resting energy expenditure, where false matches experienced a 20 kcal/d increase in absolute resting energy expenditure upon completion in comparison to true matches (F +74.0±239, T +54.8±256.2 kcal/d). These findings are note-worthy as we know improvements in fat free mass are linked with reducing risk of disease and mortality.[118,119]

Additionally, we measured android fat deposition and visceral adiposity as markers of abdominal obesity. It is known that abdominal obesity, particularly excessive accumulation of visceral adipose tissue, increases ones risk of chronic disease and all-cause mortality.[120,121] Our findings demonstrate favorable changes in android fat deposition and visceral fat for false matches. While all participants experienced a reduction in android total mass (-747±863grams), a significant genotype effect was observed such that false matches lost an average of about 179.4 more grams of android total mass upon completion (F -849.1±882.8, T -669.7±855.4 grams). Further while all participants reduced android fat mass (-532±528 grams), a trend in genotype with large effect favored false matches, as they also lost on average 168 grams more of android fat mass in comparison to true matches (F -627±583, T -459±480 grams). Additionally,

while not statistically significant, a moderate effect was observed for VAT mass, area, and volume for time x genotype interaction where false matches experienced greater reductions from baseline to completion in VAT mass (T -152.6±233.7, F -160.4±255.6 g; p=0.20, η^2_p=0.032, d=0.6) area (-31.6±48.5, F -33.3±52.9 cm^2; p=0.20, η^2_p =0.031, d=0.59) and volume (T -164.6±252.7, F -173.6±276 cm^3; p=0.22, η^2_p=0.030, d=0.58). These findings suggest potential for use of this profile in coordination with the tested diet and exercise program for reducing abdominal obesity and chronic disease risk.

While the present investigation overwhelmingly favors the false match matches genotype in relation to the tested diets for body composition variables, these results contrast recently reported 3-month preliminary findings.[122] Among the preliminary findings, while no significant difference in BW change was observed (T -4.33±3.6, F -3.91±3.9 kg, p=0.36), significant differences for reduction in fat mass (T -3.81±2.5, F -1.92±3.2 kg, p=0.01) and body fat percentage (T -2.15±2.3, F 0.01±2.1 %, p=0.002), and better retention of fat free mass (T -0.76±1.8, F -2.16±2.3 kg, p=0.042) was observed in favor of true matches. Therefore, evidence from the preliminary findings and present investigation suggest a genetic impact on markers of body composition related to health and disease risk; however, it is clear that more research is needed to identify the combination of genes and allelic variants to best predict diet and exercise prescription within a weight management program for optimization of health acutely (i.e. < 3-months) and more long-term (> 3-months).

Furthermore, as with any weight management program, the behavioral aspect must be considered. In contrast to the present investigation, data from preliminary

findings were collected during the spring and summer months. It has been demonstrated through previous research that time of year, specifically fall and winter months and the holiday season, play a significant role in reduction of physical activity, increase in energy intake, and alteration in body composition (i.e. increase fat mass and body fat percentage).[123-126] Data from the present investigation was collected from April 2014-May 2015 with rolling admission into the weight loss program. Thus, differences between the present investigation and preliminary findings may be associated with holiday interference and differences in time of year in relation to study course among participants secondary to rolling admission.

Fitness

While all participants experienced a significant increase in absolute and relative peak aerobic capacity from baseline to completion (absolute VO_2 +0.2±0.2 L/min, p=0.00; relative VO_2 +3.7±3.2 ml/kg/min), a trend in time x genotype x diet interaction with a large effect was observed for absolute and relative VO_2 peak favoring false matches in MC. These findings support the notion of greater outcomes observed in false matches, as false match MC demonstrated the greatest improvements in cardiorespiratory fitness.

In addition a significant diet effect and time x diet interaction was observed for lower body strength in favor of MC. From these results we can conclude that MC is most beneficial in terms of improving strength. These findings are consistent with previous research conducted in our lab comparing the macronutrient distribution used in MC to other diets in relation to impact on markers of fitness.[26,112,113]

Biochemical Markers

All participants experienced reductions in total cholesterol (-7.2±36.0 mg/dL), LDL (-2.5±29.3 mg/dL), and triglycerides (-20.9±57.9 mg/dL), and an increase in HDL cholesterol (+4.6±13.3 mg/dL) from baseline to completion. We observed significant diet effects and time x diet interactions favoring MC for total cholesterol (MC -25.2±31.3, LC +7.7±33.1 mg/dL), LDL (MC -13.6±28.6, LC +6.7±26.9 mg/dL), and triglycerides (MC -37.1±65.7, LC -7.6 ± 47.7 mg/dL). These findings are consistent with a previous investigation in our lab comparing similar macronutrient distribution to other diets.[114] Furthermore a significant time x diet interaction was observed for HDL favoring LC (LC +8.9±12.8, MC -0.6±12.2 mg/dL). These findings are expected considering LC total cholesterol increased steadily overtime; thus we would expect the observed increases in HDL and LDL.

We did not observe any genotype effects for total cholesterol and LDL, which is consistent with Dopler-Nelson and colleagues[9] findings; however, we did observe a trend in genotype x diet interaction with a large effect for total cholesterol, and a significant genotype x diet interaction for LDL, where true MC was favored (cholesterol: T-MC -26.0±32.1, F-MC -23.5±32.0, F-LC +7.0±31.8, T-LC +8.5±35.8 mg/dL; LDL: T-MC -15.8±26.7, F-MC -8.6±34.2, F-LC +3.7±28.1, T-LC +10.1±26.3 mg/dL). Furthermore a significant time x genotype interaction for triglycerides favoring false matches upon completion was observed (F -35.5±49.1 mg/dL, T -9.9±62.3), which contrasts Dopler-Nelson and colleagues[9] results. For HDL cholesterol, there was no significant genotype effect or trend observed, which contrasts Dopler-Nelson and

colleagues[9] results, as they observed a significant increase in HDL for true matches. Difference between studies regarding blood lipids is likely related to differences in dietary composition as previously discussed.

Regarding markers related to insulin resistance, a significant diet effect was observed favoring LC, such that LC experienced a reduction in fasting blood glucose upon completion (LC -0.02±13.0, MC +3.2±9.2 mg/dL, p=0.01). Although blood glucose levels increased slightly in MC upon completion, levels remained within normal limits. Further, this observed change might be attributed to dietary habits of participants prior to the testing session, such as length of fast between testing sessions (8 hours versus 12 hours), size and dietary components of last meal.

In addition, a significant genotype effect was observed for fasting insulin and glucose/insulin ratio, along with a trend towards significance with a large effect in HOMA-IR favoring false matches. While fasting insulin levels were greater in false matches at each time point in comparison to true matches (T: baseline 11.6±6.4, 6-months 13.5±6.4, F: baseline 16.2±8.0, 6-months 16.3±7.2 μIU/L), levels remained relatively stable throughout the course of the study as opposed to increasing slightly as observed in true matches. These findings are congruent with blood glucose results for true and false matches over time (T: baseline 89.7±9.3, 6-months 92.2±9.7, F: baseline 91.5±10.0, 6-months 91.5±11.1 mg/dL). Coordinately false matches experienced an increase in glucose/insulin ratio upon completion (F +0.4±4.1, T-1.5±3.8, p=0.03) and reduction in HOMA-IR (F-0.06±1.3, T0.5±1.2, p=0.06, η^2_p=0.075, d=0.92). Overall

these findings suggest improvements in glucose metabolism favoring false matches over true.

Psychosocial Evaluation

We found the MC diet to promote the most favorable results with regards to satiation and diet quality, whereas LC exhibited improved results with self-esteem levels. A significant time x diet interaction was observed for diet quality favoring MC upon completion, with an average rating of diet quality greater than one unit in MC compared to LC (MC +2.3±2.0, LC +1.14±2.0). Along with this a time x diet trend with moderate effect was observed for reported feeling of fullness, where overall participants in MC reported greater satiation upon completion from baseline (MC +0.61±1.8, LC -0.86±1.6). Interestingly, a trend in diet with a moderate effect was observed for self-esteem score, where individuals in LC reported greater rating of self-esteem at all time points including overall from baseline to completion (LC +2.0±2.6, MC +1.6±3.5).

Regarding genotype, a significant time x genotype interaction was observed for self-classified weight (i.e. perception of over or underweight independent of actual weight status) with regards to body image such that false matches exhibited the greatest reduction in self-classification of overweight in comparison to true matches (F -0.5±0.7, T -0.2±0.7). Related to findings favoring MC and false matches, a significant time x genotype x diet interaction was observed for social physical anxiety such that false match MC exhibited the greatest reductions in social physical anxiety over time in comparison to other genotype x diet combinations.

Conclusions

Overall, results showed that both diet interventions in coordination with the structured exercise program elicited improvements in anthropometrics, body composition, resting energy expenditure, fitness, blood lipid profile, and some psychosocial variables. Additionally, false matches experienced favorable results among the majority of variables in comparison to true matches. Thus, findings suggest MC prescription for individuals with the low CHO genotype per the tested genetic profile.

Considering the relatively small sample size of the present investigation, significant differences and trends containing moderate to large effect sizes in response to genotype, and observed health benefits facilitating disease prevention, more research is warranted testing this genetic profile. Moreover, since only some of the candidate genes in the tested profile are considered functional single nucleotide polymorphisms with clinical significance (ADRB3rs4994, ADRB2 rs1042713 and rs 1042714), more research is necessary to identify the ideal combination of genes and allelic variants to best predict diet and exercise prescription within a weight management program.

Furthermore, the pre-investigation power analysis suggested a goal sample size of 80 participants. This analysis was based on previous research from our laboratory assessing changes in fat mass between diet groups, and change in body weight between genotype in the Dopler-Nelson investigation[9]. Post-hoc power analyses regarding the moderate and large effect sizes related to body composition and fat deposition in the present investigation suggest a sample size ranging from 400-800 participants in order to detect statistically significant differences between genotype for body composition and

fat deposition variables. These findings further support the necessity of conducting the present investigation with a larger sample size. Overall, future investigations should take the following points into consideration: larger sample size, degree of CHO and fat restriction within the tested diets, incorporation of a structured exercise program, time of year data is collected, and uniform admission into the study.

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APPENDIX A

NUTRIGENETIC STUDIES[117]

Study	Candidate Genes	Design	Methods	Results

Mutch et al. 2007[7]	TMEM132A
	QPRT
	CLDN5
	PTGDS
	ESAM
	FMOD
	FAM69B
	IF127
		• 10 weeks
		• 53 participants from NUGENOB study
		• Males & females
		• Retrospective genotype matching based on weight loss
		  ○ responder: 8-12 kg wt loss
		  ○ non-responder: < 4 kg wt loss
			• Randomly assigned to hypocaloric diet (~600 kcal deficit):
			  ○ low fat, high CHO diet: 20-25% kcal fat, 60-65% kcal CHO, 15% kcal protein
			  ○ high fat, low CHO diet: 40-45% kcal fat, 40-45% kcal CHO, 15% kcal protein
			• 3-day weighed food log at 0 & 10 wks
			• One day weighed food log at 2,5,7 wks
			• Weekly contact with RD
			• No exercise component
				• Candidate genes significantly increased in non-responders –vs-responders
				• Responders to weight loss had less expression of candidate genes
				• No difference between weight loss outcomes and diet intervention

Dopler-Nelson et al. 2010[9]	FABP2 (rs1799883)
	PPARG (rs1801282)
	ADRB3 (rs4994C3)
	ADRB2 (rs1042713 & rs1042714R)
		• 12 months
		• 141 participants from AtoZ weight loss trial
		• Retrospective genotype matching
		  ○ true or false match to diet group based on genotype
			• Randomly assigned to diet group:
			  ○ Atkins (≤ 20 g/d CHO for 2-3 mo, then ≤50 g/d CHO
			  ○ Zone (40% kcal CHO, 30% kcal fat, 30% kcal protein)
			  ○ LEARN (55-60% kcal CHO, < 10% kcal sat fat)
			  ○ Ornish (≤10% kcal fat)
			• Weekly meeting RD x 2 mo, then random follow-up between 2-12 mo
			• Random 3-day food recalls via NDSR
			• BW, body composition, WC, HC, BP, fasting insulin and BG, blood lipid profile measured at 0,2,6,12 mo
			• Exercise was encouraged
				• BW reduction, true match versus false match (p=0.005)
				• 5.3% loss in BW in true, 2.3% loss in BW in false match (p<0.05)
				• True matches to lowest CHO (Atkins) and fat (Ornish) diets had greatest weight loss, 6.8% total weight loss in true versus 1.4% total weight loss in false (p=0.03)
				• More favorable changes in lipids in true matches.

Arkadianos et al.	ACE INS/DEL	• 12 month, blinded, RCT	• Control group followed	• 5.6% reduction

2007[8]	APOC3 3175C>G
	CBS 699C>T
	CETP 279G>A
	COLIA1 GSpIT
	GSTMI
	GSTP1 313A>G, 341C>T
	GSTT1
	IL61595C>G
	MTRR 66A>G
	MTHFR 1298A>C, 677C>T
	MTR 275A>G
	NOS3 894G>T
	PPARG Pro12Ala
	SOD2 -28C>T
	SOD3 760C>G
	TNFalpha -308G>A
	VDR CTaqIT, TBsmIC, TFokIC
		• 50 participants in nutrigenetic group
		  ○ 22 female, 28 male
		• 43 participants in control group
		  ○ 18 female, 25 male
		• Prospective genotype matching to diet
		  ○ specific alterations in dietary Rx based on variations in candidate genes
		• Physicians blinded to treatment groups
			low-glycemic index, Mediterranean style diet
			  ○ 38% kcal CHO, 46% kcal fat, 16% kcal protein
			• Nutrigenetic group followed same diet with alterations pending genotype
			• Regular clinical visits for all pts
			• BW measured and fasting blood sample collected at baseline and completion
			• Home exercise routines provided
				in BMI (1.93 kg/m^2) in nutrigenetic group versus 2.2% gain (0.51 kg/m^2) in control group ($p < 0.023$)
				• 57% of pts in nutrigenetic group with pre-diabetes had reduced BG versus 25% in control group ($p < 0.046$)

CHO = carbohydrate, RD = registered dietitian, RCT = randomized controlled trial, wks = weeks, mo = months, pts = patients, Rx = prescription, BG = blood glucose				

APPENDIX B

WEIGHT LOSS INTERVENTIONS[117]

Study	Design	Dietary & Exercise Intervention	Methods	Results
FABP2 (rs1799883)				
de Luis et al. 2008[14]	• 2 months • 204 obese, AH adults ○ 50 males & 154 females • Randomized into diet groups	• Low fat diet: 1500 kcal/d, 52% kcal CHO, 27% kcal fat, 20% kcal protein • Low CHO diet: 1507 kcal/d, 38% kcal CHO, 36% kcal fat, 26% kcal protein • Aerobic exercise encouraged (walking), 60 min x 3x/wk	• Measures at 0, 2 mo: REE, WC, HC, BW, BP, BG, fasting insulin, CRP, blood lipid profile, adipocytokines • Dietary data collected at 0 & 8 wks via 3-day food records	• All participants: weight loss and fat mass loss at 2 mo ($p < 0.05$) • Mutant-type: reduced fat mass with lower CHO diet ($p < 0.05$) • Wild-type: reduced cholesterol, TG, insulin, and leptin for both diets ($p < 0.05$)
Martinez-Lopez et al 2013[13]	• 2 months • 109 overweight and obese, AH adults • 20 male, 89 female	• 1000 kcal/d for women, 1200 kcal/d for men • 55% kcal CHO, 30% kcal fat, 15% kcal protein • Lipid breakdown: < 7% kcal sat fat, 10-15% PUFA, 10% PUFA, < 200 mg/d dietary cholesterol, 2 g/d from plant stanols/sterols	• Measures at 0, 1, 2 mo: BW, BF%, WC, HC, RMR, BP, BG, insulin, blood lipid profile, CRP • Dietary data collected at 0, 1, 2 mo via 24-	• All participants: reduction in BW. BMI BF%, WC, WHR, SBP, BG, insulin, and blood lipids at 2 mo ($p < 0.05$) • Mutant-type: greater reductions in BW, BMI, WC, WHR, and CRP ($p < 0.05$)

		• 25 g/d fiber • No exercise intervention	hr dietary recall	
de Luis et al. 2006[15]	• 3 months • 69 obese, AH adults	• 1520 kcal/d, 52% kcal CHO, 25% kcal fat, 23% kcal protein • Aerobic exercise encouraged, 60 min at least 3x/wk	• Measures at 0, 3 mo: REE, WC, HC, BW, BP, BG, fasting insulin, CRP, blood lipid profile, adipocytokines, oxygen consumption • Dietary data collected at 0, 3 mo via 3-day food records	• All participants: decrease in BMI, BW, WC, and increase in oxygen consumption at 3 mo ($p < 0.05$) • Mutant-type: reduction in BG at 3 mo ($p < 0.05$) • Wild-type: reduction in FM, LDL, and leptin at 3 mo ($p < 0.05$)

de Luis et al 2012[16]	• 3 months
	• 111 obese, AH adults
		• 1459 kcal/d, 45.7% kcal CHO, 34.4% kcal fat, 19.9% kcal protein
		• Lipid breakdown: 21.8% sat fat, 55.5% MUFA, 22.7% PUFA (7 g/d n-6 FA, 2 g/d n-3 FA)
		• Walking only for 2-3 hr/wk
			• Measures at 0, 3 mo: BW, FFM, FM, BP, BG, HbA1c, insulin, blood lipids, adipocytokines
			• Dietary data collected at 0, 3 mo via 3-day food records
			• Weekly dietary monitoring by RD via phone
				• All participants: reduction in BMI, BW, FFM, WC, SBP ($p < 0.05$)
				• Mutant-type:
				  ○ reduction in BMI, BW, FFM, FM, WC at 3 mo ($p < 0.05$)
				  ○ reduction in in total cholesterol, LDL, insulin, & HOMA at 3 mo($p < 0.05$)

			call	
de Luis et al 2013[17]	• 3 months • 122 obese, AH adults	• 1342 kcal/d, 46.6% kcal CHO, 34.1% kcal lipids, 19.2% kcal protein • Lipid breakdown: 21.7% sat fat, 67.5% MUFA, 10.8% PUFA • Walking only for 2-3 hr/wk	• Measures at 0, 3 mo: BW, FFM & FM via BIA, WC, HC, BP, BG, insulin, blood lipids, CRP, adipocytokines • Dietary data collected at 0, 3 mo via 3-day food records	• All participants: reduction in BMI, BW, WC at 3 mo ($p < 0.05$) • Wild-type: reduction in FM, insulin, and leptin at 3 mo ($p < 0.05$)
PPARG (rs1801282)				
Curti et al 2013[21]	• 9 months • 134 adults with pre-diabetes or metabolic syndrome	• Medication Group: 850 mg metformin 2x/d, lifestyle intervention • Lifestyle Group: o 16-session curriculum covering diet, exercise, and behavior modification. o Individual meetings weekly x 8 mo, then monthly thereafter. o Low-fat,	• Measures at 0, 9 mo: BW, BMI, WC, BP, CRP, BG, insulin, blood lipids • Dietary data collected at 0, 9 mo via 24-hr dietary recall • Physical activity measured at 0, 9 mo via IPAQ	• All participants: reduced BW ($p < 0.001$), WC ($p=0.01$), BG ($p=0.041$), insulin ($p < 0.001$), apolipoprotein B ($p < 0.001$), and increased HDL ($p < 0.001$) at 9 mo • Mutant-type: reduced BP at 9 mo ($p < 0.001$)

		hypocaloric diet ○ 150 min/wk of physical activity. • Dietary Rx for both groups: 500-1000 kcal/d deficit, 55% kcal CHO, < 30% kcal fat, 8-10% kcal sat fat, ~ 15% kcal protein, < 300 mg/d cholesterol		
Franks et al 2007[18]	• 12 months • 3,234 obese men & women with pre-diabetes • Participants from the U.S. Diabetes Prevention Program • Randomized into a control group, medication group, lifestyle group	• Consistent with Curti and colleagues (see above)	• Measures at 0, 12 mo: BW, WC, FM • Dietary intake was measured at 0,12 mo via a food frequency questionnaire	• Mutant-type, medication group: reduced BW at 12 mo (p=0.01) • Mutant-type, lifestyle group: reduced BW at 12 mo (p=0.04)
Lindi et al 2002[20]	• 36 months • 490 overweight & obese adults with pre-diabetes ○ 161 men, 329 women • Participants from Finnish Diabetes Prevention Study	• Individuals met with an RD for dietary counseling 7 times within the first year and every 3 months thereafter until completion of the study • Specific dietary goals included consuming < 30% kcal from fat, < 10%	• Measures at 0, 36 months: BW, BMI, WC, HC, BG, and insulin • Dietary data was collected 4x/yr via 3-day food records	• Mutant-type, control group: at 36 mo, Ala/Ala had greater chance of developing type 2 DM versus wild-type (p < 0.05) • Mutant-type, Intervention group: ○ Higher risk of

	• Multicenter, RCT • Randomized into control or intervention group	kcal sat fat, and 15 g fiber/1000 kcal consumed • 30 min/d exercise was encouraged		developing type 2 DM in Ala/Ala versus wild-type allele ($p > 0.05$) ○ Reduced BW at 36 mo in Ala/Ala versus wild-type ($p=0.043$) ○ Greater reduction in BW at 36 mo in Ala/Pro versus wild-type ($p > 0.05$)
Nicklas et al 2001[72]	• 18 months ○ 6 mo intervention ○ 12 mo maintenance • 70 obese, AH, postmenopausal women	• 6 month weight loss intervention: ○ weekly group meetings with RD for dietary instruction, education, counseling ○ goal to reduce total caloric intake 250-350 kcal/d ○ Supervised walking 1 d/wk at 50-60% HRR, unsupervised walking 2 d/wk • 12 month maintenance: met with RD bi-weekly	• Measures at 0, 6 mo: BW, body composition via DXA, maximal oxygen uptake, RMR via indirect calorimetry, BG, insulin	• Mutant-type: reduced BW, BG, and insulin at 6 mo ($p < 0.001$)

		for the first 6 mo, no meetings during the last 6 mo		
Garaulet et al 2011[19]	• 1465 overweight & obese, AH men & women • Length of study individualized pending time to reach goal weight ○ Goal weight determined considering a weight loss of 0.5-1.0 kg/wk	• 600 kcal deficit based on calculated energy needs via the Harris-Benedict Equation (included activity factors) • Resulted in about 1200-1800 kcal diet for women and 1500-2000 kcal diet for men • 50% kcal CHO, 35% kcal fat (< 10% sat fat, 20% MUFA), 15-20% kcal protein • Exercise: 10,000 steps/d and at least 30 minutes of moderate-intensity exercise	• Measures at 0, completion: BW, body composition via BIA, WC, HC, BP, blood lipid profile, BG, and insulin • Dietary data was collected at 0, completion via 24-hr recall	• Mutant-type: greater percentage of weight loss from 0 when consuming lower fat diet (p=0.286) • Wild-type: greater percentage of weight loss from 0 when consuming a higher fat diet (p=0.037)
ADRB3 (rs4994)				
Rawson et al 2002[79]	• 34 obese, AH, postmenopausal women • Length of study individualized, based on Metropolitan Life Insurance Tables ○ Average length of study 13.5 ±	• 1200 kcal/d, 55% kcal CHO, < 30% kcal fat, < 7% kcal sat fat, ~ 15% kcal protein, < 200 mg/d cholesterol • No exercise intervention	• Measures at 0, completion: BW, body composition, RMR, TEE, TEF via doubly labeled water technique	• All participants: reduced body mass, BMI, BF%, FFM, and FM ($p < 0.05$) at completion • No difference between genotypes

	2.6 months			
Shiwaku et al 2003[81]	• 3 months • 76 normal & overweight, AH women • Behavioral weight loss intervention	• Individualized dietary counseling promoting caloric restriction from baseline intake • Group sessions emphasizing implementation of healthy lifestyle habits • 7000 steps/d	• Measures at 0, 3 months: BW, BP, WC, HC, tricep skinfolds, body composition via BIA, blood lipids • Dietary compliance measured via food frequency questionnaires • Exercise compliance measured via physical activity questionnaire	• All participants: exhibited significant reductions in BW, BP, EC, HC, tricep skinfold, LDL, LDL to HDL ratio, and phospholipids upon completion ($p < 0.05$), with no difference between genotypes
Tahara et al 2010[82]	• 3 months • 57 overweight & obese, AH men • Behavioral weight loss intervention	• At least one individualized dietary counseling session with RD promoting caloric restriction from baseline dietary intake • Three group sessions (baseline, mid-point, completion) emphasizing implementation of	• Measures weekly: BW & WC • Questionnaires to assess dietary and exercise compliance completed at 3 mo	• All participants: reduced BW, WC ($p < 0.05$) at 3 mo • No difference between genotypes

		healthy lifestyle habits • 10,000 steps/d		
Bea et al 2010[83]	• 12 months • 148 normal weight & overweight/obese, AH postmenopausal women • Secondary analysis from a block randomized resistance training trial ○ 320 sedentary individuals randomized into exercise or control group	• No dietary intervention • High-intensity resistance training & moderate impact weight-bearing exercise • 75 min x 3 d/wk • 2 x 6-8 repetitions at 70-80% 1RM • 1RM measured and adjusted every 6-8 weeks	• Measures at 0, 12 months: body composition via DXA	• All participants: increase in lean soft tissue ($p < 0.05$) • No significant differences between genotype

Phares et al 2004[22]	• 6 months
	• 70 overweight, AH, men (29) & women (41)
		• No caloric restriction
		• 55% kcal CHO, 30% kcal fat, 15% kcal protein
		• Endurance exercise 3 d/wk
		  ○ progressed in intensity (50-70% Vo2 max) & time (20-40 min) x 10 wks
		  ○ then participants trained for 40 min at 70% Vo2max for remaining 14
			• Measures at 0, 6 months: Body composition via DXA, Vo2 max, oral glucose tolerance test
			• Dietary compliance measured with food records collected at 0, 2, 4, 6 mo
				• All participants: reduced BF%, % trunk fat, and FM ($p < 0.05$) at 6 mo
				• Mutant-type: greater reduction in BF% ($p=0.027$), % trunk fat ($p=0.03$), FM ($p=0.037$) at 6 mo

		weeks • Walking for 45-60 min/d x 1 d/wk during last 14 wks		
Lee et al 2006[23]	• 3 months • 80 overweight, AH women	• Individualized, weekly, dietary counseling with RD emphasizing reduction of intake from baseline • 60 min supervised, moderate-intensity, aerobic exercise weekly • 10,000 steps/d	• Measures at 0, 3 months: BW, WC, BF% via brozek equation, tricep and subscapular skinfold thickness, blood lipids • Dietary compliance measured via 2-day food records at 0, 3 months	• All participants: reduced BW, BMI, BF%, WC, and total cholesterol ($p < 0.01$) at 3 mo • Wild-type: o reductions in HDL ($p < 0.05$), LDL ($p < 0.05$), TG ($p < 0.01$) o greater reductions in BW, BMI ($p < 0.01$)
de Luis et al 2013[17]	• 3 months • 260 obese, AH, men (55) & women (166) • Randomized into diet group differing in fat content	• MUFA diet: o 1342 kcal/d o 46.6% kcal CHO, 34.1% kcal fat, 19.2% kcal protein o 21.7% sat fat, 67.5% MUFA, 10.8% PUFA • PUFA diet: o 1459 kcal/d	• Measures at 0, 3 months: BW, BP, body composition via BIA, BG, insulin, blood lipids • Dietary compliance via 3-day food records	• All participants: reduced BW, BMI, FM, and WC at 3 mo ($p < 0.05$) • Mutant-type, MUFA: o greater reduction in WC ($p > 0.05$) versus wild • Wild-type, MUFA: o greater reduction in BMI ($p < 0.05$) versus mutant

		○ 45.7% kcal CHO, 34.4% kcal fat, 19.9% kcal protein ○ 21.8% sat fat, 55.5% MUFA, 22.7% PUFA • 60 min/d aerobic activity, 3 d/wk	collected at 0, 3 months	• Mutant-type, PUFA: ○ greater reductions in BW, WC, insulin versus wild ($p < 0.05$) • Wild-type, PUFA: ○ reduced BG, insulin, TC, LDL, TG ($p < 0.05$) ○ greater reductions in BMI, FM, WHR, HOMA versus mutant ($p < 0.05$)
ADRB2 (rs1042713)				
Saliba et al 2014[95]	• 7 weeks • 109 obese, AH women	• Individual diet Rx with 600 kcal deficit • 3 individual dietary counseling sessions & 2 group sessions • One group session providing information on how to increase physical activity from baseline	• Measures at 0, 7 weeks: BW	• No significant differences among allele patterns and weight loss outcomes
Ruiz et al 2011[25]	• 3 months • 78 obese, AH women	• Individualized dietary prescription with 600 kcal deficit • Weekly dietary	• Weekly Measures: BW • Measures at 0, 3 months: BW,	• No significant differences among allele patterns and weight loss outcomes

		counseling sessions with RD	body composition via DXA, WC, RMR • Dietary compliance measured via 3-day food records at 0, 3 months, and 1-day food records at weeks 2, 5, 7	
Verhoef et al 2014[96]	• 5 months • 150 overweight & obese, AH men (39) & women (111)	• Very low calorie diet x 2 mo followed by instruction to maintain BW for last 3 months • Diet was provided & consisted of 50 g CHO/d, 7 g fat/d, 52 g protein/d	• Measures at 0, 2, 5 months: BW, WC, HC, & body composition via BOD POD	• All participants: reduced BW, BMI, FM, percent FM, WC, HC at 5 mo ($p < 0.001$) • No significant differences among allele patterns and weight loss outcomes
ADRB2 (rs1042714)				
Saliba et al 2014[95]	See above	See above	See above	• No significant differences among allele patterns and weight loss outcomes
Bea et al 2010[83]	See above	See above	See above	• Mutant-type: increase in lean soft tissue in exercise group versus control ($p < 0.05$)

				• Wild-type: no change in lean soft tissue in exercise group
Ruiz et al 2011[25]	See above	See above	See above	• Mutant-type: greater reduction in BW (p=0.002) & LM at 3 mo (p=0.001)
Rauhio et al 2013[24]	• 12-months • 62 obese, AH, postmenopausal women	• 700 kcal/d x 3 mo, with weekly dietary counseling with RD • 9 mo weight maintenance period • Daily physical activity log recording activity type, duration, and perceived intensity	• Measures at 0, 3, 12 mo: BW, WC, body composition via DXA	• All participants: lost weight with favorable change in body composition • Wild-type: reduced gynoid fat percentage at 3 mo ($p < 0.03$)
AH = apparently healthy, min = minutes, x/wk = times per week, mo = months, REE = resting energy expenditure, WC = waist circumference, HC = hip circumference, BW = body weight, BP = blood pressure, BG = blood glucose, fasting insulin, CRP = c-reactive protein, wks = weeks, BF% = body fat percentage, SBP = systolic blood pressure, WHR = waist to hip ratio, hr/wk = hours per week, FM = fat mass, FFM = fat free mass, BIA = bioelectrical impedance, DM = diabetes mellitus, IPAQ = international physical activity questionnaire, HRR = heart rate reserve, DXA = dual x-ray absorptiometry, RMR = resting metabolic rate, TEE = total energy expenditure, TEF = thermic effect of food, 1RM = one repetition maximum, LM = lean mass				

APPENDIX C

RECRUITMENT FLYER

Want to get fit and lose weight?

Participants Needed for a Study

Researchers in the Exercise & Sport Nutrition Laboratory (ESNL) at Texas A&M University are recruiting approximately 320 women between the ages of 18 and 60 to participate in a weight loss program. Participants will be randomized into one of four intervention groups involving varying exercise and nutritional requirements for 24 weeks. Eligible participants will receive $300 for completing the study. Eight visits approximately one month apart will be required.

For more information call:

Exercise & Sport Nutrition Laboratory (ESNL)
Department of Health & Kinesiology (HLKN)
1700 Research Parkway
Suite # 2500
979-458-1743/979-458-1715

APPENDIX D

PARTICIPANT ELIGIBILITY SCREENING

Texas A&M University: Exercise & Sport Nutrition Laboratory

Trial: Effects of Diet Type Selection Based on Response to a Carbohydrate Intolerance Questionnaire and Genetic Screening on Success to a Weight Loss and Exercise Program - Entrance Criteria

Phone Script: *"Hello this is the Exercise & Sport Nutrition Laboratory. I am going to ask you a few general questions to see if you qualify for the study you expressed interest in."*

Gender:

1. Are you female?
Yes – Possible FAM No – Screen Failure

Age:

1. Are you between the ages of 18 & 60? (they must be 60 when they sign the consent, they may turn 61 during the study)
Yes – Possible FAM No – Screen Failure

Exercise History:

1. Have you participated in a planned exercise program within the last three months?
Yes – Screen Failure No – Possible FAM

2. Do you exercise more than 30 minutes per day, 3 days per week?
Yes – Screen Failure No – Possible FAM

3. Have you experienced recent weight change of ±7 lbs. within the last 3 months?
Yes – Screen Failure No – Possible FAM

Exclusion Criteria:

1. Are you pregnant or nursing, or plan to become pregnant during the next 12 months? Have you recently been pregnant in the past 12 months?
Yes – Screen Failure No – Possible FAM

2. Do you have any uncontrolled metabolic disorder including known electrolyte abnormalities; heart disease, arrhythmias, diabetes, thyroid disease, or hypogonadism; a history of hypertension, hepatorenal, musculoskeletal, autoimmune, or neurological disease?
Yes – Screen Failure No – Possible FAM

3. Are you currently taking thyroid, hyperlipidemic, hypoglycemic, anti-hypertensive, or androgenic medications?
Yes – Screen Failure No – Possible FAM

4. Have you taken ergogenic levels of nutritional supplements that may affect muscle mass (e.g., creatine, HMB), anabolic/catabolic hormone levels (androstenedione, DHEA, etc.), or weight loss (e.g., ephedra, thermogenics, etc.) *within the past three months?*
Yes – Screen Failure No – Possible FAM Not Sure – Consult w/ESNL Staff prior to testing

5. Are you willing to take part in a regular moderate exercise program?
Yes – Possible FAM No – Screen Failure

BMI: Do you have a BMI greater than 22?
Minimum Body Weight Needed for a BMI = 22

Height(ft./in.)	Minimum Wt. (lbs.)	Height(ft./in.)	Minimum Wt. (lbs.)
4'10"	105	5'9"	149
4'11"	109	5'10"	153
5'0"	112	5'11"	157
5'1"	116	6'0"	162
5'2"	120	6'1"	166
5'3"	124	6'2"	171
5'4"	128	6'3"	176
5'5"	132	6'4"	180
5'6"	136	6'5"	185
5'7"	140	6'6"	190
5'8"	144		

Yes – Possible FAM No – Screen Failure

Summary: If the potential participant meets all conditions for a possible FAM, please schedule them.

APPENDIX E

INFORMED CONSENT

Project Title: Effects of Diet Type Selection Based on Response to a Carbohydrate Intolerance Questionnaire and Genetic Screening on Success to a Weight Loss and Exercise Program

You are invited to take part in a research study being conducted by Dr. Richard Kreider, a researcher from Texas A&M University and funded by Curves International. The information in this form is provided to help you decide whether or not to take part. If you decide to take part in the study, you will be asked to sign this consent form. If you decide you do not want to participate, there will be no penalty to you, and you will not lose any benefits you normally would have.

Why Is This Study Being Done?
The purpose of this study is to determine if stratification of individuals based on responses to a Carbohydrate Intolerance Questionnaire (CIQ), genetic screening, and/or DNA methylation affects weight loss success and/or health outcomes of women following the Curves moderate carbohydrate, high protein, low fat diet (30% CHO, 45% PRO, 25% FAT) or the Curves carbohydrate restricted, high protein, moderate fat diet (20% CHO, 45% PRO, 35% FAT).

Why Am I Being Asked To Be In This Study?
You are being asked to be in this study because you are a female between the ages of 18 and 60 years of age with a Body Mass Index (BMI) > 22 and/or a body fat percentage > 30%. You will not be allowed to participate in this study if you report a recent weight change of plus or minus 7 lbs. within the past 3 months. In addition you will not be allowed to participate in this study if you report any uncontrolled metabolic or cardiovascular disorder; including known electrolyte abnormalities, heart disease, arrhythmias, diabetes, thyroid disease, or a history of hypertension, hepatorenal, musculoskeletal, autoimmune, or neurological disease; if you are taking any weight loss supplements and/or ergogenic levels of nutritional supplements within the last 3 months that may affect body composition and/or anabolic/catabolic hormone levels; a history of pregnancy or lactation within the past 12 months or intentions to become pregnant during the next 12 months; participation in a regular exercise program within the past 3 months; or, the presence of any absolute or relative contraindications for exercise testing or prescription as outlined by the American College of Sports Medicine unless your personal physician feels the condition is controlled, would not be a limitation for you to participate in the study, and clears you for participation. If you do not

qualify for this study we will keep your contact information (phone number and/or e-mail) and contact you at a later date for potential entry into a similar study.

How Many People Will Be Asked To Be In This Study?
Approximately 320 people will be invited to participate in this study locally.

What Are the Alternatives to being in this study?
The alternative to being in the study is not to participate.

What Will I Be Asked To Do In This Study?
You will be asked to not exercise for 48 hours nor eat or drink calorie containing drinks for 12 hours before each testing session/visit. You will also be asked to record all food and drinks you eat and drink on food record forms for four days (including one weekend day) prior to all of the testing sessions/visits. Your participation in this study will last up to approximately six months and include eight visits (visit 1 ~ 1 hour/visit2,5 and 8 ~ 3 hours/visit 3,4,6, and 7 ~ 1.5 hours). These visits are detailed below and in Table 1.

Visit 1 (week one) – Familiarization
This visit will last about one hour. During this visit details of the study will be explained, human subject consent forms will be signed, personal and medical history information will be completed, a carbohydrate intolerance questionnaire will be completed, and you will have a general physical that will include measurement of fasting blood to determine if you can participate in the study. You will donate approximately 5 ml (1 teaspoon) of fasting blood from a vein in your arm according to standard procedures. Three cheek swabs will then be taken from your inner cheek for a genetic screening. We will be evaluating DNA to assess which diet may be more effective from a metabolism viewpoint. The samples will be destroyed after analysis. You will also be weighted and have your height measured.

Visit 2, 5 and 8 (week 0, 12 and 24) – (T1, T4 and T7)
These visits will last about three hours. During these visits you will first be asked to complete a physical activity questionnaire, a quality of life inventory, a social physique anxiety scale, a self-esteem scale, a body image questionnaire and an eating satisfaction inventory. These items will take about 30 minutes to complete. The samples will be destroyed after analysis. You will then have your resting energy expenditure determined. This will take about 30 minutes. You will then donate approximately 20 milliliters (4 teaspoons) of blood from a vein in your arm. Blood samples will be obtained by standard/sterile procedures using a needle inserted into a vein in your arm. This will take about 15 minutes. You will then have your total body composition measured, total body water determined, hip/waist measurements determined, resting blood pressure determined and heart

rate measured. Collectively these tests will take about 30 minutes. You will then be prepared to perform a maximal treadmill test. This test will take about 30 minutes to complete. You will then perform a one repetition maximum and 80% of 1 repetition maximum endurance repetition test on the bench press and hip/leg sled using standard procedures. These tests will take about 30 minutes to complete. In the event of an emergency during an exercise test proper emergency response protocols (calling 9-911 for serious injury or a medical emergency, calling Biosafety/EHS for cleanup assistance or spill team response, calling UPD for incidents in public areas, retrieving AED located in the lab, performing CPR or other First Aid techniques, etc.) will be followed by the Exercise & Sport Nutrition Laboratory (ESNL) staff depending on the severity of the emergency.

Visit 3, 4, 6 and 7 (week 4,8,16 and 20) – (T2, T3, T5 and T6)
These visits will last about one and a half hours. The same tests will be performed at visits 3,4,6 and 7 minus the cheek swabs and the exercise tests (maximal treadmill test, bench press test and hip/leg press test).

After the familiarization and baseline testing you will be matched according to BMI, age and body fat percentage and randomly assigned to one of four groups including: 1.) CIQ-Negative – Genetic Screen high carbohydrate recommended; 2.) CIQ-Negative – Genetic Screen high protein recommended; 3.) CIQ-Positive – Genetic Screen high carbohydrate recommended; or, 4.) CIQ-Positive – Genetic Screen high protein recommended. You will then be randomized to follow the Curves Complete moderate carbohydrate, high protein, low fat diet (30% CHO, 45% PRO, 25% FAT) (CC-I) or the Curves Complete II carbohydrate restricted, high protein, moderate fat diet (20% CHO, 45% PRO, 35% FAT) (CC-II) and supervised resistance based exercise program. This will involve consuming 1,400 kcals/day for 1 week and 1,500 kcals/day at the prescribed macronutrient intakes for 23 weeks. Meal plans on the Curves Complete diets will be provided with limited food options for the first two weeks. Thereafter, more variety in food choices will be provided to meet macronutrient goals. Additionally, the Curves Complete diets will be designed by a dietitian with a goal of providing foods with low amounts of saturated fat. You will also be asked to take the Curves Essential 2 Go-Nutra Stock which includes a Time Released Biomultiple multiple vitamin, a Bioavailable Calcium supplement and an Omega-3 supplement. In addition if you expected to exercise four days per week using the Curves 30 minute circuit training program. Each circuit style workout consists of 14 resistance exercises that work all major muscle groups. These are set up with floor-based calisthenics exercises (e.g., running/skipping in place, arm circles, Zumba dance, etc.) designed to maintain an elevated heart rate. You may also be asked to wear a heart rate monitor. All exercise sessions will be held in the Exercise and Sport Nutrition Laboratory. Research Assistants will monitor your exercise sessions and record your attendance. You will also be encouraged to walk for 30 minutes at a brisk pace

and/or accumulate 10,000 steps per day on non-circuit training days. The International Physical Activity Questionnaire (IPAQ), daily physical activity logs and daily steps recorded from a pedometer will be used to assess physical activity patterns.

Table 1. Assessment and Timeline Overview

Familiarization	Baseline (T1)	4 Weeks (T2)	8 Weeks (T3)	12 Weeks (T4)	16 Weeks (T5)	20 Weeks (T6)	24 Weeks (T7)
Familiarization Session Complete Paperwork Review Medical history Physical Exam Fasting Blood Genetic Screening Determination of Qualifications to Participate Group Assignment: 1)+CIQ,GEN-HC 2)+CIQ,GEN-HP 3)-CIQ,GEN-HC 4)-CIQ,GEN-HP Randomized Diet Assignment: CC-I (30%C, 45%P, 25%F) CC-II (20%C, 45%P,35%F) Phase I – 1,400 kcals/d for 1 week Phase II – 1,500 kcals/d for 23 weeks	Diet Record Review IPAQ[a] Body Weight Hip and Waist Measurements Resting Energy Expenditure Resting BP[b] and HR[c] Body comp/water Fasting Blood Gene Expression DNA Methylation Maximal Cardiopulmonary Exercise Test 1 rep and 80% 1 rep Bench Press and Leg Press Measures Survey Completion[d]	Diet Record Review IPAQ Body Weight Hip and Waist Measurements Resting Energy Expenditure Resting BP[a] and HR[b] Body comp/water Fasting Blood Survey Completion[d]	Diet Record Review IPAQ Body Weight Hip and Waist Measurements Resting Energy Expenditure Resting BP[a] and HR[b] Body comp/water Fasting Blood Survey Completion[d]	Diet Record Review IPAQ Body Weight Hip and Waist Measurements Resting Energy Expenditure Resting BP[a] and HR[b] Body comp/water Fasting Blood Gene Expression DNA Methylation Maximal Cardiopulmonary Exercise Test 1 rep and 80% 1 rep Bench Press and Leg Press Measures Survey Completion[d]	Diet Record Review IPAQ Body Weight Hip and Waist Measurements Resting Energy Expenditure Resting BP[a] and HR[b] Body comp/water Fasting Blood Survey Completion[d]	Diet Record Review IPAQ Body Weight Hip and Waist Measurements Resting Energy Expenditure Resting BP[a] and HR[b] Body comp/water Fasting Blood Survey Completion[d]	Diet Record Review IPAQ Body Weight Hip and Waist Measurements Resting Energy Expenditure Resting BP[a] and HR[b] Body comp/water Fasting Blood Gene Expression DNA Methylation Maximal Cardiopulmonary Exercise Test 1 rep and 80% 1 rep Bench Press and Leg Press Measures Survey Completion[d]

[a]International Physical Activity Questionnaire; [b]Blood Pressure; [c]Heart Rate;
[d]Standardized quality of life (SF-36), social physique anxiety, self-esteem, body image, and eating satisfaction inventories
CC-I - Curves Complete Diet I (Phase I 1,400 kcals/d, Phase II 1,500 kcals/d at 30% C, 45% P, 25% F) and Exercise Program
CC-II - Curves Complete Diet II (Phase I 1,400 kcals/d, Phase II 1,500 kcals/d 20% C, 45% P, 35% F) and Exercise Program

You may be removed from the study by the investigator for these reasons:

- You do not show up for your scheduled testing sessions/visits and the investigators are unable to contact you to reschedule.
- You do not follow your assigned diet protocol.
- You do not follow your assigned exercise protocol.

Are There Any Risks To Me?

The things that you will be doing are greater than risks that you would come across in everyday life. Although the researchers have tried to avoid risks, you may feel that some questions/procedures that are asked of you will be stressful or upsetting. You do not have to answer anything you do not want to. You will be exposed to a low level of radiation during the body composition test, which is similar to the amount of natural background radiation you would receive in one month while living in College Station Texas. In addition, a very low level of electrical current will be passed through your body during the body water test. This analyzer is commercially available and has been used in the health care/fitness industry as a means to assess body composition and body water for over 20 years. The use of these analyzers have been shown to be a safe method of measuring body composition and total body water and are approved by the FDA. You will donate about 1 teaspoon (5 milliliters) of blood during the initial familiarization/screening visit and then about 4 teaspoons (20 milliliters) at each of the seven testing sessions throughout the study using standard procedures. These procedures may cause a small amount of pain when the needle is inserted into the vein as well as some bleeding and bruising. You may also experience some dizziness and/or faint if you are not used to having blood drawn. The exercise tests that will be performed may cause symptoms of fatigue, shortness of breath, and/or muscular fatigue/discomfort. The exercise tests may also cause short-term muscle soreness and moderate fatigue for several days following the tests. You may also experience muscle strains/pulls during the exercise testing and/or training program. However, exercise sessions will be conducted by trained staff and monitored to ensure you follow appropriate exercise guidelines. You will follow a prescribed dietary regimen involving consuming 1,400 or 1,500 calories per day during various phases of the program. In addition, one group will eat a high percentage of calories in the form of protein. Although the total amount of total protein is not excessive (up to 169 grams/day) it may be higher than you are used to eating and may exceed recommended protein intake for active individuals. As a result, you may experience weight loss or gain, feelings of hunger or fullness, and/or changes in appetite and/or mood during various phases of the dietary intervention. In addition your risk to participation in this study may be greater if you have medical clearance to participate with a controlled medical condition. The likelihood of any of these occurring is slim.

Are There Any Benefits To Me?

The direct benefit to you by being in this study is to know more about your health and fitness status from the tests to be performed. However, even if no individual benefit is obtained, you will be paid for your participation.

Will There Be Any Costs To Me?
Aside from your time, there are no costs for taking part in the study.

Will I Have To Pay Anything If I Get Hurt In This Study?
If you suffer any injury as a result of taking part in this research study, please understand that nothing has been arranged to provide free treatment of the injury or any other type of payment. However, all needed facilities, emergency treatment and professional services will be available to you, just as they are to the community in general. You should report any injury to Dr. Richard Kreider at 979-845-1333. You will not give up any of your legal rights by signing this consent form.

Will I Be Paid To Be In This Study?
You will receive a total of $300 ($20 for the Familiarization and $40 for each additional testing session T1-T7) in one check at the end of the study. Payment will occur after finishing all eight sessions and after all study materials (food records, etc.) have been turned in to the study staff. You will be pain on a prorated basis if you are unable to complete the entire study.

Will Information From This Study Be Kept Private?
The records of this study will be kept private. No identifiers linking you to this study will be included in any sort of report that might be published. Research records will be stored securely and only ESNL staff will have access to the records.

Information about you will be stored in locked file cabinets in a locked file room in an ID card swipe access controlled laboratory. Computer files will be protected with a password. This consent form will be filed securely in an official area.

People who have access to your information include the Principal Investigator and research study personnel. Representatives of regulatory agencies such as the Office of Human Research Protections (OHRP) and entities such as the Texas A&M University Human Subjects Protection Program (HSPP) may access your records to make sure the study is being run correctly and that information is collected properly.

The agency that is funding this study (Curves International) and the institution(s) where study procedures are being performed (Texas A&M University) may also see your information. However, any information that is sent to them will be coded with a number so that they cannot tell who you are. Representatives from these entities can see information that has your name on it if they come to the study site to view records. If they are any reports about this study, your name will not be in them.

Information about you and related to this study will be kept confidential to the extent permitted or required by law.

Who may I Contact for More Information?

You may contact the Principal Investigator, Richard Kreider, PhD, to tell him about a concern or complain about this research at 979-845-1333 or rkreider@hlkn.tamu.edu. You may also contact the Co-Investigator/Laboratory Research Associate, Chris Rasmussen, at 979-458-1741 or crasmussen@hlkn.tamu.edu.

For questions about your rights as a research participant; or if you have questions, complaints, or concerns about the research, you may call the Texas A&M University Human Subjects Protection Program office at (979) 458-4067 or irb@tamu.edu.

What if I Change My Mind About Participating?

This research is voluntary and you have the choice whether or not to be in this research study. You may decide to not begin or to stop participating at any time. If you choose not to be in this study or stop being in the study, there will be no effect on your student status, medical care, employment, evaluation, relationship with Texas A&M University, etc. Any new information discovered about the research will be provided to you. This information could affect your willingness to continue your participation.

STATEMENT OF CONSENT

I agree to be in this study and know that I am not giving up any legal rights by signing this form. The procedures, risks, and benefits have been explained to me, and my questions have been answered. I know that new information about this research study will be provided to me as it becomes available and that the researcher will tell me if I must be removed from the study. I can ask more questions if I want. A copy of this entire consent form will be given to me.

_____ _____

Participant's Signature Date

_____ _____

Printed Name Date

INVESTIGATOR'S AFFIDAVIT:

Either I have or my agent has carefully explained to the participant the nature of the above project. I hereby certify that to the best of my knowledge the person who signed this consent form was informed of the nature, demands, benefits, and risks involved in his/her participation.

_____ _____

Signature of Presenter Date

_____ _____

Printed Name Date

APPENDIX F

GENERAL HEALTH QUESTIONNAIRE

Title Page Pg 1

General Screening Form

Study: _____ **IRB:** _____

Texas A&M, College Station, TX

Screening# ☐☐☐

Subject Initials ☐☐☐

Consent Date ☐☐ ☐☐ ☐☐☐☐ (mm dd yyyy)

Screening Date ☐☐ ☐☐ ☐☐☐☐ (mm dd yyyy)

Subject ID ☐☐☐

Personal Data

Pg 2

Visit: SCREENING **Screening #:** ☐☐☐

Name: _____

Address: _____

Phone #: _____

E-mail: _____

Local PCP: _____ ☐ None

_____

Demographics

Pg 3

Visit: SCREENING **Screening #:** ☐☐☐

Sex: ☐ M ☐ F

DOB: ☐☐ ☐☐ ☐☐☐☐ Age at enrollment: _____ y
mm dd yyyy

Race:
(Mark all which apply)

- ☐ White
- ☐ Black or African American
- ☐ Native Hawaiian or Other Pacific Islander
- ☐ Asian
- ☐ American Indian/Alaska Native
- ☐ Unknown

Ethnicity:
(Mark only 1)

- ☐ Hispanic or Latino
- ☐ Not Hispanic or Latino
- ☐ Unknown

General Health & Physical Exam

Pg 4

Visit: SCREENING Screening #: ☐☐☐

PMHx: _____

_____

_____

_____

_____

Surgical Hx: _____

_____

Allergies and drug reactions: _____

_____

Medications:

_____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____
_____ _____ _____

SHx: Lives with: _____ Where: _____

Occupation Hx: _____

Smoking: Duration: _____ PPD x _____ Yrs EtOH: _____
Former smoker: when stopped: _____ Duration: _____ PPD x _____ Yrs

Vital signs:

HR: ☐☐☐ m T: ☐☐ . ☐ ☐ °C ☐ °F

BP: ☐☐☐ / ☐☐☐ mmHg SaO2: ☐☐☐ %

Anthropometry:
Height: ☐☐☐ . ☐ cm Weight: ☐☐☐ . ☐ kg BMI: ☐☐ . ☐ kg/r

General Health & Physical Exam

Visit: SCREENING Screening #: ☐☐☐

ROS: fever chills sweats wtΔ fatigue appetite sleep
Skin: itching rash sores susp. moles/lesions- healing recentΔ
Head: dizzy fainting HA/LOC trauma
Eyes: correction Δvision-double tearing itching/redness
Ears: Δhearing ringing earache vertigo/tinnitus
Nose: epistaxis rhinorrhea allergies
Mouth/Throat: bleeding gums sore mouth/throat swollen neck
CV: angina palpitations DOE orthopnea/PND edema
Pulm: SOB wheeze cough hemoptysis TB
Hematologic: bruise /bleed easily transfusion hx
GI: dysphagia N / V abd pain GERD hematochezia jaundice
GU: freq urgency hesitancy dys- hematuria incont UTI's stones
Genital: testicular masses hernias
Endocrine: polyuria polydipsia skin/hair ? thyroid hx
Vascular: claudication DVT hx
MSK: jt pain stiffness arthritis gout
Neuro: numbness weakness/atrophy seizure/tremor
Psych: depression anxiety recent memoryΔ
Female: regular dysmenorrhea pregnancies menopause
Breast: skinΔ lumps pain discharge

PE: Gen: Well
Skin: cap refill: no rash lesions:
Head: no trauma no bruising no masses
Eyes: PERRLA EOMI no ptosis sclera clear
Ears: good acuity TM: nl reflex/intact
Nose: nl
Mouth/Throat: nl/pink, moist mucous membranes no lesions
Neurological: Alert & oriented×3, nl MS via conversation
Cranial Nerves: II - XII intact/nl
Motor: 5/5 UE/LE's bil
Sensation: intact LT UE/LE's
DTRs: symmetric/nl biceps knee ankle
Gait/Station: nl
Neck: no LAD no masses no bruits no JVD supple stiff
Chest: CTA bil equal expansion
Extremities: no C/C/E Major jts: no swelling full ROM
Heart: Reg no M/R/G
Pulses Bil: PT / DP: 2+
Abdomen: soft, NT/ND BS + no masses / organomegaly

Visit: SCREENING

General Health & Physical Exam

Screening #: ☐☐☐

Assessment: _____

Blood Draw: ☐Y ☐N _____

Blood draw performed by: _____

Lab Results Reviewed: ☐Y ☐N

Eligible based on General Health and Physical Exam: ☐Y ☐N

_____ Date: ☐☐ ☐☐ ☐☐☐☐
Signature of staff member performing exam mm dd yyyy

_____ Date: ☐☐ ☐☐ ☐☐☐☐
Signature of Principal Investigator (page 2-13) mm dd yyyy

APPENDIX G

PHYSICIAN CLEARANCE FORM

Dear Provider: One of your patient's would like to participate in a study titled "Effects of Diet Type Selection Based on Response to a Carbohydrate Intolerance Questionnaire and Genetic Screening on Success to a Weight Loss and Exercise Program" that is being conducted by the Exercise & Sport Nutrition Laboratory (ESNL) at Texas A&M University. In order to do so, she must meet the selection criteria described below and/or have approval from her personal physician to participate in the study. The study will involve having sedentary and overweight female participants participate in the Curves exercise and weight loss program for 24 weeks. The assessments to be performed are listed below. Please check the test/tests you **do not** feel comfortable having your patient complete (if any). In addition please staple a copy of your letterhead to this form to verify that it has been reviewed.

_____Fasting blood

_____Fasting resting energy expenditure (REE)

_____Bench press/Leg press assessments

_____Bioelectrical Impedance Analysis (BIA)

_____Diet intervention (see table attached)

_____Bone densitometry (DEXA)

_____BodyMetrix Ultrasound assessment

_____Maximal cardiorespiratory stress test (Bruce protocol)

Details about these specific tests are included below and in the attached participant consent form. If you feel she meets the entrance criteria and/or any existing medical condition that she may have is under control and **would not** be a limitation for her to participate in the study, please sign the medical clearance below.

Selection Criteria

Approximately 80 sedentary and overweight female participants (BMI > 22 and/or body fat percentage > 30%) between the ages of 18 and 60 will participate in this study. I understand that in order to participate in this study, a trained individual will examine me to determine whether I qualify to participate.

Participants **will not** be allowed to participate in this study if they:

1. have recent history of weight change (±7 lb within 3 months);
2. have any metabolic disorders including known electrolyte abnormalities; heart disease, arrhythmias, diabetes, thyroid disease, or hypogonadism; a history of hypertension, hepatorenal, musculoskeletal, autoimmune, or neurological disease; if they are taking thyroid, hyperlipidemic, hypoglycemic, anti-hypertensive, or androgenic medications;
3. have been pregnant or lactating within the past 12 months or are planning to become pregnant during the next 12 months;
4. have participated in a planned exercise program or have exercised regularly (> 30 min/d 3 days/wk) within the past three months;
5. have taken any weight loss medications and/or dietary supplements that may affect muscle mass or body weight during the three month time period prior to beginning the study;

6. have any absolute or relative contraindications for exercise testing or prescription as outlined by the American College of Sports Medicine;

The only exception to these selection criteria will be if the prospective participant has a medical condition or history that the participant's personal physician feels is controlled and therefore would not be a limitation for them to participate in the study.

Medical Clearance

I medically clear _____ to participate as a participant in this study.

Name _____ Date _____

Signature _____

Diet Breakdown.

Diet	Kcals	Macronutrients	Diet Content (%)	g/d	Kcals/ d	g/kg/d (90 kg)
Curves Complete I –Moderate Carbohydrate / High Protein / Low Fat Diet (CC-I)						
1 Week	1,400 kcals/d	CHO PRO FAT	30 45 25	105 158 39	420 630 350	1.17 1.75 0.43
23 Weeks	1,500 kcals/d	CHO PRO FAT	30 45 25	113 169 42	450 675 375	1.25 1.88 0.47
Curves Complete II –Carbohydrate Restricted / High Protein / High Fat Diet (CC-II)						
1 Week	1,400 kcals/d	CHO PRO FAT	20 45 35	70 158 54	280 630 490	0.78 1.75 0.60
23 Weeks	1,500 kcals/d	CHO PRO FAT	20 45 35	75 169 58	300 675 525	0.83 1.88 0.65

Blood Samples. Participants will fast overnight for twelve (12) hours and then donate approximately 1 teaspoon (5 milliliters) of fasting blood once and 4 teaspoons (20 milliliters) of fasting blood 7 times throughout the duration of the 24 week study. Blood samples will be obtained using standard phlebotomy procedures using standard sterile venipuncture of an antecubital vein by laboratory technician's trained in phlebotomy in compliance with guidelines established by the Texas Department of Health and Human Services. The phlebotomists and lab technicians will wear personal protective clothing (gloves, lab coats, etc.) when handling blood

samples. Participants will be seated in a phlebotomy chair. Their arm will be cleaned with a sterile alcohol wipe and sterile gauze. A standard rubber tourniquet will then be placed on the brachium. An antecubital vein will be palpated and then a 23 gauge sterile needle attached to a plastic vacutainer holder will be inserted into the vein using standard procedures. Two serum separation vacutainer tubes (red tops) and one EDTA vacutainer tube (purple top) will be inserted into the vacutainer holder for blood collection in succession using multiple sample phlebotomy techniques. Once samples are obtained, the vacutainer holder and needle will be removed. The needle will be discarded as hazardous waste in a plastic sharps container. The site of the blood draw will then be cleaned with a sterile alcohol wipe and gauze and a sterile Band-Aid will be placed on the site. The blood collection tubes will be labeled and placed in a test tube rack for later analysis.

Resting Energy Expenditure Assessment. Resting energy expenditure assessments will be made according to standard protocols using the Parvo Medics TrueOne 2400 Metabolic Measurement System. This will involve the participants lying down on an exam table, having a light blanket placed over them to keep warm and inserting ear plugs in their ears to reduce distractions. A see through metabolic canopy will then be placed over their neck and head so that metabolic measurements can be obtained. The participant will lie motionless without going to sleep for 15-minutes. Metabolic measurements will then be obtained to determine resting oxygen uptake and energy expenditure.

Body Composition Assessments (BIA & DEXA). Participants will undergo body composition tests in the ESNL. Prior to each assessment, height will be measured using standard anthropometry and total body weight will be measured using a calibrated electronic scale with a precision of +/-0.02 kg. Total body water will then be estimated using a Xitron 4200 Bioelectrical Impedance Analyzer (*San Diego, CA*) which measures bio-resistance of water and body tissues based on a minute low energy, high frequency current (500 micro-amps at a frequency of 50 kHz) transmitted through the body. This analyzer is commercially available and has been used in the health care/fitness industry as a means to assess body composition and body water for over 20 years. The use of this device has been approved by the Food and Drug Administration (FDA) to assess total body water and the current to be used has been deemed safe. This is measured through four electrodes placed on the body: one electrode will be placed on the posterior surface of the right wrist, in between the radial and ulna styloid processes (wrist bones), another electrode will be placed on the posterior surface of the right hand at the distal base of the second metacarpal; the third electrode will be placed on the anterior surface of the right foot at the distal end of the first metatarsal. Participants will lie on a table in the supine position and electrodes will be connected to the analyzer. After they are connected, age, gender, weight, height, and activity level are entered into the unit by the technician. After the unit has measured the resistance, which takes approximately 30 seconds, the unit then calculates total body water and body water percent.

Body composition/bone density will then be determined using a calibrated Hologic Discovery W dual-energy x-ray absorptiometry (DEXA) by qualified personnel with limited x-ray technology training under the supervision of Richard B. Kreider, PhD, MX. The DEXA body composition test will involve having the participant lie down on their back in a standardized position in a pair of shorts/t-shirt or a gown. A low dose of radiation will then scan their entire body for approximately six (6) minutes. The DEXA segments regions of the body (right arm, left arm, trunk, right leg, and left leg) into three compartments for determination of fat, soft tissue (muscle), and bone mass. Radiation exposure from DEXA for the whole body scan is approximately 1.5mR per scan. This is similar to the amount of natural background radiation a person would receive in one month while living in College Station, TX. The maximal permissible x-ray dose for non-occupational exposure is 500 mR per year. Total radiation dose will be less than 5mR for the entire study. Since women of child bearing age may serve as subjects in this study, each subject will

complete a questionnaire related to their menstrual cycle timing, sexual activity, use of birth control pills, and desire to become pregnant (see attached). DEXA tests will be performed within 14-days of the onset of their period in menstruating women of child bearing age who do not use oral contraceptives according to NCRP and ARP radiology standards in order to reduce the possibility of exposure of an unknown fetus to radiation.

Fat layer thickness and localized muscle layer thickness will then be determined using a BodyMetrix BX2000 utilizing ultrasound technology. Seven sites will be used including the chest, axilla, tricep, scapula, waist, hip and thigh. When used with BodyView software it can be used to estimate total body fat percentage.

Strength Tests. All strength/exercise tests will be supervised by certified lab assistants experienced in conducting strength tests using standard procedures. Strength testing will involve the participants performing one repetition maximum (1 RM) on the isotonic bench press and the Nebula Fitness Olympic Power Station. Participants will warm-up (2 sets of 8 – 10 repetitions at approximately 50% of anticipated maximum) on the bench press. Participants will then perform successive 1 RM lifts starting at about 70% of anticipated 1RM and increasing by 5 – 10 lbs until they reaches their 1RM. Participants will then rest for 10 minutes and warm-up on the Nebula 45° Leg press (2 sets of 8 – 10 repetitions at approximately 50% of anticipated maximum). They will then perform successive 1RM lifts on the leg press starting at about 70% of anticipated 1RM and increasing by 10 – 25 lbs until reaching the subject's 1RM.

Cardiopulmonary Exercise Tests. Cardiopulmonary exercise tests will be performed by trained exercise physiologists in accordance to standard procedures described by the American College of Sports Medicine's (ACSM) *Guidelines for Exercise Testing and Prescription*. This will involve preparing the participant's skin s for placement of 10 ECG electrodes. Electrode sites will be cleansed with a sterile alcohol gauze using a circular motion. The site will be allowed to air dry or will be dried with a gauze pad. Electrodes will then be placed on the right subclavicular fossa (RA), left subclavicular fossa (LA), right abdomen (RL), left abdomen (LL), 4^{th} intercostals space at the right sternal border (V1), 4^{th} intercostals space at the left sternal border (V2), equidistant between V2 and V4 (V3), 5^{th} intercostal space at the midclavicular line (V4), 5^{th} intercostal space at the anterior axillary line (V5), and 5^{th} intercostals space at the axillarly line (V6) of the chest. The participant will then be attached to an ECG. Resting blood pressure, heart rate, and a 12-lead ECG will be obtained. The exercise specialist will then review the 12-lead ECG to ensure that no contraindications for exercise testing are apparent based on the ACSM guidelines. Participants will then be seated on a treadmill. A sterile mouthpiece attached to a head harness will be secured on them. The participant will then have a nose clip placed on their nose. Resting expired gases will be collected using the Parvo Medics 2400 TrueOne Metabolic Measurement System. Once the participant is ready to begin the test protocol, they will be instructed to straddle the treadmill with both legs while the treadmill is turned on at a speed of 1.7 mph and at a 0% grade. The participant will then use one foot to repeatedly swipe the belt in order to gauge the speed of the motion. Once they are familiar with this speed, they will step onto the belt while still gripping the handrail with both hands. Once the participant becomes comfortable walking on the treadmill, he/she will let go of the handrail and begin walking freely. The participant will then perform a standard symptom-limited Bruce treadmill maximal exercise test using the following speeds and grades:

Stage Duration(min.)	Speed	Grade(%)
1 3	1.7	10
2 3	2.5	12
3 3	3.3	14
4 3	4.2	16
5 3	5.0	18
6 3	5.5	20
7 3	6.0	22

The participant will be encouraged to exercise to their maximum unless they experiences clinical signs to terminate the exercise test as stated by the ACSM's *Guidelines for Exercise Testing and Prescription* (i.e., angina, dyspnea, dizziness, a decline in systolic blood pressure, dangerous dysrhythmias (increasing or multi-form premature ventricular contractions, ventricular tachycardia, supraventricular tachycardia, new atrial fibrillation, or A-V block), lightheadedness, confusion, ataxia, cyanosis, nausea, excessive rise in systolic blood pressure over 250 mmHg or diastolic over 120 mmHg, chronotropic impairment, failure of the monitoring system, or other signs or symptoms for terminating the test). The test may also be terminated at the request of the participant. Once the exercise test is complete, the participant will observe a 3-6 minute active recovery period followed by a 3-6 minute seated recovery period. The normal exercise time to maximum of the Bruce treadmill protocol for untrained women is typically about 9 minutes (near the completion of stage III or just entering stage IV). Heart rate (HR), ECG tracings, and expired gases will be monitored continuously throughout the exercise test. Blood pressure (BP) and ratings of perceived exertion (RPE) will be obtained toward the end of each stage. Participants will be asked to report any unusual signs or symptoms to the exercise specialists during the exercise test. These tests will determine maximal aerobic capacity and anaerobic threshold to determine the effects of the exercise training on fitness and exercise capacity.

APPENDIX H

RADIATION CONSENT

Texas A&M University: Exercise & Sport Nutrition Laboratory

Trial: Effects of Diet Type Selection Based on Response to a Carbohydrate Intolerance Questionnaire and Genetic Screening on Success to a Weight Loss and Exercise Program

Radiation Exposure Questionnaire for Women of Child Bearing Age

Radiation exposure may affect fetal development. Although the DEXA test will only expose you to a small amount of radiation (1.5mR per scan), you should be aware that there is a possibility that if you become pregnant during the course of the study that the x-ray exposure may be harmful to the fetus. Therefore, it is important to conduct x-ray tests within 10-14 days of the start of a female's menstrual cycle if the she is of child bearing age, sexually active, and/or is not taking birth control pills. The following questionnaire must be completed so that we know when it is an appropriate time to conduct the DEXA body composition tests. Please be assured that this information will be kept confidential within the limits permitted by law.

Current Age? _____
Age of first period? _____
Date of last period? _____
Normal length of menstrual cycle? _____
Do you use birth control pills? _____
Are you pregnant or have a desire for pregnancy? _____

Note: If you happen to get pregnant during the course of this study, you must notify research assistants so that appropriate precautions can be made.

I confirm that I have completed this questionnaire honestly and agree to notify researchers within the ESNL of any change in the length of my menstrual cycle and/or pregnancy status.

_____ _____
Name Date

_____ _____
Staff Signature Date

APPENDIX I

FOOD LOG

Exercise and Sport Nutrition Laboratory

Effects of Diet Type Selection Based on Response to a CIQ and Genetic Screening on Success to a Weight Loss and Exercise Program - Food Record

Name: _____ Day: 1 2 3 4 (Circle One)

Instructions:

1) Record everything that you eat for 3 weekdays AND 1 weekend day
2) Precisely record the food item (brand if applicable), preparation method, and TOTAL quantity consumed
3) Break down mixed dishes or recipes by listing their component parts
4) For dairy and meat products, indicate fat level (i.e. low fat, extra lean, 2%, etc.)

FOOD ITEM	PREPARATION METHOD (i.e. baked, fried, grilled, etc.)	QUANTITY							
		gm	mL	cups	T or tsp.	oz.	Pieces	Sm, Med, Lg	Other
MEAL 1:									
MEAL 2:									
MEAL 3:									
MEAL 4:									

APPENDIX J

EATING SATISFACTION SURVEY

Texas A&M University: Exercise & Sport Nutrition Laboratory
Trial: Effects of Diet Type Selection Based on Response to a Carbohydrate Intolerance Questionnaire and Genetic Screening on Success to a Weight Loss and Exercise Program

Eating Satisfaction Survey

NAME _____ Date _____

INSTRUCTIONS

Circle the number or dot between numbers that best indicates the degree you have felt the following symptoms during the last week:

Appetite

None Low Moderate High Severe
0 . . . . . 1 . . . . . 2 . . . . . 3 . . . . . 4 . . . . . 5 . . . . . 6 . . . . . 7 . . . . . 8 . . . . . 9 10

Hunger

None Low Moderate High Severe
0 . . . . . 1 . . . . . 2 . . . . . 3 . . . . . 4 . . . . . 5 . . . . . 6 . . . . . 7 . . . . . 8 . . . . . 9 10

Satisfaction from Food

None Low Moderate High Severe
0 . . . . . 1 . . . . . 2 . . . . . 3 . . . . . 4 . . . . . 5 . . . . . 6 . . . . . 7 . . . . . 8 . . . . . 9 10

Feeling of Fullness

None Low Moderate High Severe
0 . . . . . 1 . . . . . 2 . . . . . 3 . . . . . 4 . . . . . 5 . . . . . 6 . . . . . 7 . . . . . 8 . . . . . 9 10

Amount of Energy

None Low Moderate High Severe
0 . . . . . 1 . . . . . 2 . . . . . 3 . . . . . 4 . . . . . 5 . . . . . 6 . . . . . 7 . . . . . 8 . . . . . 9 10

Overall Quality of Diet

None Low Moderate High Severe
0 . . . . . 1 . . . . . 2 . . . . . 3 . . . . . 4 . . . . . 5 . . . . . 6 . . . . . 7 . . . . . 8 . . . . . 9 10

APPENDIX K

ROSENBERG SELF-ESTEEM SCALE

Rosenberg Self Esteem Scale

Circle the appropriate number for each statement depending on whether you strongly agree, agree, disagree, or strongly disagree with it.

	Strongly agree	Agree	Disagree	Strongly disagree
On the whole, I am satisfied with myself.	1	2	3	4
At times I think I am no good at all.	1	2	3	4
I feel that I have a number of good qualities.	1	2	3	4
I am able to do things as well as most other people.	1	2	3	4
I feel I do not have much to be proud of.	1	2	3	4
I certainly feel useless at times.	1	2	3	4
I feel that I'm a person of worth, at least on an equal plane with others.	1	2	3	4
I wish I could have more respect for myself.	1	2	3	4
All in all, I am inclined to feel that I am a failure.	1	2	3	4
I take a positive attitude toward myself.	1	2	3	4

APPENDIX L

SOCIAL PHYSICAL ANXIETY SCALE

Social Physique Anxiety Scale

Please answer the following questions as accurately as you possibly can. For each item, indicate the degree to which the statement is characteristic or true of you. Mark each answer using the five point scale that best represents your response to each item.

Key: 1=not at all true 2= slightly true 3=moderately true 4=very true 5=extremely true

1. I am comfortable with the appearance of my physique/figure _____
2. I would never worry about wearing clothes that might make me look too thin or overweight. _____
3. I wish I wasn't so uptight about my physique/figure. _____
4. There are times when I am bothered by thoughts that other people are evaluating my weight or muscular development. _____
5. When I look in the mirror, I feel good about my physique/figure. _____
6. Unattractive features of my physique/figure make me nervous in certain social situations. _____
7. In the presence of others, I feel apprehensive about my physique/figure. _____
8. I am comfortable with how fit my body appears to others. _____
9. It would make me uncomfortable to know that others were evaluating my physique/figure. _____
10. When it comes to displaying my physique/figure to others, I am a shy person. _____
11. I usually feel relaxed when it is obvious that others are looking at my physique/figure. _____
12. When in a bathing suit, I often feel nervous about the shape of my body. _____

APPENDIX M

BODY IMAGE

THE MBSRQ-AS

INSTRUCTIONS--PLEASE READ CAREFULLY

The following pages contain a series of statements about how people might think, feel, or behave. You are asked to indicate the extent to which each statement pertains to you personally.

Your answers to the items in the questionnaire are anonymous, so please do not write your name on any of the materials. In order to complete the questionnaire, read each statement carefully and decide how much it pertains to you personally. Using a scale like the one below, indicate your answer by entering it to the left of the number of the statement.

EXAMPLE:

_____ I am usually in a good mood.

In the blank space, enter a **1** if you **definitely disagree** with the statement;
enter a **2** if you **mostly disagree**;
enter a **3** if you **neither agree nor disagree**;
enter a **4** if you **mostly agree**;
or enter a **5** if you **definitely agree** with the statement.

There are no right or wrong answers. Just give the answer that is most accurate for you. Remember, your responses are confidential, so please be completely honest and answer all items.

1

1	2	3	4	5
Definitely Disagree	Mostly Disagree	Neither Agree Nor Disagree	Mostly Agree	Definitely Agree

_____ 1. Before going out in public, I always notice how I look.

_____ 2. I am careful to buy clothes that will make me look my best.

_____ 3. My body is sexually appealing.

_____ 4. I constantly worry about being or becoming fat.

_____ 5. I like my looks just the way they are.

_____ 6. I check my appearance in a mirror whenever I can.

_____ 7. Before going out, I usually spend a lot of time getting ready.

_____ 8. I am very conscious of even small changes in my weight.

_____ 9. Most people would consider me good-looking.

_____ 10. It is important that I always look good.

_____ 11. I use very few grooming products.

_____ 12. I like the way I look without my clothes on.

_____ 13. I am self-conscious if my grooming isn't right.

_____ 14. I usually wear whatever is handy without caring how it looks.

_____ 15. I like the way my clothes fit me.

_____ 16. I don't care what people think about my appearance.

_____ 17. I take special care with my hair grooming.

_____ 18. I dislike my physique.

continued on the next page

1	2	3	4	5
Definitely Disagree	**Mostly Disagree**	**Neither Agree Nor Disagree**	**Mostly Agree**	**Definitely Agree**

_____ 19. I am physically unattractive.

_____ 20. I never think about my appearance.

_____ 21. I am always trying to improve my physical appearance.

_____ 22. I am on a weight-loss diet.

For the remainder of the items use the response scale given with the item, and enter your answer in the space beside the item.

_____ 23. I have tried to lose weight by fasting or going on crash diets.

1. Never
2. Rarely
3. Sometimes
4. Often
5. Very Often

_____ 24. I think I am:

1. Very Underweight
2. Somewhat Underweight
3. Normal Weight
4. Somewhat Overweight
5. Very Overweight

_____ 25. From looking at me, most other people would think I am:

1. Very Underweight
2. Somewhat Underweight
3. Normal Weight
4. Somewhat Overweight
5. Very Overweight

continued on the next page

26-34. Use this 1 to 5 scale to indicate how dissatisfied or satisfied you are with each of the following areas or aspects of your body:

1	2	3	4	5
Very Dissatisfied	**Mostly Dissatisfied**	**Neither Satisfied Nor Dissatisfied**	**Mostly Satisfied**	**Very Satisfied**

_____ 26. Face (facial features, complexion)

_____ 27. Hair (color, thickness, texture)

_____ 28. Lower torso (buttocks, hips, thighs, legs)

_____ 29. Mid torso (waist, stomach)

_____ 30. Upper torso (chest or breasts, shoulders, arms)

_____ 31. Muscle tone

_____ 32. Weight

_____ 33. Height

_____ 34. Overall appearance

APPENDIX N

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

   ☐ Yes

   ☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

   _____ **days per week**

   ☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.