SUPPLEMENTARY MATERIAL

SUBJECTS AND METHODS

Study design

The study was a prospective, randomized controlled, feasibility trial of an 8-week diet counseling intervention for veterans enrolled in the MOVE! program with continued assessment to week 24, between November 2012 to March 2014. The MOVE! program is an 8-week, evidence-based weight management program for overweight and obese veterans that is established in all Veterans Administration hospitals.[29] The study took place through Veterans Administration of San Diego Healthcare System (VASDHS) and its community clinics. This study received IRB approval (protocol # H130174). It was also registered with ClinicalTrials.gov (NCT01859403). All authors had access to the study data and had reviewed and approved the final manuscript.

Participants

Veterans with a physician's referral to weight management clinic and a BMI $\geq$ 30.0 were recruited from those enrolled in the VASDHS MOVE! program. Inclusion criteria for this study were willingness to purchase and consume two Healthy Choice meals per day, keep a food log, have no known food allergies, have access to a freezer and microwave, understand and consent to the study, and attend the MOVE! program during the initial 8 weeks. Subjects were excluded if they drank 6 or more caffeinated beverages per day; had an active substance abuse or dependence disorder within the past year; had a surgical gastrointestinal procedure, with exception of distal appendectomy; had acute infections or use of antibiotic therapy; had a cognitive disorder or psychiatric hospitalization in the past 6 months, or suicidal ideation

identified in the past year; ≤GFR of 30 ml/min; New York Heart Association functional classification of congestive heart failure above class I; edema requiring diuretics (not including hydrochlorothiazide); abnormal EKG reading, high dose oral corticosteroids; abnormal TSH, sodium or potassium concentrations; fasting LDLs > 190 mg/dL; triglycerides ≥ 1000 mg/dL; or hemoglobin ≤ 10 g/dL. All participants provided written informed consent.

Diet Assignment

Participants entered the study on their normal diet. The baseline visit was 3-4 weeks prior to start of MOVE! program initiation. After baseline measurements were taken, participants provided saliva for genetic analysis (Pathway Genomics, Inc., San Diego, CA; Figure S1). Participants were then randomly assigned to either the genetics-guided therapy (GT) group or standard therapy (ST) groups. Randomization, which was performed prior to receipt of nutrigenetic report, was non-stratified, two-group, concealed allocation, using the Research Randomizer website.[30]

In the GT group, participants and researchers were unblinded to the diet match and participants were informed of their nutrigenetic report. GT participants were matched to one of four possible diet types: balanced, low-carbohydrate, low-fat, or Mediterranean based on their report. They received a meal plan, lists of foods to incorporate in the plan, and samples of menus (similar to the MOVE! packet of literature given to ST group) to assist adherence to their diet and to obtain their caloric goal (**Online Material: Meal Plan**). The macronutrient guidelines of the different diets for the GT participants are shown in **Table S2.**

In the ST group, participants and researchers were blinded to the nutrigenetic report. These participants were given the balanced diet plan. To aid in simplicity and adherence, all diet

plans (for both ST and GT participants) incorporated Healthy Choice (ConAgra Foods®, Inc.) entrees at lunch and dinner (**Online Material: Sample Menu**) for the first 8 weeks of the study, for which participants were fully reimbursed upon delivery of receipts. At the conclusion of the study, ST participants were provided their nutrigenetic reports.

The macronutrient composition of each diet plan was based on a compilation of research studies that showed the benefit of that particular diet plan on patients with a high risk polymorphism. For example, the macronutrient composition of the Mediterranean diet plan was based on refs 17-19 and 20-22 (see **Table S1**). All participants were provided access to a website to track their diet and exercise (fatsecret.com). This website also displayed detailed macronutrient data to enable the study dietitian to track dietary adherence and provide individualized counseling to participants at weekly group visits. To ensure macro- and micro-nutrients were within USDA guidelines and fit each diet's macronutrient requirements, all diet plans were analyzed with The Food Processor ® version 10.12 (ESHA Research, Salem, OR).

During weeks 1-8, all participants received weekly face-to-face group counseling based on their diet match. During weeks 9-24 participants were asked to continue to report dietary intake into the food log. To encourage use of the diet tracking website, participants were paid one dollar per day of entry, which was tallied weekly and paid in one lump sum at week 24. No further formal dietary counseling was given during this time.

In the first 8 weeks of the study, macronutrient composition was assessed by food diaries (via website as described in methods) and weekly in-person counseling and review of diet. Macronutrient data was reviewed with every patient during these in-person visits. During weeks 9-24 participants were reimbursed for use of self-reported dietary intake food logs. However,

besides receipts from Healthy Choice Meals, we did not have any additional evidence that patients were compliant with the self-reported diets in their food logs.

Anthropometric, Energy, and Impedance Assessments

At baseline, week 8, and week 24 each participant underwent measurements of height, weight, calculated BMI, waist circumference, hip circumference, and had a physical exam. Body weight was measured to the nearest 0.1 kg via a Weight-Tronix Scale (Scale Electronics Development, New York, NY, USA) by trained nursing staff. Resting metabolic rate (RMR) was collected using an indirect calorimeter system (MedGem®; Microlife Medical Home Solutions, Inc., Golden, CO, USA) to calculate each participant's daily caloric requirement. Bioelectrical impedance analysis (BIA) measurements was acquired using the Tanita® leg-to-leg system (model TBF – 300A; Arlington Heights, IL; USA) at baseline, week 8, and week 24. An EKG was performed to evaluate for bradycardia, rapid heart rate or other arrhythmia or active ischemia at the baseline visit.

Laboratory Measurements

Fasting blood samples were collected at baseline, week 8, and week 24. A CBC, basic chemistry panel, 25-hydroxy vitamin D, thyroid stimulating hormone, alanine transaminase, lipid panel, ultra-sensitive C reactive protein (US-CRP) and insulin were drawn. Individual lab values that were 2.5 standard deviations from the mean were considered erroneous and were not included in further analysis. Fasting homeostatic model assessment of insulin resistance (HOMA-IR) was calculated based on fasting serum glucose and insulin concentrations.

Salivary Nutrigenomics Testing

Salivary samples from participants were sent to Pathway Genomics and the Pathway Fit Test® (a genomic array) was performed. Based on the SNP alleles for seven genes, and using a proprietary algorithm, Pathway Fit Test® makes a recommendation to a specific diet (**Figure S1**). The genes (and reference SNP [rs] number) used to make these dietary recommendations were APOA2 (rs5082), ADIPOQ (rs17300539), FTO (rs9939609), KCTD10 (rs10850219), LIPC (rs1800588), MMAB (rs2241201), and PPARG (rs1801282); (**Table S1**).

Statistics

The primary, pre-specified study goal was to compare the percentage of participants achieving ≥5% weight loss in the GT vs. ST groups at 8 weeks. This is mainly because a patient's success in the MOVE! program is assessed at the end of their 8 week enrollment. However, since most of those studying obesity are concerned with long-term outcomes of an intervention, the secondary outcome was the percentage of participants in each group achieving ≥5% weight loss at 24 weeks.

Given paucity of data, a pre-specified power and sample size analysis was not done. Since the aim was to understand the direction and magnitude of differences in GT vs. ST, 50 participants were recruited in this single site recruitment structure. Participants were recruited in batches prior to starting the MOVE! program. This trial was completed due to meeting enrollment goal of at least 50 participants. Based on a 25 participants per group assumption, this study had the ability to detect a 30% absolute difference in the proportion of individuals achieving ≥ 5% weight loss 24 weeks after randomization, assuming 80% power, and a two-sided alpha of 0.05. For this calculation, it was assumed that the control group rate would be similar to previous publications on MOVE! program (~18% success rate [28]).

Since this was a feasibility study, per protocol analyses for all participants was performed (**Figure 1**). Analyses were performed using the Statistical Package for Social Science (SPSS) version 20.0 (SPSS, Inc., Chicago, IL) and GraphPad Prism 5 (GraphPad Software, La Jolla, CA). A two-sided alpha of 0.05 was used for declaring statistical significance. Differences in means were evaluated utilizing student t-tests when comparing two primary groups, or a one-way analysis of variance (ANOVA), if comparing multiple subclasses, with Dunns multiple comparison post-hoc test. For comparisons of categorical variables, Fisher Exact test was used. The Wilson procedure with a correction for continuity was used to assess the confidence interval for the difference between two independent proportions. For adherence data, a Pearson's correlation was performed. In order to assess whether this genotype is a good prognosticator of weight loss from dietary/behavioral intervention, the sensitivity, specificity, positive predictive value, and negative predictive value were calculated for different weight loss thresholds. The threshold with the best results is reported but other thresholds are shown in the supplementary table (**Table S3**).

Table S1: Nutrigenetic genes used for dietary recommendations.

Gene	Symbol/SNP	Polymorphism	Dietary Response	Reference
Adiponectin	Adipoq (rs17300539)	G/G – insulin resistance, metabolic syndrome	Mediterranean diet	17-19
Apolipoprotein A-II	ApoA2 (rs5082)	C/C – higher BMI	Low fat diet	15, 16
Fat mass and obesity-associated protein	FTO (rs9939609)	A/A – higher BMI	Mediterranean diet	20-22
K channel tetramerization domain containing 10	KCTD10 (rs10850219)	G/G – low HDL and high cholesterol	Low carbohydrate diet	23
Hepatic triglyceride lipase	LipC (rs1800588)	T/T – low HDL and high cholesterol	Low fat diet	24, 25
Methylmalonic aciduria cblB type	MMAB (rs2241201)	G/G – high LDL	Low carbohydrate diet	23
Peroxisome proliferative activated receptor gamma	PPARγ (rs1801282)	C/C – high LDL, type 2 diabetes mellitus	Low fat diet	26, 27

Note: Polymorphism column shows the variant that is associated with dysmetabolism and its associated trait. Dietary response column shows the diet that improved dysmetabolism in those with these variants in observational studies.

Table S2: Macronutrient Guidelines of the Different Diets Used in this Study.

	Carbohydrates	Fats	Proteins
Balanced Diet	55%	25%	20%
Low Carbohydrate Diet	40%	30%	30%
Low Fat Diet	55-60%	20%	20-25%
Mediterranean Diet	45%	35%	20%

Table S3: Estimates of Sensitivity, Specificity, Positive Predictive Value, and Negative Predictive Value of Using BDG as a Prognosticating test of weight loss at 6 months.

	0% Weight Loss	1% Weight Loss	2% Weight Loss	3% Weight Loss	4% Weight Loss	5% Weight Loss	6% Weight Loss
Sensitivity	38%	40%	43%	47%	56%	42%	33%
Specificity	100%	100%	100%	100%	94%	75%	70%
Positive Predictive Value	100%	100%	100%	100%	90%	50%	30%
Negative Predictive Value	27%	32%	41%	50%	68%	68%	72%

Supplemental Figures

Figure S1: Sample report from Pathway Genomics. Through a proprietary algorithm, Pathway Genomics makes a recommendation of the most appropriate diet for each participant (A) on the basis of their genotype for 6 genes (B). In this case, the participant is recommended to go on a low fat diet.

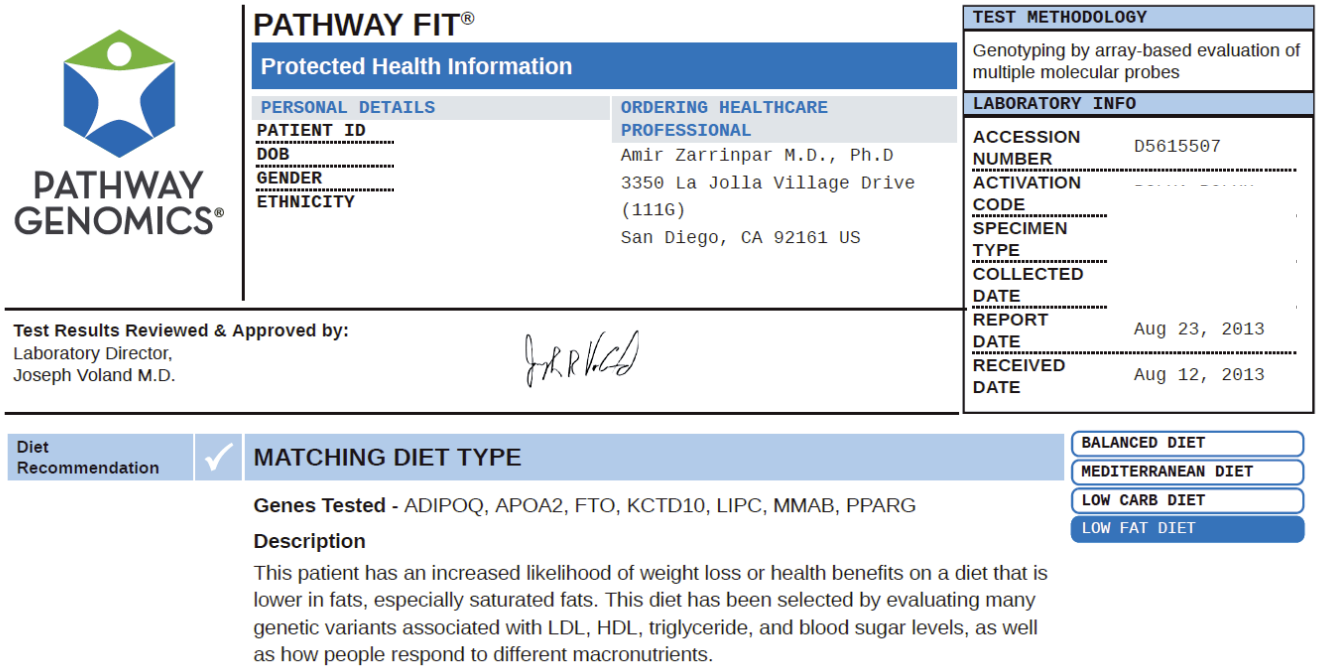
Figure S2: Lipid profile changes in the genotype guided therapy (GT) and the standard therapy (ST) groups. (A) Percentage LDL loss by participants at 8 and 24 weeks. Though this was significant at 8 weeks, it was no longer so at 24 weeks. Note that a negative number on this graph implies that LDL levels in serum went up. (B) Percentage HDL loss by participants at 8 and 24 weeks. (C) Triglycerides loss by participants at 8 and 24 weeks. (* $p < 0.05$).

Figure S3: Glucose homeostasis and Insulin resistance in the genotype guided therapy (GT) and the standard therapy (ST) groups. (A) Percentage decrease in fasting blood glucose by participants at 8 and 24 weeks. (B) HOMA-IR reduction from baseline by participants at 8 and 24 weeks. (C) Percentage decrease in glycated hemoglobin by participants at 8 and 24 weeks.

Figure S4: Adherence and weight loss by diet received. (A) There was no significant difference in adherence by diet received ($p = 0.52$, one-way ANOVA). (B) There was no significant difference in weight loss by diet received ($p = 0.52$, one-way ANOVA). Please note that in this graph, diet received refers to the dietary intervention the patient received, NOT their genotype.

Figure S1

A



B

MATCHING DIET TYPE

GENE/LOCUS	MARKER	GENOTYPE	STRENGTH
ADIPOQ	rs17300539	G/G	■■■□
APOA2	rs5082	C/C	■■■■
FTO	rs9939609	T/T	■■■□
KCTD10	rs10850219	G/G	■■■□
LIPC	rs1800588	C/C	■■■□
MMAB	rs2241201	G/C	■■■□
PPARG	rs1801282	C/C	■■■□

Figure S2

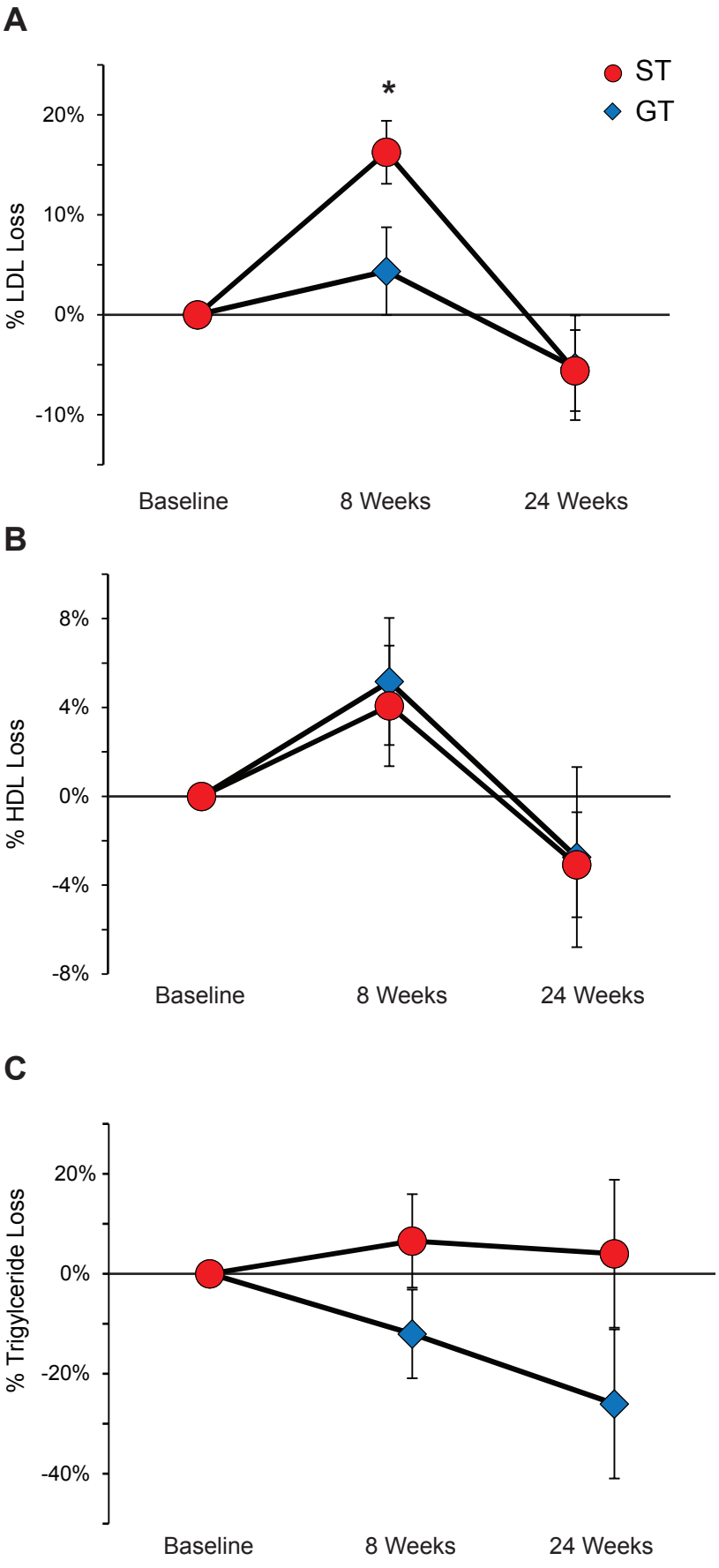

A
ST
GT
*
20%
10%
0%
-10%
% LDL Loss
Baseline
8 Weeks
24 Weeks
B
8%
4%
0%
-4%
-8%
% HDL Loss
Baseline
8 Weeks
24 Weeks
C
20%
0%
-20%
-40%
% Triglyceride Loss
Baseline
8 Weeks
24 Weeks

Figure S3

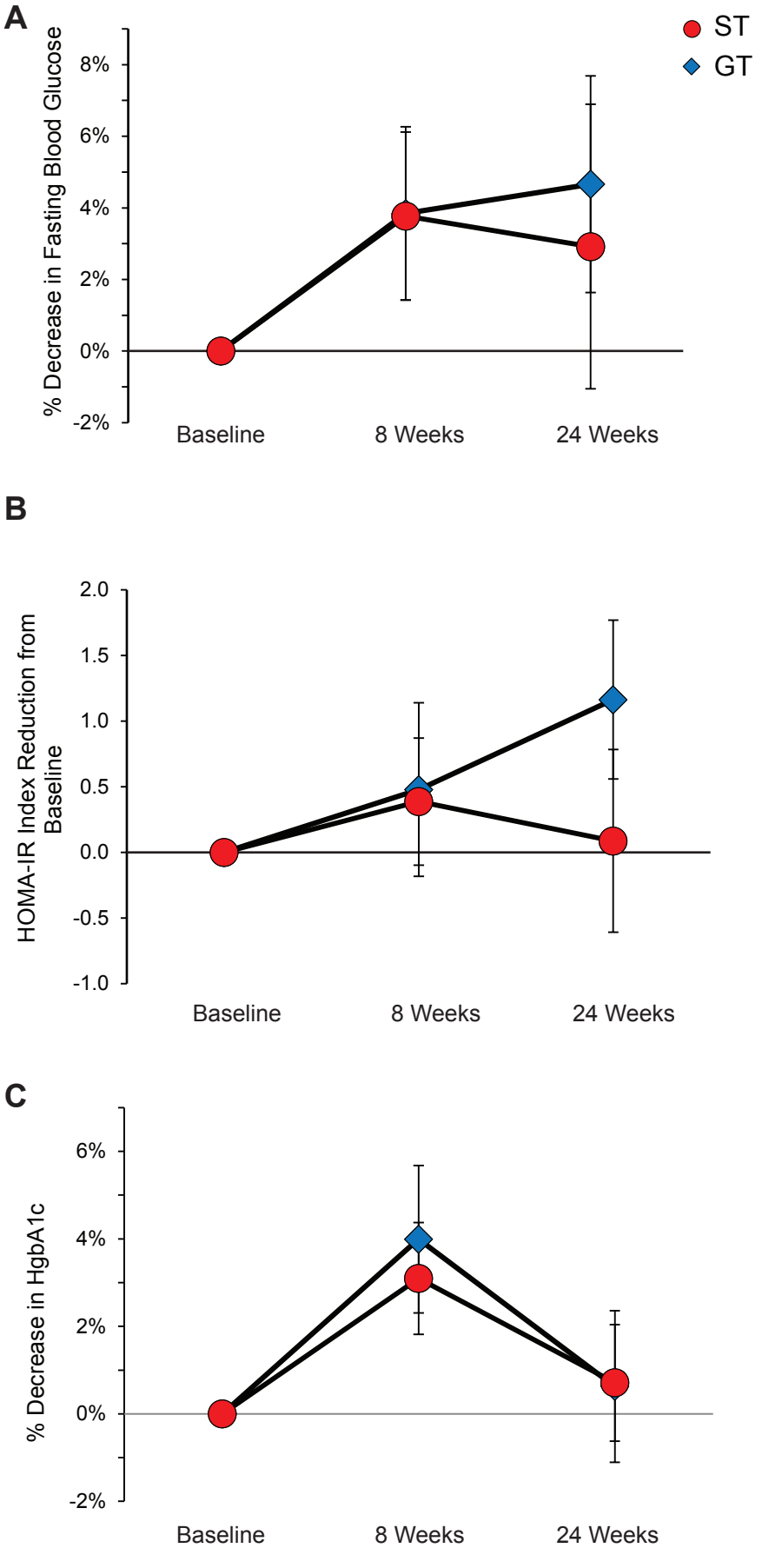
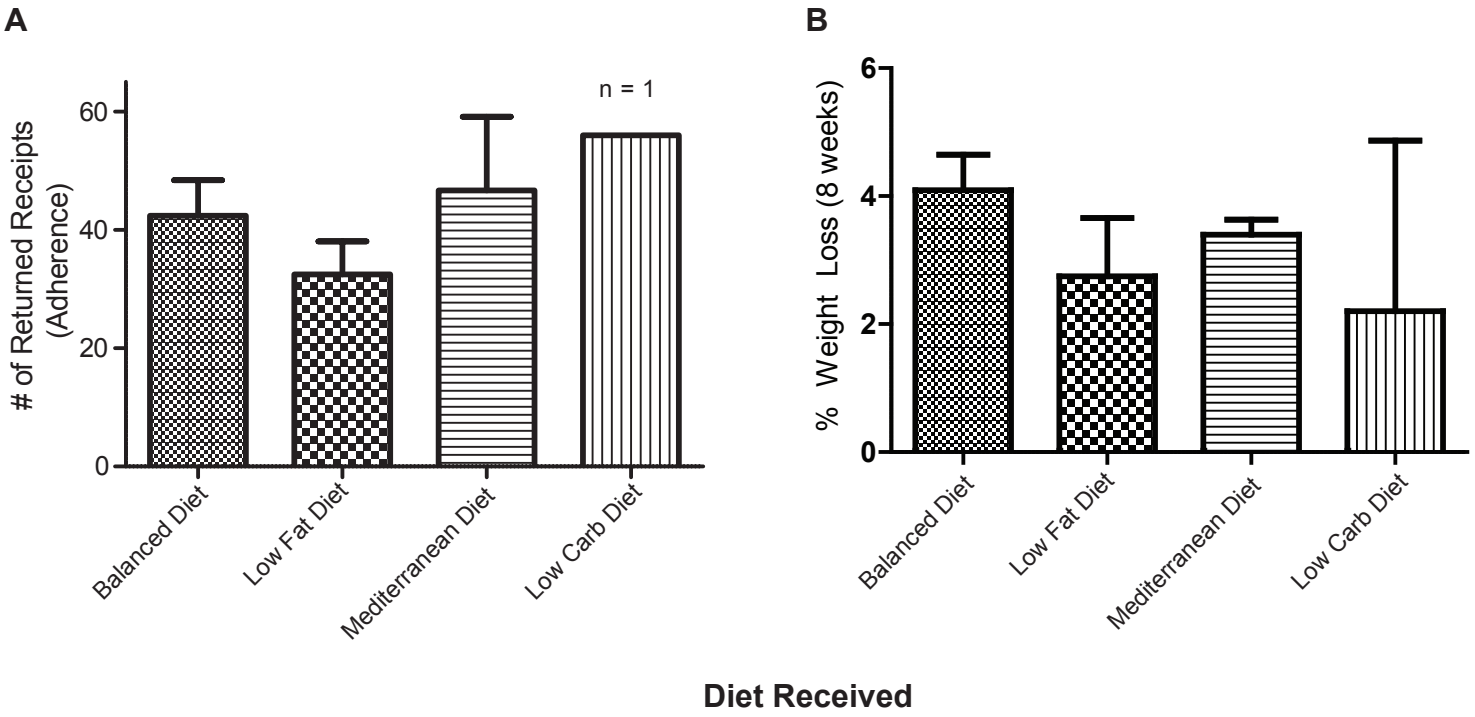

A
ST
GT
% Decrease in Fasting Blood Glucose
8%
6%
4%
2%
0%
-2%
Baseline
8 Weeks
24 Weeks
B
HOMA-IR Index Reduction from Baseline
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
Baseline
8 Weeks
24 Weeks
C
% Decrease in HgbA1c
6%
4%
2%
0%
-2%
Baseline
8 Weeks
24 Weeks

Figure S4


A
# of Returned Receipts (Adherence)
60
40
20
0
n = 1
Balanced Diet
Low Fat Diet
Mediterranean Diet
Low Carb Diet
B
% Weight Loss (8 weeks)
6
4
2
0
Balanced Diet
Low Fat Diet
Mediterranean Diet
Low Carb Diet
Diet Received

Balanced Diet Meal Plan

Nutrient Percentage Breakdown: 25% fat 55% carbohydrate 20% protein

Sample Breakfast Options

(Pick one entrée for breakfast)

Option Code	*Entrees*
B1	**Bran flakes** • ¾ cup Bran flakes topped with • ½ banana in • 1 cup skim milk
B2	**Waffle topped with berries** • 2 whole grain waffle with • 2 tbsp sugar-free syrup and • ½ cup fresh/frozen berries
B3	**Yogurt topped with strawberries** • 1 cup fat-free yogurt with • ½ cup strawberries • 1 hardboiled egg
B4	**Egg white scramble** • 4 egg whites scrambled with • ½ cup sautéed fresh spinach in • ½ tbsp olive oil • 2 slices of whole grain toast • 2 slice whole grain toast
B5	**Cottage cheese with melon** • 1 cup low fat (2%) cottage cheese with • ½ cup cubed melon • 1 multigrain English muffin
B6	**Ham, egg, cheese scramble** • 1 oz reduced fat ham and • 4 egg white and • 1 slice (1oz) cheese scramble in 1 tbsp skim milk • 1 banana • 1 slice whole grain toast
B7	**Oatmeal** • 1 cup cooked regular/quick/ instant oatmeal • 1/8 cup natural granola • 1 large egg, scrambled with • 1 tbsp skim milk •

Sample Lunch/Dinner Healthy Choice Meals

Pick one entrée for lunch and one for dinner and supplement with 1 additional serving of lean protein and 1 additional serving of vegetable.

Option Code	**Healthy Choice Entrees**	Calories*
M1	Rosemary Chicken and Sweet Potatoes	180
M2	Chicken Romano Fresca	230
M3	Portabella Parmesan Risotto	220
M4	Honey Balsamic Chicken	220
M5	Lemon Herb Shrimp	200
M6	Sesame Glazed Chicken	330
M7	Roasted Chicken Verde	230
M8	Sundried Tomato Chicken	320
M9	Salisbury Steak	170
M10	Slow Roasted Turkey Medallions	210
M11	Bacon and Smokey Cheddar Chicken	250
M12	Chicken Alfredo Florentine	210
M13	Ravioli Florentine Marinara	230
M14	Honey Ginger Chicken	320
M15	Spicy Caribbean Chicken	300
M16	Garlic Herb Shrimp	260
M17	Pineapple Chicken	380

Lean Protein

Please eat 1 additional serving with lunch and dinner.

Option Code	**Protein**
P1	2 hardboiled eggs
P2	1 oz low sodium beef/turkey/duck/ostrich jerky
P3	1 (1.5 oz) bake chicken drumstick with skin
P4	½ (3.5 oz) baked chicken breast with skin
P5	2 oz baked chicken thigh with skin
P6	1 (3.2 oz) baked chicken wing (with skin)
P7	3 oz baked/broiled salmon
P8	3 oz baked/broiled catfish
P9	3 oz baked/broiled tilapia
P10	3 oz baked/broiled halibut
P11	3 oz baked/broiled cod
P12	3 oz broiled lean beef (sirloin, tenderloin)
P13	3 oz broiled New York steak, top loin, strip steak
P14	3 oz (2 thin slices or 1 thick slice) roast beef
P15	3 oz broiled pork loin
P16	2 oz slice of turkey deli meat
P17	3 oz canned tuna in water
P18	1 cup black beans
P19	1 cup pinto/kidney beans
P20	¼ cup roasted almonds (unsalted)

Vegetable Samples

Please eat 1-2 additional serving with lunch and dinner. (May also be used for snacking.)

Option Code	Vegetable	Calories*
V1	**Mixed green and tomato salad** • ½ cup mixed green salad with • ½ cup fresh tomato, • 2 tbsp fat free French/Italian dressing	80
V2	**Sautéed green beans** • ½ cup boiled fresh/frozen green beans	35
V3	**Steamed broccoli** • ½ cup steamed fresh/frozen broccoli	30
V4	**Steamed mixed vegetables** • ½ cup steamed fresh/frozen mixed vegetables	60
V5	**Spinach and mushroom salad** • ¾ cup spinach salad topped with • ¼ cup chopped mushroom • 2 tbsp fat free balsamic vinaigrette	70
V6	**Baby carrots** • 10 fresh baby carrot sticks with • 1 tbsp fat free ranch dressing	45-75
V7	**Celery sticks** • 1 large fresh stalk celery with • 1 tbsp fat free ranch dressing	30
V8	**Sautéed squash/zucchini** • ½ cup baked squash/zucchini, lightly seasoned with herbs/pepper	20
V9	**Mixed green and mushroom salad** • ¾ cup fresh mixed green salad with • ¼ cup chopped mushroom, • 2 tbsp fat free balsamic vinaigrette	75
V10	**Sautéed mustard greens** 1 cup fresh/frozen mustard greens boiled	35

Snack Samples

Fruit Samples

(Servings per day depends on calories: will be discussed with dietitian)

Option Code	**Fruit**	Calories*
F1	1 small (4oz) apple	55
F2	1 small (6") banana	90
F3	1 small (4oz) peach	45
F4	1 small (5 oz) pear	75
F5	17 grapes	50
F6	1 cup cantaloupe	55
F7	1 cup melon	60
F8	½ cup canned peaches in water	40
F9	½ cup canned fruit salad in water	35
F10	½ cup canned pineapple in own juice	75

Dairy Samples

(Servings per day depends on calories: will be discussed with dietitian)

Option Code	**Dairy**	Calories*
D1	8 oz skim milk	90
D2	8 oz light soy milk, unsweetened	70
D3	1 cup (6 oz) Greek-style yogurt	100
D4	½ cup (4 oz) low fat (1%) cottage cheese	80
D5	1 string cheese (2% milk reduced fat)	70

Dessert substitutes

(Eat only 1-2 times a week)

Option Code	Desserts	Calories*
S1	Jell-O gelatin, sugar free, 1 snack cup (3.2 oz) 0 carbs, 0 fat	10
S2	Jell-O chocolate pudding, sugar free, 1 snack cup (3.7 oz) 13g carbs, 1.5g fat	60
S3	Dole/Dreyer's frozen fruit bar (variety pack), fat free, 1 bar 12g carbs	50
S4	Ice cream sorbet ½ cup 28g carbs, 0.5g fat	130
S5	Quaker rice cakes, 2 piece 14g carbs, 0g fat	70
S6	Air popped popcorn, 2 cup 12.4g carbs, 0.8g fat	60
S7	Smart Ones giant fudge bars, 1 bar 20g carb, 0g fat	80
S8	Popsicle fudgsicle bars, no sugar added, 1 bar 10g carbs, 1g fat	40
S9	Healthy Choice fudge bar, 1 bar 13g carbs, 1g fat	80
S10	Snackwell's devil's food cookie cakes, fat free, 1 cookie 12g carbs, 0g fat	50
S11	Breyers chocolate cookies and cream, fat free ice cream, ½ cup 25g carb, 0g fat	110
S12	Meringue cookies, 6 cookies 14g carbs, 0g fat	55
S13	Hood fat free frozen yogurt, ½ cup 20g carbs, 0g fat	90

***Caloric values determined by direct package labels. If not available, by The Food Processor ® version 10.12(ESHA Research, Salem, OR).**

Balanced Diet Sample Menu Plan: 1420 kcals

	Ingredient	Quantity
Breakfast	Bran flakes cereal	¾ cup (30 g)
	Milk, 2%	1 cup (246 g)
	Banana, medium	½ fruit (59 g)
Snack	Yogurt, flavored, low fat (1%)	8 oz (113 g)
	Canned pineapple in own juice	½ cup (90 g)
Lunch	Healthy Choice Lemon Herb Shrimp	1 entrée (247 g)
	Broiled steak, top loin	2 oz (56 g)
	G &M Salad	
	fresh mixed greens with	1 cup (36 g)
	chopped mushroom,	½ cup (44 g)
	balsamic vinaigrette	2 Tbsp (30 g)
Snack	String cheese, 2% milk (reduced fat)	1 piece (21 g)
	Strawberries	1¼ cups (184 g)
Dinner	Healthy Choice Bacon & Smokey Cheddar Chicken	1 entrée (245 g)
	Black beans, cooked	½ cup (127 g)
	Fresh asparagus, boiled, seasoned with herbs	6 spears (90 g)
	Sorbet, chocolate	½ cup (70 g)
Dessert	Sorbet, chocolate	½ cup (70g)