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The effects of separate and combined dietary weight loss and exercise on fasting ghrelin concentrations in overweight and obese women: a randomized controlled trial

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Abstract

Objective—Compensatory metabolic changes that accompany weight loss, e.g., increased ghrelin, contribute to weight regain and difficulty in long-term weight loss maintenance; however, the separate effects of long-term caloric restriction and exercise on total circulating ghrelin in humans is unknown.

Design—A 12-month randomized controlled trial comparing: i) dietary weight loss with a 10% weight loss goal ('diet'; n=118); ii) moderate-to-vigorous intensity aerobic exercise for 45 min/

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Author Contributions

CM, KEFS and AM had full access to all of the data in the study and take responsibility for its integrity and the accuracy of the analysis; CM, KEFS, CW, CMA, GLB, and AM established the study concept and design; KEFS, AK, KLC, GLB, and AM acquired data; CM, KEFS, LX, AM analyzed and interpreted data; CM and KEFS drafted the manuscript; KEFS, II, AK, KLC, CMA, GLB, AM provided critical revision of the manuscript for important intellectual content. LX and CM performed statistical analyses; AM obtained funding; LX provided administrative, technical, or material support; KEFS and AM supervised the study.

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day, 5 days/week ('exercise'; n=117); iii) dietary weight loss and exercise ('diet + exercise'; n=117); or iv) no-lifestyle-change control (n=87). Participants: 439 overweight or obese postmenopausal women (50-75 y).

Measurements—Fasting total serum ghrelin was measured by radioimmunoassay at baseline and 12 months. Fasting serum leptin, adiponectin, and insulin were also measured.

Results—Fasting total ghrelin significantly increased in the diet + exercise arm (+7.4%, $p=0.008$) but not in either the diet (+6.5%, $p=0.07$) or exercise (+1.0%, $p=0.53$) arms compared to control. Greater weight loss was associated with increased ghrelin concentrations, regardless of intervention. Neither baseline ghrelin nor body composition modified the intervention effects on changes in total ghrelin. The 12-month change in total ghrelin was inversely associated with changes in leptin, insulin, and insulin resistance, and positively associated with change in adiponectin.

Conclusions—Greater weight loss, achieved through a reduced calorie diet or exercise, is associated with increased total ghrelin concentrations in overweight or obese postmenopausal women.

Keywords

caloric restriction; lifestyle; satiety; hormones

Introduction

Ghrelin is an enteric peptide and the only known circulating appetite-stimulating (orexigenic) hormone.¹ It is implicated in short-term control of food intake as well as long-term body weight regulation.²

Ghrelin circulates in proportion to body weight (with higher levels of ghrelin seen with lower body weight), and generally responds in a compensatory fashion to weight change (increasing with weight loss, decreasing with weight gain).^{3,4} Ghrelin response to weight loss has been primarily examined in the settings of caloric restriction or surgical intervention, although altered ghrelin concentrations have been observed in response to weight loss through exercise.⁵⁻⁷ A recent study suggested that exercise-induced weight loss may increase fasting ghrelin and hunger sensations, but at the same time, it may also balance the orexigenic drive by increasing satiety after a meal and improving the sensitivity of the appetite control system.⁶ These observations may account, in part for the mixed findings with respect to the role of ghrelin changes on weight regain.⁸

To our knowledge, no studies have compared the separate and combined effects of long-term (12 months) caloric restriction and aerobic exercise on total circulating ghrelin concentrations in humans. This is an important issue; compensatory metabolic changes that accompany weight loss, including increased ghrelin, are hypothesized to contribute to weight regain and difficulty in long-term weight loss maintenance.^{9,10}

The purpose of the present study was to examine the independent and combined effects of 12 months of dietary weight loss and/or aerobic exercise on total ghrelin in overweight and

obese postmenopausal women, and to assess the degree to which changes are associated with body composition, select adipokines and other metabolic parameters including leptin, adiponectin, glucose, insulin, and insulin resistance as assessed by the homeostasis assessment model (HOMA), that may also have roles in regulating energy balance, hunger and satiety.^{11,12}

We hypothesized that ghrelin would significantly increase in the diet and diet + exercise groups compared with controls, and that the magnitude of increase would be proportional to the amount of weight lost.

Methods

Design

The Nutrition and Exercise in Women (NEW) study was a 12-month randomized controlled trial to test the effects of dietary weight loss and/or exercise on circulating hormones and other outcomes.¹³ Study procedures were reviewed and approved by the Fred Hutchinson Cancer Research Center Institutional Review Board in Seattle, WA. All participants provided written informed consent.

Setting and participants

Participants were overweight or obese (BMI ≥ 25 or BMI ≥ 30 kg/m² (≥ 23 kg/m² if Asian-American), postmenopausal women (50-75 y) from the greater Seattle area. They were recruited through media and mass mailings (Fig. 1). Exclusion criteria included: diagnosed diabetes; fasting blood glucose ≥ 126 mg/dL or use of diabetes medications; use of postmenopausal hormone therapy; history of invasive cancer within the past 10 years, excluding basal or squamous cell skin cancer; alcohol intake >2 drinks/day; current smoking; abnormal screening labs (e.g., hematocrit <32 or >48 , white blood cell count <3.0 or >15.0 , potassium <3.5 or >5.0 , creatinine >2.0) or contraindication to the study interventions for any reason (e.g., abnormalities on screening physical, abnormal exercise tolerance test, uncontrolled hypertension, history of cardiac arrest or stroke, recent (within 6 months) myocardial infarction, pulmonary edema, myocarditis, pericarditis, unstable angina, pulmonary embolism/deep vein thrombosis, orthostatic hypotension, moderate/severe asthma, uncontrolled arrhythmia, uncontrolled congestive heart failure, 3rd degree heart block, left bundle branch block, myocarditis, thrombophlebitis); participation in another structured weight loss program or use of weight loss medications; additional factors that might interfere with measurement of outcomes or with the success of the intervention (e.g., inability to attend facility-based sessions).

Randomization and interventions

Eligible women were randomized to: 1) dietary weight loss ('diet'; N=118); 2) moderate-to-vigorous intensity aerobic exercise ('exercise'; N=117); 3) combined diet and exercise ('diet + exercise'; N=117); or 4) control (no intervention) (N=87). Computerized random assignment, using permuted blocks randomization to achieve a proportionally smaller control group, was stratified according to BMI (≥ 30 or <30 kg/m²) and race/ethnicity.

The dietary weight loss intervention was a modification of the Diabetes Prevention Program¹⁴ and Look AHEAD¹⁵ lifestyle behavior change programs with goals of 1200-2000 kcal/day, <30% calories from fat, and 10% weight loss by 6 months with maintenance thereafter. Participants met individually with a dietitian at least twice, followed by weekly group meetings (5-10 women) for 6 months. Thereafter, they attended monthly group meetings in addition to biweekly phone or e-mail contact. Women completed daily food logs for at least 6 months or until they reached their 10% weight loss goal. Food logs, weekly weigh-ins, and session attendance were tracked to promote dietary adherence.

Participants who did not meet their weight loss goal by 6 months were encouraged to continue weight loss efforts, and were offered additional sessions; women who reached their goal were allowed to continue losing weight but were monitored to ensure that their BMI did not drop below 18.5 kg/m².

The exercise intervention progressed to 45 minutes of moderate-to-vigorous intensity exercise at a target heart rate of 70-85% observed maximum, 5 days/week by the 7th week. Participants attended 3 supervised sessions/week at the study facility and exercised 2 days/week at home. They recorded exercise mode, duration, peak heart rate, and perceived exertion at each session. Activities of 4 metabolic equivalents (METs)¹⁶ were counted towards the prescribed target.

Women randomized to diet + exercise received separate sessions and were instructed not to discuss diet during supervised exercise. The control group was instructed not to change their diet or exercise habits for 12 months.

Outcomes and follow-up

All study measures were obtained and analyzed by trained personnel who were blinded to the participants' randomization status.

We collected demographic information, medical history, and dietary intake (via a 120-item self-administered food frequency questionnaire)¹⁷ at baseline and 12 months. At both time points, participants wore pedometers (Accusplit, Silicon Valley, CA) for 7 consecutive days to determine an average daily step count. We assessed cardiorespiratory fitness (VO₂max) using a maximal graded treadmill test according to a modified branching protocol.¹⁸

BMI was calculated from weight and height, measured to the nearest 0.1 kg and 0.1 cm, respectively, with a balance beam scale and stadiometer. We measured waist circumference to the nearest 0.5 cm at the minimal waist. Body composition was measured on a DXA whole-body scanner (GE Lunar, Madison, WI).

Fasting venous blood samples (50 mL) were collected during clinic visits prior to randomization and at 12 months. Participants ate no food and drank only water for 12 hours prior to the blood draw, and were requested not to exercise for the preceding 24 hours. Blood was processed within 1 hour, centrifuged in refrigerated centrifuges kept between 4 and 8 degrees C. Samples were subsequently stored at -70°C. The blood specimens, collected between February, 2005 and July, 2009, were frozen until June, 2010 when the assays were performed; the samples had not been previously thawed.

Blood analysis

Blood samples were analyzed in batches with each participant's samples assayed simultaneously. The number of samples from each arm was approximately equal. Participant randomization dates were similar, and the sample order was random. Assays were performed at the University of Washington Northwest Lipid Research Laboratories.

We measured total, immune-reactive serum ghrelin by radioimmunoassay using the Millipore total human ghrelin assay (Millipore, Billerica, MA) with limits of detection of 110 to 10,000 pg/ml. The intra- and inter-assay coefficients of variation (CV) were 11.8% and 15.9%, respectively.

Serum insulin was quantified by a 48-hour, polyethylene glycol-accelerated, double antibody radioimmunoassay. The intra-assay CV was 4.5%. We used a Clinical Chemistry Autoanalyzer with the hexokinase method to quantify glucose. The intra- and inter-assay CVs were 1.1% and 3.5%, respectively. The homeostasis assessment model (HOMA-IR= fasting insulin (mU/L) $\times$ fasting glucose (mmol/L)/22.5) was calculated as a surrogate measure of whole-body insulin resistance.¹⁹ Adiponectin was measured in serum samples using a radioimmunoassay (Linco Research) with ¹²⁵I-labeled murine adiponectin and anti-adiponectin antibody; serum leptin was quantified using a Linco Research Human Leptin radioimmunoassay that utilizes ¹²⁵I-labeled Human Leptin, and the double antibody/PEG technique (Millipore, Billerica, MA). Intra- and inter-assay CVs for adiponectin were 8.4% and 9.8%, respectively; for leptin, they were 9.1% and 14.4%, respectively.

Statistical Analysis

For the main analyses, all available data were used without imputation for missing values. Pearson correlation coefficients were calculated between total ghrelin and baseline anthropometric and blood measures. Descriptive data were presented as means (standard deviation, SD). Due to non-normal distributions, blood parameters were log-transformed prior to further analysis, and these data are presented as geometric means with 95% confidence intervals (CI) unless otherwise indicated.

The mean change in fasting serum total ghrelin between baseline and 12 months in the diet, exercise, and diet + exercise arms were computed and compared to the change among controls using the generalized estimating equation (GEE) modification of linear regression to account for intra-individual correlation over time. The intervention effects were examined based on the assigned treatment at randomization, regardless of adherence or study retention (i.e., intent-to-treat). We used Bonferroni correction (two-sided alpha: 0.05/3=0.016) to adjust for multiple comparisons. The potential moderating effects of baseline ghrelin concentrations and BMI were also tested by including appropriate interaction terms in the models described above.

Subsequently, the effect of weight loss on total ghrelin was examined using a stratified analysis (<5%, 5-9.9%, and 10% weight loss)^{20,21} performed within each intervention arm. These analyses were adjusted for age, race/ethnicity and baseline BMI.

Unstandardized bivariate regression coefficients were also calculated for the change in fasting total ghrelin associated with other metabolic parameters (leptin, adiponectin, glucose, insulin, HOMA-IR) in women randomized to diet, exercise, or diet + exercise.

All statistical analyses were performed using SAS software version 9.1 (SAS Institute, Cary, NC).

Results

Participants

At 12 months, 398 of 438 participants completed physical exams and provided a blood sample, 397 underwent a DXA scan, and 371 completed a treadmill test; 39 did not complete the study (Fig.1). One participant randomized to diet + exercise was excluded from analysis due to missing baseline blood measures. A second individual (exercise) was excluded from the analyses because both baseline and 12 month ghrelin measurements were below the assay's limit of detection (<110.0 pg/mL). Baseline characteristics of study participants are shown in Table 1.

Intervention Fidelity

Data on intervention adherence, weight loss, and body composition changes in this trial have been previously reported.¹³ The mean weight change was -2.4% ($p=0.03$) in the exercise arm, -8.5% ($p<0.001$) in the diet arm, and -10.8% ($p<0.001$) in the diet + exercise arm, compared to -0.8% among controls. Women in all intervention groups significantly reduced waist circumference (exercise: $p=0.002$; diet and diet + exercise: $p<0.001$) and % body fat (all $p<0.001$) compared to controls. Lean mass decreased significantly in the diet arm ($p=0.005$) but was preserved in both the exercise arm and the diet + exercise arm (both $p>0.10$).

Percent of daily calories from fat decreased in both the diet and diet + exercise arms (-6.7% and -8.0% , respectively). In both diet groups, women attended an average of 27 diet counseling sessions (86%). Women randomized to exercise participated in moderate-to-vigorous activity for a mean (SD) of 163.3 (70.6) mins/week, while women randomized to diet + exercise participated for 171.5 (62.9) mins/week. Both groups significantly increased average pedometer steps/day and VO_2max compared to baseline.

Baseline Associations

At baseline, there were significant inverse correlations between fasting total ghrelin and BMI ($r = -0.34$, $p<0.0001$), waist circumference ($r = -0.33$, $p<0.0001$), % body fat ($r = -0.11$, $p=0.02$), fat mass ($r = -0.25$, $p<0.0001$), and lean mass ($r = -0.30$, $p<0.0001$). Total ghrelin was also inversely associated with fasting insulin ($r = -0.36$, $p<0.0001$), glucose ($r = -0.16$, $p<0.0006$), HOMA-IR ($r = -0.35$, $p<0.0001$), and leptin ($r = -0.20$, $p<0.0001$), and was positively associated with adiponectin ($r = 0.31$, $p<0.0001$). Ghrelin was not significantly associated with age.

Intervention Effects

Compared to controls, there was a significant increase in ghrelin among women randomized to diet + exercise (+100 pg/mL [7.4%], $p=0.008$). The change in ghrelin was not significantly different from controls among women randomized to diet (+87 pg/mL [6.5%], $p=0.07$) or to exercise (+14 pg/mL [1.0%], $p=0.53$) (Table 2). However, increases in ghrelin were significantly associated with a greater magnitude of weight loss in each study arm (Table 3).

Among women who lost 5-10% of body weight, ghrelin increased by a mean 26 pg/mL [2.6%] in the exercise arm ($p=0.32$ vs. controls), 60 pg/mL [4.2%] in the diet arm ($p=0.18$ vs. controls), and 108 pg/mL [8.4%] in those randomized to diet+ exercise ($p=0.03$ vs. controls). Among women who lost 10% of body weight, ghrelin increased 148 pg/mL [10.7%] in the diet arm ($p=0.006$ vs. controls) and 132 pg/mL [9.2%] in the diet + exercisers ($p=0.0011$ vs. controls). Too few women randomized to exercise lost 10% of body weight for valid analysis in this group. Higher concentrations of fasting ghrelin and greater % body fat at baseline did not modify the intervention effects (results not shown).

The intervention effects on other blood parameters have been previously published.^{22,23} Compared to controls, both diet alone and diet + exercise had significant effects on leptin (diet: -6.3 ng/mL, -27.1%; diet + ex: -9.5 ng/mL, -40.1%), adiponectin (diet: 1.2 μ g/mL, 9.5%; diet + ex: 0.8 μ g/mL, 6.6%), glucose (diet: -2.3 mg/dL, -2.4%; diet + ex: -2.7 mg/dL, -2.8%), insulin (diet: -32.8 μ IU/mL, -22.3%; diet + ex: -3.0 μ IU/mL, -24.0%), and HOMA-IR (diet: -0.63, -24.3%; diet + ex: -0.66, -26.4%). No significant effects of exercise alone on these analytes were observed. The observed twelve-month changes in ghrelin were inversely associated with the changes in leptin ($p<0.001$), insulin ($p<0.001$), glucose ($p=0.049$), and HOMA-IR ($p<0.001$), and positively associated with the change in adiponectin ($p=0.004$) (Table 4).

Discussion

Changes in circulating levels of total ghrelin are an important adaptation to weight loss that acts as a compensatory signal to restore body weight.^{9,10} Increased ghrelin has been observed following both diet-induced^{3,24} and exercise-induced⁷ weight loss, as well as in response to aerobic exercise training without significant weight change.²⁵ However, to our knowledge the separate and combined effects of dietary weight loss and exercise on ghrelin have not been directly compared in overweight and obese women.

We observed a significant rise in total ghrelin among women randomized to diet + exercise but not among women randomized to diet as we had expected. This may be due, in part, to the large variability in ghrelin responses to the dietary weight loss program, or to elements of meal timing and/or macronutrient composition²⁶ that were not assessed in the present study. Nevertheless, we observed a significant association between the magnitude of weight loss and the rise in serum ghrelin, consistent with previous reports.^{3,7,24} Furthermore, this trend was significant regardless of the behavioral weight loss strategy used.

It remains unclear which parameters of body composition or metabolism are sensed by the systems that regulate ghrelin during alterations in energy balance. Purnell et al.²⁷ previously reported a significant inverse association between the rise in 24-hour ghrelin after 3 months of weight loss and change in fat-free mass, independent of adiposity. Bivariate associations in the present study showed strong correlations between changes in ghrelin and changes in total weight, waist circumference, BMI, and % body fat, but not with changes in lean mass. We also observed associations with changes in leptin and adiponectin, as well as with insulin and insulin resistance in the direction that would be expected with weight loss, supporting ghrelin's role in long-term energy homeostasis;^{28,29} however, the timing of the change in ghrelin as it relates to alterations in body composition and in adipokines and other metabolic hormones implicated in energy regulation could not be determined. The change in ghrelin for a given magnitude of change in weight, lean mass, or % body fat did not differ significantly according to study arm. This suggests that overall weight loss, irrespective of the method through which it is achieved, is the primary driver of changes in fasting total ghrelin among overweight and obese postmenopausal women.

In a study of 78 obese women, Labayen et al.³⁰ reported that women with lower ghrelin levels were more resistant to fat mass loss during a 12-week lifestyle intervention compared to women with higher baseline ghrelin concentrations. In this study, we saw no evidence that weight loss over 12 months was significantly different between women with higher baseline ghrelin concentrations compared with lower, nor were the intervention effects on fasting ghrelin modified by baseline adiposity.

Ghrelin circulates in two major forms, acyl ghrelin and des-acyl ghrelin. The acylated form is considered to be the bioactive form that interacts with the ghrelin receptor (GHS-R1a),³¹ subsequently mediating ghrelin's effects on appetite and body weight regulation. However, the acylated form is unstable due to rapid degradation in blood, so the majority of ghrelin (>90%) circulates in the des-acylated form. The ratio of acyl and des-acyl ghrelin remain constant over a wide array of conditions that affect ghrelin levels, hence total ghrelin levels (acyl plus des-acyl) are a reasonable surrogate for the more difficult to measure acyl ghrelin.³²⁻³⁴ Recent evidence suggests that desacyl ghrelin may be even more responsive to weight change than acylated forms. In a sample of 552 young men participating in a 6 month structured exercise program, the observed increase in des-acyl ghrelin was significantly associated with the reduction in weight, fat mass, % body fat, and waist circumference, but not with the change in fat-free mass.³⁵ These findings are consistent with our observations of total ghrelin changes in our sample of overweight and obese postmenopausal women. The assay used in our study measured total ghrelin, thus, it reflects a mixture of acyl and desacyl ghrelin forms, which does represent a limitation of the present study.

The use of more specific assays to characterize ghrelin changes, as well as their time course during weight loss and weight loss maintenance, will make important contributions in future studies. Replication of these findings in other populations will also be informative since our findings may not be generalizable to other populations, including men. The present study also has a number of strengths, including its large size, adequate power to examine the separate and combined effects of dietary weight loss and aerobic exercise on ghrelin, and its long duration relative to the majority of previous studies of weight loss and ghrelin.

In summary, our results suggest that the adaptive response of ghrelin to weight loss is similar regardless of whether weight loss is achieved through caloric restriction alone, aerobic exercise, or a combination, and that changes in ghrelin are significantly associated with concurrent adaptive changes in leptin, adiponectin, insulin and insulin resistance. Whether different lifestyle behaviors have a significant effect on the magnitude of weight regain beyond 12 months remains an important area for future investigation.

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Flow of participants through the NEW study.

Table 1
Select baseline characteristics of randomized women

Variable	Mean (SD)
Age (y)	57.9 (5.0)
Ethnicity (%)	%
Non-Hispanic White	84.9
Non-Hispanic Black	8.0
Hispanic	2.8
Other (American Indian, Asian, or Unknown)	4.3
Weight (kg)	83.6 (11.8)
BMI (kg/m ²)	30.9 (4.0)
Waist circumference (cm)	94.6 (10.1)
Body fat (%)	47.2 (4.3)
	5727
Pedometer steps/day (7 d average)	(2273)
VO ₂ max (ml/kg/min)	22.9 (4.0)
Average Dietary Intake (FFQ)	
	1934
Total calories (kcal/day)	(638.4)
Relative % calories from fat	34.3 (6.9)
Relative % calories from carbohydrate	48.0 (8.2)
Ghrelin (pg/mL) *	1452 (623)
Leptin (ng/mL)	25.7 (10.5)
Adiponectin (µg/mL)	13.8 (5.9)
Insulin (µIU/mL)	12.9 (8.1)
Glucose (mg/dL)	96.4 (8.2)
HOMA-IR	3.12 (2.14)

Values derived from FFQ were truncated <600 kcal and >4000 kcal.

%calories from macronutrient= (total calories from macronutrient/total daily intake)

HOMA-IR= Homeostasis Assessment Model for Insulin Resistance.

* one participant excluded due to ghrelin below assay detection limit.

Table 2
Baseline and 12-month total ghrelin [geometric mean, 95% Confidence Interval (CI)],
according to intervention arm

	Total Ghrelin (pg/mL)							
	Baseline			12 months			Change	<i>p</i> *
	N	Mean	95% CI	N	Mean	95% CI	(%)	
Control	87	1290	1179, 1412	80	1313	1203, 1434	23 (1.8%)	ref
Exercise	116	1336	1229, 1451	105	1350	1247, 1462	14 (1.0%)	0.53
Diet	118	1332	1248, 1422	105	1419	1319, 1527	87 (6.5%)	0.07
Diet + Exercise	116	1359	1259, 1466	108	1459	1351, 1575	100 (7.4%)	0.008

* GEE model comparing changes between each intervention group and control, adjusted for age, race/ethnicity and baseline BMI.

Table 3
12-month change [geometric mean (95% CI)] in total ghrelin (pg/mL), stratified by % weight loss

Total Ghrelin (pg/mL)				
		Baseline	Change	
	N	Geo Mean (95% CI)	Geo Mean (95% CI)	%
CONTROL	80	1319 (1202-1448)	-6 (-58,46)	0.5
EXERCISE				
0% loss (no change or gain)	29	1546 (1336, 1788)	-135 (-232, -38)	8.7
<5% loss	46	1343 (1103, 1636)	8 (-67, 51)	0.6
5-10% loss	30	1160 (1015, 1325)	26 (-42, 94)	2.2
Ptrend			0.01	
DIET				
0% loss (no change or gain)	10	1066 (842, 1348)	51 (-44, 145)	4.8
<5% loss	18	1362 (1147, 1619)	-92 (-147, -9)	6.8
5-10% loss	27	1416 (1262, 1588)	60 (-32, 152)	4.2
10% loss	49	1380 (1235, 1541)	148 (42, 254)	10.7
Ptrend			0.0023	
DIET+EXERCISE				
0% loss (no change or gain)	4	1089 (787, 1508)	-33 (-73, 7)	3.0
<5% loss	14	1241 (1009, 1526)	44 (-143, 55)	3.6
5-10% loss	21	1286 (1024, 1614)	108 (22, 194)	8.4
10% loss	69	1438 (1320, 1566)	132 (70, 194)	9.2
Ptrend			0.0041	

ptrend across weight loss groups, within each intervention arm; adjusted for age, race/ethnicity and baseline BMI.

Table 4
Bivariate regression coefficients^a for unit change in fasting total ghrelin vs. change in metabolic parameters, adjusted for age, baseline BMI, race/ethnicity, and intervention arm, excluding controls

Variable	12-MO CHANGE		
	Regression Coefficient	Std Error	p
Weight (kg)	-15.5	3.0	<0.0001
BMI (kg/m ²)	-46.2	7.9	<0.0001
Waist circumference (cm)	-10.3	2.3	<0.0001
% Body Fat	-22.5	4.0	<0.0001
Lean Mass (kg)	-2.65	8.8	0.763
Insulin (μU/mL)	-12.8	2.7	<0.0001
Glucose (mg/dL)	-3.44	2.3	0.133
HOMA-IR	-44.3	10.0	<0.0001
Leptin (ng/mL)	-10.7	2.0	<0.0001
Adiponectin (μg/mL)	10.5	4.6	0.024

^aRegression coefficients are not standardized.