Effect of Lifestyle Intervention on Cardiometabolic Risk Factors: Results of the POWER-UP Trial

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Abstract

Objective—To investigate the effects of three weight loss interventions on cardiometabolic risk factors including blood pressure, lipids, glucose, and markers of insulin resistance and inflammation. We also examined whether categories of incremental weight change conferred greater improvements on these parameters.

Methods—This 2-year trial was conducted in a primary care setting and included 390 obese participants who were randomly assigned to one of three interventions: 1) Usual Care [quarterly primary care provider (PCP) visits that included education about weight management]; 2) Brief Lifestyle Counseling (quarterly PCP visits plus monthly behavioral counseling provided by a trained auxiliary healthcare provider); or 3) Enhanced Brief Lifestyle Counseling (the same care as described for the previous intervention, plus weight loss medications or meal replacements). The primary outcome was change in cardiometabolic risk factors among groups.

Results—At month 24, participants in Enhanced Brief Lifestyle Counseling lost significantly more weight than those in Usual Care (4.6 vs. 1.7 kg), with no other significant differences between groups. Enhanced Brief Lifestyle Counseling produced significantly greater improvements in HDL cholesterol and triglyceride levels at one or more assessments, compared with the other two interventions. Markers of insulin resistance also improved significantly more in this group throughout the 2 years. Collapsing across the three groups, greater weight loss was associated with greater improvements in triglycerides, HDL cholesterol, and markers of insulin resistance and inflammation at month 24, but was not significantly associated with reductions in blood pressure, total cholesterol, and LDL cholesterol at any time.

Conclusions—Enhanced Brief Lifestyle Counseling, which produced the largest weight loss, was generally associated with the greatest improvements in cardiovascular risk factors. These findings suggest that an intensive weight loss intervention, delivered in a primary care setting, can help obese individuals improve some cardiometabolic risk factors.

Keywords

lifestyle intervention; weight loss; cardiometabolic risk factors; lipids; insulin resistance

Introduction

Weight loss has been found to ameliorate several modifiable cardiovascular disease (CVD) risk factors. It is associated with: reductions in blood pressure; improved glycemic control; decreased total cholesterol, LDL cholesterol, and triglycerides; and increased HDL cholesterol.[1–3] Greater weight loss typically confers larger improvements in cardiometabolic risk factors,[3] but even modest weight loss of 5–10% has been shown to produce beneficial effects.[3–5]

Numerous studies have demonstrated the efficacy of behavioral interventions to promote weight loss and improve health outcomes in overweight and obese adults.[3–7] However, few trials have been conducted in routine clinical settings.[8–11] To address this need, the National Heart, Lung, and Blood Institute (NHLBI) recently supported three independent studies to evaluate the effectiveness of weight loss interventions delivered in primary care. The three participating institutions formed a collaborative research group to undertake the Practice-based Opportunities for Weight Reduction (POWER) trials.[12] The three individual studies included POWER-UP (University of Pennsylvania), POWER Hopkins (Johns Hopkins), and Be Fit, Be Well (Harvard University/Washington University).[12] Common components were used in all three studies to standardize comparisons, but each site implemented its own behavioral intervention.[13–15]

The POWER-UP trial provided opportunity to examine the effects of modest weight loss on cardiometabolic risk factors in obese individuals with increased risk for CVD. This 2-year trial included obese men and women who were randomly assigned to a usual care condition or one of two lifestyle interventions of varying intensity (described below). POWER-UP's methods and main results have been published previously.[13] This paper expands upon our previous report of the effects of the three interventions on traditional cardiometabolic risk factors.[13] We hypothesized that both lifestyle interventions would result in greater improvements in blood pressure, lipids, glucose, and markers of insulin resistance and inflammation than the usual care intervention. We also examined whether greater weight change would confer greater improvements in these parameters.

Methods and Procedures

Participants

Three hundred and ninety obese adults were recruited from six primary care practices in the University of Pennsylvania Health System to participate in the POWER-UP trial. Eligible participants were aged 21 yr and older, had a body mass index (BMI) of 30–50 kg/m², an elevated waist circumference (102 cm for men; 88 cm for women), and at least one other criterion for the metabolic syndrome.[16] Main exclusion criteria included having: uncontrolled blood pressure; recent cardiovascular events; weight change 5% over the preceding 6 months; active participation in a weight loss program; prior or planned use of bariatric surgery; serious co-morbid conditions (e.g., severe psychiatric illness, end-stage renal disease); use of medications known to cause significant (5%) long-term changes in weight; or pregnancy. The study was approved by the Institutional Review Board at the University of Pennsylvania, and all participants provided written informed consent.

Interventions

Eligible participants were randomly assigned to one of three interventions, as reported in detail in the main outcomes paper.[13] Interventions included: 1) Usual Care, in which participants met quarterly with their PCP and received approximately 5–7 minutes of education about weight management; 2) Brief Lifestyle Counseling (Brief LC), which included the quarterly PCP visit and 10–15 minutes of monthly behavioral counseling delivered by an auxiliary health care provider (typically a medical assistant) who was trained as a lifestyle coach; and 3) Enhanced Brief Lifestyle Counseling (Enhanced Brief LC), in which pharmacologic therapy (sibutramine or orlistat) or meal replacements were added to the same quarterly PCP visit and behavioral intervention to further enhance weight loss. (Participants who were initially taking sibutramine were switched to orlistat or meal replacements after this medication was withdrawn from the U.S. market in October 2010 amid concerns of increased risk of CVD events. This option was also offered in November 2009 after the Food and Drug Administration [FDA] issued an alert concerning the safety of sibutramine.)

All participants were prescribed the same diet and physical activity goals but were provided different amounts of behavioral support to reach them. Participants who weighed <250 lb were prescribed a balanced diet of 1200 to 1500 kcal/d (1500 to 1800 kcal/d for participants who weighed 250 lb), which consisted of approximately 15 to 20% kcal from protein, 20 to 35% kcal from fat, and the remainder from carbohydrate. All participants were instructed to gradually increase their physical activity to 180 minutes per week and were given a pedometer, a calorie-counting book,[17] and handouts from NHLBI's Aim for a Healthy Weight.[18]

Outcomes and Measurements

The primary outcome was the change in cardiometabolic risk factors including blood pressure, lipids, fasting glucose, markers of insulin resistance, and high-sensitivity C-reactive protein (hs-CRP). As a secondary outcome, we quantified the change in cardiometabolic risk factors associated with increasing categories of weight change.

Measurements were obtained in a standardized fashion by trained, certified staff members at baseline and months 6, 12, and 24.[13,19] Weight was measured on a calibrated scale (Tanita BWB-800), and height was measured using a wall-mounted stadiometer. Lipids, glucose, insulin, and hs-CRP were measured following a 9-hour overnight fast by standardized methods described previously.[19–20] All laboratory assays were performed at the William Pepper Laboratory of Clinical Medicine at the Hospital of the University of Pennsylvania. Insulin resistance was estimated using the homeostasis model assessment (HOMA-IR index) formula ([fasting insulin (uU/mL) * fasting glucose (mmol/L)]/22.5), with greater insulin resistance indicated by higher HOMA-IR values.[21] Demographic data including gender, age, race/ethnicity, educational level, and income level were collected by a self-report questionnaire at baseline.

Statistical Analysis

The distributions of baseline characteristics were examined for each intervention group. Continuous variables were reported as means [standard deviations (SD)] when normally distributed or as medians [interquartile range (IQR)] when the distribution was not normal. Categorical variables were reported as frequencies.

Changes in cardiometabolic outcomes at 12 and 24 months in the intention-to-treat (ITT) population were compared with the use of repeated-measures, linear mixed-effects models (for continuous outcomes) and generalized-estimating-equation models (for categorical outcomes), which controlled for age, sex, race or ethnic group, and study site. Separate mixed-effects models were fit for each outcome. Main effects of treatment group and time, as well as the treatment group x time interaction effect, were examined in the mixed-effect models using the unstructured covariance structure.

We also examined the relationships between categories of weight change and change in cardiometabolic risk factors. Participants were divided into the following categories based on their weight change from baseline to months 12 and 24: 1) gained weight or remained at baseline weight; 2) weight loss 5%; 3) weight loss >5% to 10%; and 4) weight loss >10%. Participants from all three interventions were pooled for this analysis, with adjustment for treatment condition, gender, race and age. Separate linear regression models were fit for weight and the cardiometabolic variables.

Results

Baseline Characteristics

The baseline characteristics of participants in each intervention group were similar and have been described in detail.[13] As shown in Table 1, participants were predominantly non-Hispanic, white women and had a mean (±SD) age of 51.5 (11.5) years, body weight of 107.7 (18.3) kg, and BMI of 38.5 (4.7) kg/m^2. Participants in the Usual Care group were significantly heavier and had a greater waist circumference than those in the Enhanced Brief LC group (p<0.05) but did not differ significantly from those in the Brief LC group. Fasting glucose levels were also significantly higher in the Usual Care group, relative to Enhanced Brief LC (p<0.05). Two hundred and eighty-six (73.3%) participants provided complete cardiometabolic data at month 24.

Weight Loss

As previously reported,[13] mean (±SE) weight losses at month 12 were 2.3 (0.6), 3.4 (0.6), and 7.1 (0.6) kg for the Usual Care, Brief LC, and Enhanced Brief LC groups, respectively. Weight loss differed significantly between Enhanced Brief LC and Usual Care at this time (shown in Table 2), as well as between the two lifestyle groups. By month 24, weight regain occurred in all groups, although weight loss remained significantly greater in Enhanced Brief LC than in Usual Care (p<0.05).

Weight change at months 12 and 24 was reanalyzed in the Enhanced Brief LC group after excluding the 44 participants who received sibutramine at any time (data not shown). As reported in the main outcomes paper,[13] weight loss was very similar in this group at both time points in both the full ITT and modified ITT populations.

Changes in Cardiometabolic Risk Factors

Participants in Enhanced Brief LC achieved the greatest improvements in glycemic parameters (shown in Table 2). Both fasting insulin levels and HOMA-IR declined significantly more at months 12 and 24 in these participants than in the two other conditions, indicating improved insulin resistance. Fasting glucose also declined significantly more in Enhanced Brief LC at month 12, compared to Usual Care, but this benefit was not sustained at month 24. Participants who received Enhanced Brief LC also had significantly greater improvements in HDL cholesterol and triglyceride levels at one or more assessments compared with the other two groups. Substantial reductions in triglycerides (20 mg/dl) were observed in all groups over time, but they did not differ significantly between groups at month 24. LDL cholesterol and other markers of atherogenic particles (i.e., non-HDL cholesterol) declined modestly (approximately 5–15 mg/dl) in all groups at some periods. Blood pressure was essentially unchanged from baseline values in all groups.

Changes in traditional cardiometabolic risk factors (blood pressure, lipids, and glucose) also were analyzed in the modified ITT population that excluded participants who had used sibutramine. These findings (also reported in the main outcomes paper) were very similar to those for the entire Enhanced Brief LC group.[13] Since the magnitude of weight loss was comparable in the Enhanced Brief LC group, with and without participants who used sibutramine, we did not perform additional analyses on markers of atherogenic particles, insulin resistance, or inflammation.

Relationship of Changes in Weight and Cardiometabolic Risk Factors

As shown in Table 3, participants were divided into four categories of weight change to further quantify the associations between incremental percent weight change and improvements in cardiometabolic risk factors. Greater improvements in triglycerides, HDL cholesterol, and hs-CRP were observed with increasing categories of weight loss. Insulin resistance, as indicated by HOMA-IR, also improved with greater weight loss. In contrast, the magnitude of improvement in blood pressure, total cholesterol, and LDL cholesterol did not significantly differ across categories of weight change. Glucose transiently improved in one of the higher categories of weight loss at month 12, but this effect was not sustained, and there were no differences among groups at month 24. Incremental weight loss had minimal effect on either systolic or diastolic blood pressure.

Discussion

The principal finding of this study was that lifestyle interventions delivered in primary care settings helped patients achieve modest weight losses that were associated with improvements in cardiometabolic risk factors. Enhanced Brief LC, in which meal

replacements or weight loss medications were used in conjunction with quarterly PCP visits and monthly brief lifestyle coaching, conferred the largest weight losses and generally the greatest improvements in cardiometabolic risk factors. The largest improvements were seen in markers of insulin resistance, as indicated by reduced fasting insulin levels and decrements in HOMA-IR. These benefits were sustained throughout the duration of the study. Significant changes also were observed in HDL cholesterol over time in the Enhanced Brief LC group.

All three interventions produced modest reductions in total and LDL cholesterol, triglycerides, and hs-CRP at one or more times during the trial. Net beneficial effects on lipids and inflammatory markers generally were maintained, despite some weight regain in all groups. In contrast, systolic and diastolic blood pressure were essentially unchanged in all groups.

Our findings of modest reductions in lipid parameters and minimal changes in blood pressure are similar to those reported in the POWER-Hopkins study, in which obese participants with at least one cardiovascular risk factor were randomly assigned to a self-directed control group or to one of two behavioral interventions. Weight-loss counseling was provided remotely (via phone, email, or web-based applications) or in-person, using group and individual sessions.[14] Weight loss at month 24 in the two intervention groups (−4.6 and −5.1 kg, respectively) was similar to that observed in our Enhanced Brief LC participants. We note that baseline values for blood pressure and lipids were near normal in POWER-UP and POWER Hopkins, thus, limiting the capacity to assess the potential benefits of weight loss on these outcomes.

To better describe the associations between weight change and improvements in cardiometabolic risk factors, we also examined the effects of incremental categories of weight loss, irrespective of the treatment condition. Although it is generally accepted that weight loss 5% in obese individuals induces favorable changes in numerous CVD risk factors,[1–5] we observed smaller changes in several metabolic parameters than others have previously described.[3] In the Look AHEAD (Action for Health in Diabetes) study, weight loss of 5 to <10% (compared with 2%) was associated with increased odds of achieving clinically significant improvements in systolic and diastolic blood pressure, HbA$_{1c}$, glucose, triglycerides, LDL cholesterol, and HDL cholesterol.[3] Larger weight losses (10%) were associated with greater benefits in all of these parameters, with the exception of LDL cholesterol. In contrast, we did not observe significant improvements in blood pressure, total cholesterol, LDL cholesterol, and fasting glucose with greater weight loss (i.e., 5% and 10%, compared with <5%) in the present study. Total and LDL cholesterol levels tended to improve with weight loss, but there were inconsistencies across graduated categories of weight change. (The lack of a dose-response relationship may have been attributable to the differential use of cholesterol medications in the four weight loss categories, but we were not able to confirm this hypothesis.) The Look AHEAD study included over 5,100 participants and was better powered to detect differences in cardiometabolic risk among categories of weight change. Moreover, as noted previously, POWER-UP participants had near-normal baseline values for many of the cardiometabolic variables examined.

Strengths of the present study include its diverse population, which is generally representative of primary care practices across the country and potentially makes our results generalizable to the broad population. The study also had a very high rate of adherence and follow-up over its 2-year duration, suggesting that it is possible to engage patients in behavioral weight loss programs delivered in primary care practice. Our investigation also had limitations, principally that it was not powered to detect significant differences between groups in cardiometabolic risk factors. (The study was powered on differences in weight

loss.) Thus, our nonsignificant relationships between weight loss and improvements in blood pressure, glucose, and lipids should be interpreted with caution.

Despite these limitations, clinically meaningful improvements were observed in the present study in measures of insulin resistance, triglycerides, HDL cholesterol, and hs-CRP. These results reaffirm the important benefits of providing lifestyle counseling to appropriate patients to induce weight loss. The Enhanced Brief LC approach, developed in POWER-UP, provides a potentially valuable means of achieving clinically significant weight loss (5%) in primary care practice.

Acknowledgments

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Table 1

Baseline characteristics by intervention group in the POWER-UP Trial (n = 390).

Characteristic	Usual Care (n=130)	Brief LC (n=131)	Enhanced Brief LC (n=129)	All (n=390)
Women, n (%)	98 (75.4)	110 (84.0)	103 (79.8)	311 (79.7)
Race/Ethnicity[1]				
White, n (%)	81 (62.3)	75 (57.3)	74 (57.4)	230 (59.0)
African-American, n (%)	46 (35.4)	52 (39.7)	52 (40.3)	150 (38.5)
Hispanic, n (%)	6 (4.6)	6 (4.6)	6 (4.7)	18 (4.6)
Age, yr	51.7 (12.1)	52.0 (12.2)	51.0 (10.1)	51.5 (11.5)
Weight, kg	111.2 (20.0)[2]	106.3 (17.3)	105.4 (17.2)	18 (4.6)
BMI, kg/m^2	39.0 (4.8)	38.5 (4.6)	37.8 (4.7)	38.5 (4.7)
Waist circumference, cm	119.8 (13.9)[2]	117.1 (11.9)	115.9 (11.7)	117.6 (12.6)
Total cholesterol, mg/dl	181.7 (46.8)	185.5 (35.9)	189.1 (35.5)	185.5 (39.7)
Triglycerides, mg/dl	120.5 (58.9)	120.7 (69.5)	111.5 (59.4)	117.5 (62.7)
LDL cholesterol, mg/dl	112.1 (38.7)	116.0 (31.0)	118.1 (31.3)	115.4 (33.8)
HDL cholesterol, mg/dl	44.0 (12.7)	45.4 (12.9)	48.6 (14.9)	46.0 (13.6)
Non-HDL cholesterol, mg/dl	150.6 (42.2)	155.0 (36.8)	148.0 (33.3)	151.2 (37.7)
Total/HDL cholesterol ratio	4.8 (1.6)	4.8 (1.6)	4.5 (1.3)	4.7 (1.5)
Glucose, mg/dl	112.3 (40.1)[2]	106.2 (32.2)	96.3 (22.5)	104.9 (32.9)
Insulin, uU/ml	12.8 (8.5)	13.8 (11.2)	14.0 (10.1)	13.5 (10.0)
HOMA	3.3 (2.3)	3.4 (2.6)	3.6 (3.7)	3.4 (2.9)
hs-CRP, mg/l	8.1 (6.5)	7.1 (5.9)	6.6 (6.8)	7.3 (6.4)
Systolic blood pressure, mm Hg	120.9 (18.4)	122.8 (15.6)	120.5 (14.7)	121.4 (16.3)
Diastolic blood pressure, mm Hg	76.0 (10.4)	75.9 (11.3)	76.5 (9.7)	76.2 (10.4)
Blood pressure medication	43 (33.1)	42 (32.1)	44 (34.1)	129 (33.1)
Lipid-lowering medication	81 (62.3)	77 (58.8)	83 (64.3)	241 (61.8)
Current smoking, n (%)	10 (7.7)	16 (12.3)	12 (9.3)	38 (9.8)

Note: For all continuous variables, values shown are means (SD); p>0.05 for all comparisons unless otherwise noted.

[1] Race and ethnicity were self-reported.

[2] P<0.05 for the comparison between Usual Care and Enhanced Brief LC.

Table 2

Estimated mean change in anthropometric and cardiometabolic parameters over 24 months for the modified intention-to-treat (ITT) population.

Variable	Usual Care	Brief LC	Enhanced Brief LC
Weight, kg			
Month 6	−2.0 (0.5)	−3.5 (0.5)[1]	−6.6 (0.5)[2,3]
Month 12	−2.3 (0.6)	−3.4 (0.6)	−7.1 (0.6)[2,3]
Month 24	−1.7 (0.7)	−2.9 (0.7)	−4.6 (0.7)[2]
Systolic blood pressure, mm Hg			
Month 6	−0.7 (1.3)	0.3 (1.3)	−0.1 (1.2)
Month 12	1.2 (1.3)	0.8 (1.3)	0.2 (1.2)
Month 24	1.5 (1.6)	1.5 (1.6)	−1.1 (1.6)
Diastolic blood pressure, mm Hg			
Month 6	−0.3 (0.9)	−0.2 (0.9)	−0.5 (0.8)
Month 12	−0.5 (0.8)	−0.8 (0.8)	−1.4 (0.8)
Month 24	0.2 (0.9)	−0.2 (0.9)	−0.8 (0.9)
Triglycerides, mg/dl			
Month 6	−13.7 (5.7)	−21.6 (5.8)	−25.9 (5.6)
Month 12	−16.5 (5.4)	−22.9 (5.5)[1]	−38.6 (5.4)[2,3]
Month 24	−21.6 (6.0)	−29.7 (6.1)	−33.4 (6.0)
Total cholesterol, mg/dl			
Month 6	−11.4 (3.2)	−11.2 (3.2)	−7.7 (3.1)
Month 12	−11.1 (3.1)	−10.1 (3.2)	−9.3 (3.1)
Month 24	−14.3 (3.3)	−16.6 (3.3)	−6.9 (3.3)[3]
LDL cholesterol, mg/dl			
Month 6	−8.5 (2.8)	−7.1 (2.9)	−2.3 (2.8)
Month 12	−7.9 (2.8)	−5.0 (2.8)	−3.4 (2.8)
Month 24	−11.5 (2.8)	−11.6 (2.9)	−4.1 (2.8)
HDL cholesterol, mg/dl			
Month 6	−0.4 (0.7)	−0.0 (0.7)	−0.5 (0.7)
Month 12	−0.2 (0.7)	−0.8 (0.7)	1.4 (0.7)[3]
Month 24	0.5 (0.8)	0.7 (0.8)	3.0 (0.8)[2,3]
Mean non-HDL cholesterol, mg/dl			
Month 6	−10.3 (3.0)	−10.4 (3.1)	−7.6 (3.0)
Month 12	−10.3 (3.1)	−9.6 (3.1)	−10.3 (3.0)
Month 24	−13.9 (3.1)	−17.5 (3.2)	−10.0 (3.1)
Total/HDL cholesterol ratio			
Month 6	−0.3 (0.1)	−0.3 (0.1)	−0.20 (0.1)
Month 12	−0.3 (0.1)	−0.3 (0.1)	−0.38 (0.1)
Month 24	−0.4 (0.1)	−0.5 (0.1)	−0.5 (0.1)
Glucose, mg/dl			

Variable	Usual Care	Brief LC	Enhanced Brief LC
Month 6	−0.0 (2.6)	−8.1 (2.7)[1]	−3.1 (2.6)
Month 12	1.4 (2.2)	−3.8 (2.2)	−5.9 (2.2)[2]
Month 24	0.5 (3.1)	−0.0 (3.1)	−4.8 (3.1)
Insulin, uU/ml			
Month 6	−1.2 (0.9)	−1.8 (0.9)	−4.6 (0.8)[2,3]
Month 12	−0.9 (1.1)	−1.9 (1.1)	−5.3 (1.1)[2,3]
Month 24	2.5 (1.3)	1.5 (1.3)	−3.7 (1.3)[2,3]
HOMA			
Month 6	−0.1(0.3)	−0.3 (0.3)	−1.1 (0.3)[2]
Month 12	−0.2 (0.3)	−0.6 (0.3)	−1.5 (0.3)[2,3]
Month 24	0.9 (0.4)	0.7 (0.4)	−1.1 (0.4)[2,3]
hs-CRP, mg/l			
Month 6	−0.1 (0.6)	−0.3 (0.6)	−1.3 (0.5)[2]
Month 12	−1.4 (0.6)	−0.7 (0.6)	−1.4 (0.6)
Month 24	−1.5 (0.6)	−1.5 (0.6)	−0.4 (0.7)

Note: Values shown are means (SE). The data for the three intervention groups are model-based estimates for the intention-to-treat population. All models were adjusted for age, gender, race, and treatment site.

[1] p < 0.05 for pairwise comparison between Usual Care and Brief Lifestyle Counseling

[2] p < 0.05 for pairwise comparison between Usual Care and Enhanced Brief Lifestyle

[3] p < 0.05 for pairwise comparison between Brief Lifestyle Counseling and Enhanced Brief Lifestyle Counseling

Table 3

Estimated mean change in metabolic variables by category of weight change at months 12 and 24 (n = 390).

Change in Metabolic Variable from Baseline	Categories of Weight Change			
	Baseline weight or above	Weight loss < 5%	Weight loss 5 to < 10%	Weight loss 10%
Systolic blood pressure, mm Hg				
Month 12	–0.7 (1.7)[1]	2.8 (1.4)[1]	–0.1 (1.6)[1]	–0.7 (2.0)[1]
Month 24	–1.8 (1.9)[1]	1.3 (1.8)[1]	–2.5 (2.3)[1]	–0.7 (2.7)[1]
Diastolic blood pressure, mm Hg				
Month 12	–1.4 (1.1)[1,2]	0.2 (0.9)[1]	–0.6 (1.1)[1]	–3.8 (1.3)[2]
Month 24	–2.0 (1.1)[2]	0.8 (1.1)[1]	–1.4 (1.4)[1,2]	–1.2 (1.6)[1,2]
Total cholesterol, mg/dl				
Month 12	–9.0 (3.8)[1]	–13.5 (3.3)[1]	–11.10 (4.0)[1]	–12.1 (5.0)[1]
Month 24	–16.2 (3.6)[2]	–12.7 (3.6)[1,2]	–2.3 (4.5)[1]	–18.1 (5.2)[2]
Triglycerides, mg/dl				
Month 12	–12.0 (6.1)[1]	–25.4 (5.4)[1,2]	–35.5 (6.5)[2,3]	–53.6 (8.0)[3]
Month 24	–11.9 (6.6)[1]	–20.1 (6.5)[1]	–21.2 (8.2)[1]	–56.0 (9.6)[2]
LDL cholesterol, mg/dl				
Month 12	–6.6 (3.4)[1]	–7.8 (3.0)[1]	–3.7 (3.6)[1]	–3.2 (4.4)[1]
Month 24	–14.1 (3.1)[2]	–10.1 (3.1)[1,2]	–1.9 (3.9)[1]	–10.9 (4.5)[1,2]
HDL cholesterol, mg/dl				
Month 12	–0.0 (0.9)[1]	–0.6 (0.7)[1]	–0.3 (0.9)[1]	1.8 (1.1)[1]
Month 24	–0.5 (0.9)[1]	0.9 (0.9)[1,2]	2.7 (1.1)[2]	3.8 (1.3)[3]
Glucose, mg/dl				
Month 12	0.8 (2.6)[1]	–0.8 (2.3)[1]	–7.8 (2.7)[2]	–5.3 (3.3)[1,2]
Month 24	1.9 (3.6)[1]	0.9 (3.6)[1]	–5.5 (4.5)[1]	–2.8 (5.2)[1]
HOMA				
Month 12	0.2 (0.4)[1]	–0.6 (0.3)[1,2]	–0.9 (0.4)[2]	–2.1 (0.5)[3]
Month 24	1.2 (0.4)[1]	0.1 (0.4)[2]	–0.7 (0.6)[2,3]	–1.0 (0.6)[3]
hs-CRP, mg/l				
Month 12	–0.7 (0.8)[1]	–0.6 (0.6)[1]	–1.8 (0.8)[1]	–2.5 (1.0)[1]
Month 24	–0.2 (0.7)[1]	–1.4 (0.7)[1,2]	–3.2 (0.8)[2]	–2.9 (1.1)[2]

[*] Values shown are means (SE). The data for the categories of weight loss are model-based estimates that are adjusted for treatment condition, gender, race, and age. Missing data at each time point was assumed to be 0% change. Means with different superscripts

[1] differ significantly from each other (p<0.05).

[2] Means that share a common superscript

[3] do not differ significantly.