Effects of moderate-fat (from monounsaturated fat) and low-fat weight-loss diets on the serum lipid profile in overweight and obese men and women[1–3]

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ABSTRACT

Background: Little evidence of the effects of moderate-fat (from monounsaturated fat) weight-loss diets on risk factors for cardiovascular disease exists because low-fat diets are typically recommended. Previous studies in weight-stable persons showed that a moderate-fat diet results in a more favorable lipid and lipoprotein profile (ie, lower serum triacylglycerol and higher HDL cholesterol) than does a low-fat diet.

Objective: We evaluated the effects of energy-controlled, low-fat and moderate-fat diets on changes in lipids and lipoproteins during weight loss and subsequent weight maintenance.

Design: We conducted a parallel-arm study design in overweight and obese [body mass index (in kg/m^2): 29.8 $\pm$ 2.4] healthy men and women (n = 53) assigned to consume a low-fat (18% of energy) or moderate-fat (33% of energy) diet for 6 wk to achieve weight loss, which was followed by 4 wk of weight maintenance. All foods were provided and body weight was monitored to ensure equal weight loss between groups.

Results: The moderate-fat diet elicited favorable changes in the lipoprotein profile. Compared with baseline, HDL cholesterol was unchanged, whereas triacylglycerol and the ratios of total and non-HDL cholesterol to HDL cholesterol were lower at the end of the weight-maintenance period in the moderate-fat diet group. Despite similar weight loss, triacylglycerol rebounded, HDL cholesterol decreased, and the ratios of total and non-HDL cholesterol to HDL cholesterol did not change during the 10-wk interval in the low-fat diet group.

Conclusions: A moderate-fat weight-loss and weight-maintenance diet improves the cardiovascular disease risk profile on the basis of favorable changes in lipids and lipoproteins. There is merit in recommending a moderate-fat weight-loss diet. *Am J Clin Nutr* 2004;79:204–12.

KEY WORDS Weight loss, moderate-fat diet, monounsaturated fat, peanuts, peanut butter, lipids, lipoproteins

INTRODUCTION

The increasing prevalence of overweight and obesity constitutes a major public health crisis in the United States because of the associated increase in risk of major chronic diseases, such as coronary heart disease (1–4) and diabetes (5, 6). Lifestyle behaviors, including diet and exercise, are the cornerstone of weight control.

Typically, a diet that provides ≤30% of total calories as fat is recommended for weight loss (4), although there is an ongoing discussion about what the ideal macronutrient profile should be to optimize weight loss and maintenance of weight loss (7). Whereas weight loss has many favorable effects on risk factors for numerous chronic diseases, during the maintenance of body weight, low-fat (<25% of energy) or very-low-fat (<20% of energy) diets increase triacylglycerol concentrations, decrease HDL-cholesterol concentrations, and, in some instances, increase plasma glucose concentrations [*see* review by Parks and Hellerstein (8)]. In contrast, a moderate-fat diet (≈25–35% of energy), especially one that is higher in dietary fiber, results in lower triacylglycerol and higher HDL-cholesterol concentrations and, thus, is not associated with the untoward effects mentioned above (9). There is no dispute that weight loss alone favorably affects these risk factors (4, 10). Unfortunately, little is known about the effects of a higher-fat weight-loss diet on plasma lipids and lipoproteins. Gumbiner et al (11) reported greater beneficial effects from a weight-loss formula diet, rich in monounsaturated fatty acids (MUFAs), on lipids and lipoproteins in obese patients with type 2 diabetes than from a low-fat, high-carbohydrate, weight-reducing formula diet. Although this study provides suggestive evidence that a higher-fat weight-loss diet potentiates the effects of weight loss, additional research is needed in a cohort that is generalizable to the population at large.

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Thus, the current study was conducted to evaluate the effects of a low-fat and a moderate-fat, whole-food weight-loss diet on plasma lipids and lipoproteins in overweight and obese healthy subjects with the use of a model in which weight loss was controlled. We hypothesized that a moderate-fat, high-MUFA diet would lower serum concentrations of triacylglycerol during weight loss without affecting HDL cholesterol, whereas a low-fat diet would lower both triacylglycerol and HDL cholesterol. We further hypothesized that maintaining weight loss with a low-fat diet would cause a rebound in triacylglycerol but not in HDL cholesterol, whereas a moderate-fat diet would maintain lowered triacylglycerol concentrations without affecting HDL cholesterol. We expected that because both diets contain low amounts of saturated fat and cholesterol, LDL-cholesterol concentrations would decrease. Our hypotheses were based on our previous study, which reported favorable effects of test diets high in MUFAs provided by peanuts, peanut butter, peanut oil, or olive oil compared with the effects of a low-fat diet on lipids and lipoproteins in weight-stable subjects (12). An important aspect of our study was that we assessed 2 weight-loss diets that met current saturated fat and cholesterol recommendations; however, total fat in the 2 experimental diets differed appreciably. Establishing the cardiovascular disease (CVD) risk response to different weight-loss diets is important for the development of future lifelong diet strategies.

SUBJECTS AND METHODS

Experimental design

A parallel-arm study design was used in which the subjects were randomly assigned to receive either a low-fat or a moderate-fat (from MUFA) energy- and nutrient-controlled diet. Three cohorts were studied. Both weight-loss diets were implemented in each cohort. Subjects were fed a hypocaloric diet for 6 wk of weight loss, which was followed by a eucaloric diet for 4 wk of weight maintenance. Subjects were fed the same diet (low-fat or moderate-fat) during the entire 10-wk period. All foods were provided. On weekdays, subjects consumed breakfast and dinner meals in the Pennsylvania State University Metabolic Diet Study Center. Weekday lunches and snacks and all weekend meals were packed in coolers for take-out. Subjects were instructed to consume only foods and beverages provided by the Diet Center, except for nonenergy-containing beverages and seasonings, which were consumed ad libitum. Blood samples were collected during screening to assess the subjects' eligibility and during weeks 1, 6, and 10 of the diet-feeding period to assess changes in the study endpoints. Subjects were instructed to maintain current levels of physical activity throughout the 10-wk study period. Daily and weekly self-reporting forms were used to monitor compliance. Subjects were asked to report any changes in their health, medication use, physical activity or any instances of noncompliance with the diet (consumption of foods not provided by us or failure to consume any of the provided foods).

Statistical power analyses were conducted with the use of data from a controlled-feeding study that we recently completed, which compared the effects of 5 diets with different fat contents on lipids and lipoproteins (12). Using the estimates of variance from this study, with power set to 90%, and α set to 0.01 (one-sided), we determined that a sample size of 25 would be sufficient to detect a change of 5% for triacylglycerol, 12% for LDL cholesterol, and 7% for HDL cholesterol.

Subjects

Healthy overweight and obese (120–135% of ideal body weight) (13) men and women between 20 and 67 y of age were recruited by using methods previously described by us (14). Subjects were screened with the use of a self-reported questionnaire and via blood chemistry analysis to ensure that they were healthy and had LDL-cholesterol concentrations between the 25th and 90th percentiles, based on age and sex (15) and a triacylglycerol concentration <4.52 mmol/L (<400 mg/dL). This study was approved by the Biomedical Committee of the Institutional Review Board at The Pennsylvania State University.

Experimental diets

The 2 experimental diets were formulated to be consistent with the National Cholesterol Education Program Step II dietary recommendations (15), with 7% of energy derived from saturated fat and 200 mg cholesterol/d. The low-fat diet was formulated to contain $\approx$20% of energy from fat, and the moderate-fat diet was formulated to contain $\approx$35% of energy from fat. Our diet design was guided by the objective of replacing saturated fat with carbohydrates in the low-fat diet, whereas in the moderate-fat diet, monounsaturated fats replaced saturated fats. Peanuts, peanut butter, and peanut oil were used to provide one-half of the fat in the moderate-fat diet (*see* sample menus; **Table 1**). Diets were formulated to provide the following daily energy intakes: 5.02 MJ (1200 kcal), 6.28 MJ (1500 kcal), 7.53 MJ (1800 kcal), 8.79 MJ (2100 kcal), 10.04 MJ (2400 kcal), 11.3 MJ (2700 kcal), and 12.56 MJ (3000 kcal). Unit foods (muffins) containing the same macronutrient profile as the assigned diet were used to provide incremental changes of 418 kJ/d (100 kcal/d) as needed.

Validation of diet composition

A 6-d diet cycle was planned with the use of the NUTRITIONIST IV database (N-Squared Computing, First DataBank Division, San Bruno, CA). Chemical analysis of the diets was done to validate the macronutrient profiles of the 2 diets. Samples of the menus were prepared for validation by using the same food-preparation methods used during the study. All meals and snacks for each day of the 6-d cycle of the 62.8-MJ (1500-kcal) diet were prepared, combined in a container, and frozen at -20 °C. The sample was later thawed, finely ground, subsampled, and stored at -20 °C. Total fat was determined by ether extraction of the oven-dried sample. Protein was determined with the Kjeldahl method, and carbohydrate was determined by the difference. Saturated, monounsaturated, and polyunsaturated fatty acids (PUFAs) were analyzed by gas chromatography (Covance Laboratories Inc, Madison, WI.). Total energy was determined by using the Atwater factors of 16.74 kJ (4 kcal)/g for protein, 16.74 kJ (4 kcal)/g for carbohydrate, and 37.66 kJ (9 kcal)/g for fat. As planned, the MUFA content of the 2 diets differed significantly; the low-fat and moderate-fat diets contained 7.2% and 14.2% of energy as MUFA, respectively. The total fat content of both experimental diets was slightly lower than planned (18.3% rather than 20% for the low-fat diet and 32.8% rather than 35% for the moderate-

TABLE 1
Sample daily menus for the 7.53-MJ (1800-kcal) experimental diets

Low-fat diet	Amount	Moderate-fat diet	Amount
	g		*g*
Breakfast			
Orange juice	288.0	Orange juice	288.0
Nonfat milk	216.0	Nonfat milk	216.0
Bagel	36.0	Bagel	36.0
Sliced ham, low-fat	30.0	Peanut butter	35.2
Sliced cheese, fat-free	22.8	—	
Banana	114.0	Banana	114.0
Lunch			
Onion sandwich bun	36.0	Onion sandwich bun	36.0
Sliced roast beef, low-fat	66.0	Sliced roast beef, low-fat	54.0
Mayonnaise, fat-free	18.0	Mayonnaise, fat-free	18.0
Mustard	3.7	Mustard	3.7
Unsweetened apple sauce	300.0	Unsweetened apple sauce	160.0
Raw baby carrots	60.0	Raw baby carrots	60.0
Snack crackers, low-fat	16.8	Snack crackers, low-fat	16.8
Dinner			
Spaghetti, cooked	78.0	Spaghetti, cooked	60.0
Tomato pasta sauce	120.0	Tomato pasta sauce	85.0
Egg yolk	6.0	Egg yolk	10.3
Canola oil	9.0	Peanut oil	15.2
Parmesan cheese, fat-free	11.0	Parmesan cheese, fat-free	9.0
Cauliflower, cooked	150.0	Cauliflower, cooked	84.0
Meatball	43.2	Meatball	43.2
Dinner roll	45.6	Dinner roll	22.8
Butter	15.5		
Evening snack			
Raisins	24.0	Roasted peanuts, low-sodium	37.9
Jelly beans	50.4	Grapes	96.0
Pretzels, fat-free	20.0	Pretzels, fat-free	16.8

fat diet). As a consequence of the use of peanuts and peanut oil as a source of MUFA, the PUFA content of the diets differed; the moderate-fat diet contained 7.9% of energy as PUFAs, and the low-fat diet contained 2.5% of energy as PUFAs (**Table 2**).

Diet planning for weight loss and weight maintenance

The energy needs of the subjects were estimated on the basis of measured resting energy expenditure with the use of an indirect calorimeter (Deltatrac II; SensorMedics Corporation, Yorba Linda, CA). Measures of resting energy expenditure were taken at the beginning of the study and at the end of the weight-loss period (during week 6). Resting energy expenditure was multiplied by 1.4 to estimate the daily energy requirement. During the 6-wk weight-loss interval, subjects were fed 2.92 MJ/d (700 kcal/d) less than their estimated requirement to induce a weight-loss rate of ≈0.9 kg/wk (2 lb/wk). None of the subjects were fed <5.0 MJ/d (1200 kcal/d). Subjects were weighed each day before breakfast, and adjustments were made to the energy content of the diet as needed to maintain a steady rate of weight loss during the first 6 wk of the study and to maintain weight during the final 4 wk.

TABLE 2
Composition of the experimental diets[1]

Dietary constituent	Low-fat diet	Moderate-fat diet
Carbohydrate (% of energy)[2]	63.9	50.5
Protein (% of energy)[2]	17.8	16.8
Fat (% of energy)[2]	18.3	32.8
Saturated[3]	5.8	6.5
Monounsaturated[3]	7.2	14.2
Polyunsaturated[3]	2.5	7.9
Cholesterol (mg/d)[4]	202	202
Dietary fiber (g)[4]	17.2	17.6

[1] Based on analyses of all foods used in a 6-d menu cycle for the 6.28-MJ (1500-kcal) diets.
[2] Calculated from the results of proximate analysis.
[3] Calculated with the use of gas chromatography.
[4] Estimated by using the NUTRITIONIST IV database (N-Squared Computing, San Bruno, CA).

Laboratory analyses of endpoint measures

All blood samples were collected before breakfast (after a 12-h fast) according to a standardized protocol. Serum aliquots were stored at −80 °C. Serum concentrations of total cholesterol, HDL cholesterol, and triacylglycerol were measured by enzymatic assays. HDL cholesterol was determined after precipitation of apolipoprotein (apo) B–containing lipoproteins with dextran sulfate (molecular weight: 50 000). LDL-cholesterol concentrations were calculated with the use of the Friedewald equation (16). The within-laboratory CV was 1.9% for total cholesterol and ≤2.5% for HDL cholesterol. Apo B and apo A-I were measured with the use of rate immunonephelometry (Beckman Array; Beckman Instruments, Fullerton, CA). Concentrations of lipoprotein(a) were determined with a macra lipoprotein(a) enzyme-linked immunosorbent assay kit

TABLE 3
Characteristics of participants at study entry[1]

	Low-fat diet ($n = 25$)	Moderate-fat diet ($n = 27$)
Age (y)	45.4 ± 6.6 (31–59)[2]	42.7 ± 10.7 (22–67)
BMI (kg/m^2)	29.9 ± 2.4 (26–34)	29.8 ± 2.5 (26–36)
Male (%)	33	28
Total cholesterol (mmol/L)	5.51 ± 0.84 (4.27–7.16)	5.60 ± 0.78 (3.85–7.32)
LDL cholesterol (mmol/L)	3.48 ± 0.67 (2.30–4.81)	3.60 ± 0.61 (2.28–4.55)
HDL cholesterol (mmol/L)	1.27 ± 0.25 (0.78–1.68)	1.22 ± 0.23 (0.83–1.55)
Triacylglycerol (mmol/L)	1.65 ± 0.67 (0.65–3.26)	1.71 ± 0.81 (0.58–4.00)

[1] No significant differences were found between the diet groups (unpaired *t* tests). The lipid and lipoprotein values reported were used to assess eligibility only and were not used in the endpoint data analyses.
[2] $\bar{x}$ ± SD; range in parentheses.

(Strategic Diagnostics Inc, Newark, DE). The intraassay CV of the apolipoprotein assays was <6%.

Statistical procedures

Statistical analyses were performed with the use of SAS (STATISTICAL ANALYSIS SYSTEM, version 7.1; SAS Institute Inc, Cary, NC). A *t* test was used to test for differences between the diet groups in subjects' characteristics measured during screening and in cumulative weight loss at weeks 2–10. The probability for significance was set to $P < 0.05$. Mixed-models analyses (PROC MIXED) were used with subject, week (1, 6, and 10) and diet group (low-fat and moderate-fat) entered as factors for the analyses of lipids, lipoproteins, and other endpoint measures. For each model, a univariate procedure was used to test for normality and equality of variance. Data were transformed as needed to achieve normality. Our data analysis strategy was based on a priori hypotheses regarding the changes in lipids and lipoproteins we expected to observe within each diet group. Therefore, we used planned comparisons to compare the effects of week on each endpoint, separately within each group. Specifically, least-squares means were compared with a test for the effects of weight loss (week 1 compared with week 6) and the effects of weight maintenance (week 6 compared with week 10) and to compare final with baseline values (week 1 compared with week 10) for each endpoint for the low-fat and moderate-fat diet groups, separately. We used a Bonferroni correction to maintain the experiment-wise α at 0.05 (17). Thus, for each comparison we calculated an adjusted *P* value [adjusted $P = 1 - (1 - P)^6$]. The means reported in the paper are least-squares means ± SEMs.

The body weight of some subjects was not stable during the weight-maintenance period (*see* Results). This is not surprising given the challenges of determining precise energy intake requirements, especially after weight loss when there might have been a decrease in resting energy expenditure. Because weight gain or further weight loss could affect the endpoint measures, we chose a subset of subjects who maintained a stable body weight during the final 4-wk weight-maintenance period [within 1.4 kg (3 lb) of the values at week 6]. Twenty-nine subjects met this criterion (low-fat diet group: $n = 12$; moderate-fat diet group: $n = 17$). The mixed models described above were repeated in this cohort of weight maintainers. We tested the effects of adding week 1 values as a covariate in each of the statistical models to verify that baseline differences between groups did not alter the results.

RESULTS

Fifty-three subjects were enrolled in the study. One subject completed the weight-loss period but, because of personal scheduling problems, was unable to complete the weight-maintenance period. One subject with a baseline triacylglycerol concentration >4.52 mmol/L (400 mg/dL) was mistakenly enrolled into the study and was subsequently removed from the data analyses. Thirty-one percent of the subjects were men (low-fat diet group, $n = 7$; moderate-fat diet group, $n = 9$). Fifty-four percent of the subjects in the low-fat diet group and 56% in the moderate-fat diet group were overweight ($25 <$ body mass index < 30); the remainder of the subjects were classified as obese ($30 <$ body mass index < 36). Fifty subjects were classified as white, 2 as Black or African American, and one as Hispanic. No significant differences were found between diet groups for subjects' characteristics at screening (**Table 3**).

Weight loss

The amount of weight lost indicated that we were successful in achieving our targeted rate of 0.9 kg/wk. The average rate of weight loss exceeded our target in both diet groups during the first 6 wk of the study [1.2 ± 0.05 kg/wk (2.7 ± 0.11 lb/wk) and 1.09 ± 0.06 kg/wk (2.4 ± 0.12 lb/wk) for the moderate-fat and low-fat diet groups, respectively]. The rate of weight loss ranged from 0.67 to 1.72 kg/wk and, as planned, was not significantly different between the 2 groups ($P > 0.10$). Cumulative weight loss differed between the 2 diet groups at the end of the second week (**Figure 1**) but was not different at the end of the weight-loss period (cumulative weight lost: moderate-fat diet group, 7.2 ± 0.29 kg; low-fat diet group, 6.5 ± 0.34 kg; $P > 0.10$). Despite careful monitoring and frequent adjustments to energy intake, many subjects continued to lose some weight during the 4-wk weight-maintenance period (on average, 0.18 ± 0.05 kg/wk for the moderate-fat diet group and 0.36 ± 0.03 kg/wk for the low-fat diet group; $P < 0.004$). Most of the subjects lost 1.0–2.0 kg ($n = 28$), 5 subjects lost 2.0–2.5 kg, 14 subjects lost 0.0–1.0 kg, and 4 subjects gained 0.2–2.5 kg during the weight-maintenance period.

Effects of weight loss on endpoint measures

Both diets were effective in reducing total and LDL cholesterol concentrations during the weight-loss period. (**Table 4**).

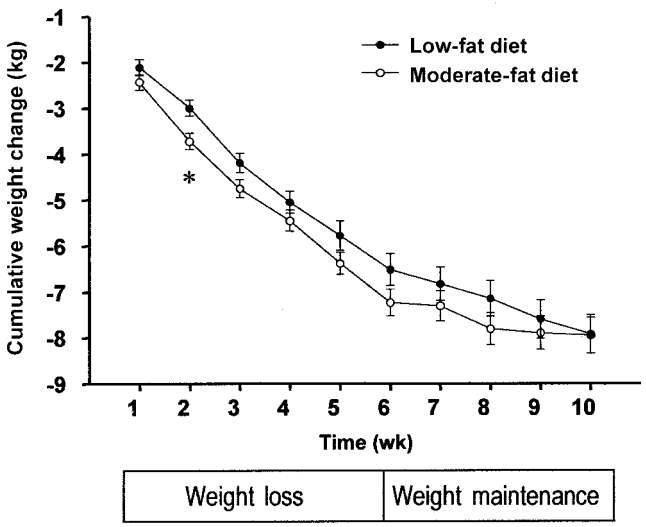

FIGURE 1. Least-squares mean (±SEM) cumulative weight loss at the end of each study week in the low-fat ($n = 25$) and moderate-fat ($n = 27$) diet groups. *Significantly different from the low-fat diet group, $P < 0.05$ (unpaired t test).

LDL cholesterol was reduced by 18% and 14% in the low-fat and moderate-fat diet groups, respectively; non-HDL-cholesterol concentrations decreased by 19% and 16%, respectively. A different pattern was observed for HDL cholesterol. Subjects who consumed the low-fat diet during weight loss experienced a significant decrease in HDL cholesterol of ≈12%. No significant change in HDL cholesterol was observed in the subjects who consumed the moderate-fat diet. The ratio of total to HDL cholesterol decreased by 8% in the low-fat diet group (adjusted $P < 0.10$) and by 11% in the moderate-fat diet group. A 10% reduction in the ratio of LDL to HDL cholesterol was observed in the moderate-fat diet group at the end of weight loss (adjusted $P < 0.05$). The 9% reduction observed in the low-fat diet group was not significant (adjusted $P = 0.10$). The ratio of non-HDL to HDL cholesterol decreased by 10% (adjusted $P < 0.10$) and 13% in the low-fat and moderate-fat diet groups, respectively, after weight loss.

Changes in apo B mirrored changes in LDL cholesterol. Both diet groups experienced significant reductions during the weight-loss period. Changes in apo A-I, however, differed from changes in HDL cholesterol. Although only the low-fat

TABLE 4
Endpoint measurements at baseline, week 6, and week 10 in all subjects[1]

	Week 1 (Baseline)	Week 6 (End of weight loss)	Week 10 (End of weight maintenance)
Total cholesterol (mmol/L)			
Low-fat diet[2]	5.60 ± 0.16[a]	4.61 ± 0.16[b]	4.85 ± 0.16[b]
Moderate-fat diet[3]	5.64 ± 0.15[a]	4.89 ± 0.15[b]	5.15 ± 0.15[b]
HDL cholesterol (mmol/L)			
Low-fat diet	1.24 ± 0.04[a]	1.09 ± 0.04[b]	1.12 ± 0.04[b]
Moderate-fat diet	1.14 ± 0.04	1.10 ± 0.04	1.12 ± 0.04
LDL cholesterol (mmol/L)			
Low-fat diet	3.53 ± 0.14[a]	2.89 ± 0.14[b]	3.00 ± 0.14[b]
Moderate-fat diet	3.75 ± 0.13[a]	3.24 ± 0.13[b]	3.48 ± 0.13[b,4]
Non-HDL cholesterol (mmol/L)			
Low-fat diet	4.36 ± 0.15[a]	3.52 ± 0.15[b]	3.73 ± 0.15[b]
Moderate-fat diet	4.50 ± 0.14[a]	3.79 ± 0.14[b]	4.03 ± 0.15[b]
Total:HDL cholesterol			
Low-fat diet	4.66 ± 0.19	4.30 ± 0.19[5]	4.40 ± 0.19
Moderate-fat diet	5.14 ± 0.18[a]	4.58 ± 0.18[b]	4.69 ± 0.19[b]
LDL:HDL cholesterol			
Low-fat diet	2.97 ± 0.15	2.71 ± 0.15	2.73 ± 0.15
Moderate-fat diet	3.40 ± 0.15[a]	3.06 ± 0.15[b]	3.18 ± 0.15[a,b]
Non-HDL:HDL cholesterol			
Low-fat diet	3.66 ± 0.19	3.30 ± 0.19[5]	3.40 ± 0.19
Moderate-fat diet	4.14 ± 0.18[a]	3.58 ± 0.18[b]	3.69 ± 0.19[b]
Triacylglycerol (mmol/L)[6]			
Low-fat diet	1.80 ± 0.13[a]	1.38 ± 0.13[b]	1.61 ± 0.13[a,b]
Moderate-fat diet	1.65 ± 0.13[a]	1.19 ± 0.13[b]	1.21 ± 0.13[b]
Apolipoprotein A-I (mmol/L)			
Low-fat diet	5.42 ± 0.18[a]	4.88 ± 0.18[b]	5.13 ± 0.18[b,4]
Moderate-fat diet	5.14 ± 0.17[a]	4.76 ± 0.17[b]	4.99 ± 0.17[a,b,4]
Apolipoprotein B (mmol/L)			
Low-fat diet	1.95 ± 0.08[a]	1.58 ± 0.08[b]	1.65 ± 0.08[b]
Moderate-fat diet	2.00 ± 0.08[a]	1.67 ± 0.08[b]	1.74 ± 0.08[b]
Lipoprotein(a) (g/L)[7]			
Low-fat diet	19.6 ± 3.4	16.4 ± 3.4	17.7 ± 3.4
Moderate-fat diet	21.6 ± 3.6	20.6 ± 3.6	23.9 ± 3.6[4]

[1] Least-squares mean ± SEM. Comparisons were made within each diet group by using the least-squares means from the mixed model, with subject, week, and diet group entered as factors and the P value adjusted for multiple comparisons. Values in the same row with different superscript letters are significantly different, adjusted $P < 0.05$.

[2] $n = 25$ for all endpoints except lipoprotein(a).

[3] $n = 27$ for all endpoints except lipoprotein(a).

[4] Different from week 6, trend for significance ($0.05 <$ adjusted $P < 0.10$).

[5] Different from baseline, trend for significance ($0.05 <$ adjusted $P < 0.10$).

[6] Data were log transformed for analysis.

[7] Data from subjects whose values were < 0.05 g/L at all time points were excluded (low-fat diet group: $n = 21$; moderate-fat diet group: $n = 19$).

diet group experienced a significant decrease in HDL cholesterol, both diet groups showed a reduction in apo A-I. As expected, both groups showed significant decreases in triacylglycerol during the weight-loss period. Finally, no significant changes were noted for lipoprotein(a) in either diet group.

Effects of weight maintenance on endpoint measures

As noted, we chose a subset of weight maintainers to test the effects of weight maintenance on the variables of interest. We found that subjects who consumed the low-fat diet had a complete reversal of the weight-loss–induced reduction in triacylglycerol during weight maintenance; subjects who consumed the moderate-fat diet showed no evidence of a rebound during this interval (**Figure 2**). Similar to the findings in the larger cohort, subjects in the low-fat diet group in this subset of weight maintainers experienced a decrease in HDL-cholesterol concentrations during weight loss. HDL-cholesterol concentrations did not change significantly in either diet group during the weight-maintenance period. Thus, HDL-cholesterol concentrations were lower at the end of week 10 than at baseline in the low-fat diet group; subjects in the moderate-fat diet group experienced no significant change from baseline.

Despite some rebounding effects, total cholesterol remained significantly lower after weight maintenance than at baseline in each diet group (**Table 5**). LDL cholesterol was 15% lower at the end of week 10 than at baseline in the low-fat diet group but was not significantly lower in the moderate-fat diet group. Although the reduction in LDL cholesterol was significant in the low-fat diet group, no significant change in LDL:HDL cholesterol was found as a result of the concurrent reduction in HDL cholesterol. Trends for significance were observed for the ≈10% reduction from baseline in total:HDL cholesterol and in non-HDL:HDL cholesterol observed in the moderate-fat diet group at the end of week 10. No change in these ratios were observed in the low-fat diet group. Concentrations of apo-B and non-HDL cholesterol at the end of 10 wk remained significantly lower than baseline in both diet groups.

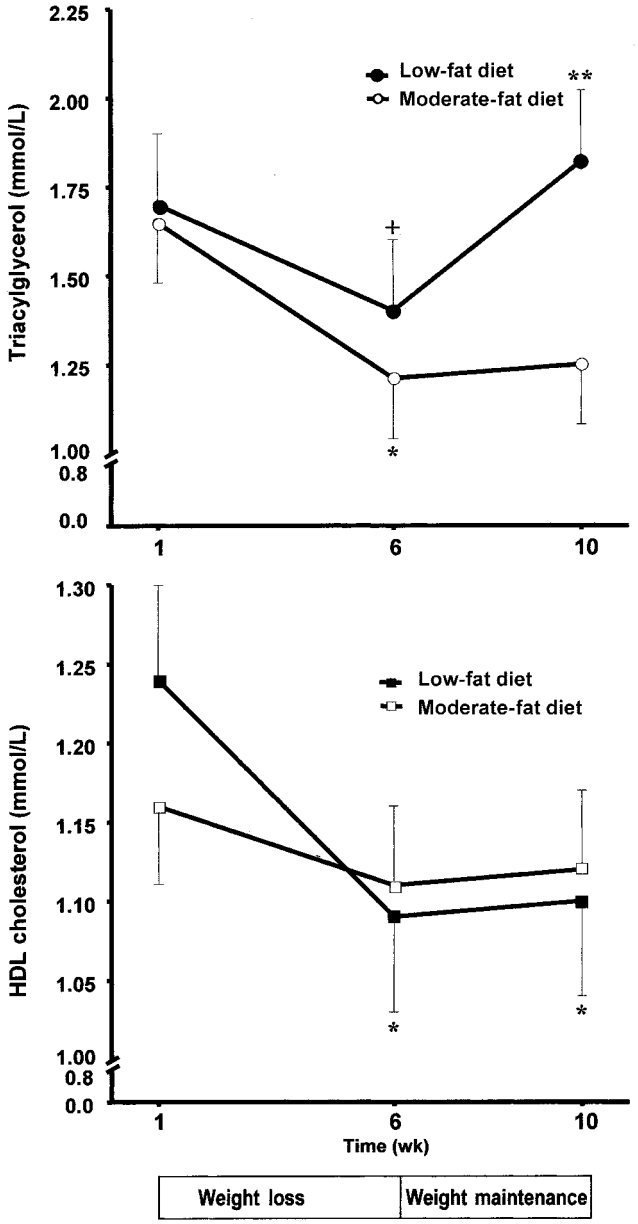

FIGURE 2. Least-squares mean (±SEM) serum triacylglycerol and HDL-cholesterol concentrations at baseline and at the end of weeks 6 and 10 in weight-stable subjects (within 1.4 kg of the weight at week 6) in the low-fat ($n = 12$) and moderate-fat ($n = 17$) diet groups. Comparisons were made within each diet group by using least-squares means from the mixed model with subject, week, and diet group entered as factors and the P value adjusted for multiple comparisons. *Significantly different from baseline, adjusted $P < 0.05$. $^{+}$Trend for significant difference from baseline, $0.05 <$ adjusted $P < 0.10$. **Significantly different from week 6, adjusted $P < 0.05$.

DISCUSSION

The findings of the current study are significant because they demonstrate that markedly lowering total fat intakes may have adverse consequences on reductions in the risk of CVD, even in response to weight loss. Despite a comparable, planned weight loss, the low-fat diet group experienced a 12% decrease in HDL cholesterol but the moderate-fat diet group experienced no change. Thus, a moderate-fat diet blunts the decrease in HDL cholesterol during weight loss. Importantly, HDL cholesterol did not increase after the 4-wk weight-maintenance period during the low-fat diet.

Numerous studies have shown that euenergetic, low-fat, high-carbohydrate diets lower HDL cholesterol compared with higher-monounsaturated fat, lower-carbohydrate diets (12, 18–20). Furthermore, a meta-analysis of 37 dietary intervention studies (21) showed that for every 1% reduction in energy from fat, HDL cholesterol decreased by 0.79%. The 14% difference in fat content between the 2 diets in the current study elicited an 8.5% decrease in HDL cholesterol, which is lower than the expected 11.1% decrease obtained when the regression equation from the meta-analysis was applied (21).

Yu-Poth et al (21) showed that HDL cholesterol increased by 0.83% for every 1-kg decrement in body weight. In a meta-analysis of 70 studies, Dattilo and Kris-Etherton (10) found that for every 1-kg decrement in body weight, HDL cholesterol increased by 0.008 mmol/L in weight-stable subjects. During weight-loss, however, HDL cholesterol decreased. In the current study, despite the loss and maintenance of 6.5 kg body weight, HDL cholesterol decreased in the low-fat diet group. Similar results were reported in 2 studies that examined the

TABLE 5
Endpoint measurements at baseline, week 6, and week 10 in the weight-stable subjects[1]

	Week 1 (Baseline)	Week 6 (End of weight loss)	Week 10 (End of weight maintenance)
Total cholesterol (mmol/L)			
Low-fat diet	5.59 ± 0.23[a]	4.50 ± 0.23[b]	4.99 ± 0.16[c]
Moderate-fat diet	5.83 ± 0.19[a]	5.02 ± 0.19[b]	5.34 ± 0.15[b]
LDL cholesterol (mmol/L)			
Low-fat diet	3.57 ± 0.20[a]	2.77 ± 0.20[b]	3.05 ± 0.20[b]
Moderate-fat diet	3.91 ± 0.17[a]	3.35 ± 0.17[b]	3.62 ± 0.13[a,b]
Non-HDL cholesterol (mmol/L)			
Low-fat diet	4.35 ± 0.21[a]	3.41 ± 0.21[b]	3.88 ± 0.21[c]
Moderate-fat diet	4.67 ± 0.18[a]	3.90 ± 0.18[b]	4.19 ± 0.18[b]
Total:HDL cholesterol			
Low-fat diet	4.69 ± 0.27	4.25 ± 0.27	4.59 ± 0.27
Moderate-fat diet	5.17 ± 0.23[a]	4.57 ± 0.23[b]	4.71 ± 0.23[a,b,2]
LDL:HDL cholesterol			
Low-fat diet	3.04 ± 0.23	2.64 ± 0.23[2]	2.83 ± 0.23
Moderate-fat diet	3.46 ± 0.19[a]	3.05 ± 0.19[b]	3.20 ± 0.19[a,b]
Non-HDL:HDL cholesterol			
Low-fat diet	3.69 ± 0.27	3.25 ± 0.27	3.59 ± 0.27
Moderate-fat diet	4.17 ± 0.23[a]	3.57 ± 0.23[b]	3.71 ± 0.23[a,b,2]
Apolipoprotein A-I (mmol/L)			
Low-fat diet	5.35 ± 0.21	4.98 ± 0.21[2]	5.29 ± 0.21
Moderate-fat diet	5.34 ± 0.17[a]	4.92 ± 0.17[b]	5.17 ± 0.17[a,b]
Apolipoprotein B (mmol/L)			
Low-fat diet	2.03 ± 0.12[a]	1.59 ± 0.12[b]	1.76 ± 0.12[b]
Moderate-fat diet	2.06 ± 0.10[a]	1.72 ± 0.10[b]	1.77 ± 0.10[b]
Lipoprotein(a) (g/L)[3]			
Low-fat diet	23.2 ± 5.4	19.4 ± 5.4	19.1 ± 5.4
Moderate-fat diet	18.3 ± 4.9	16.1 ± 4.9	19.5 ± 4.9

[1] Least-squares mean ± SEM. $n = 12$ for the low-fat diet group and $n = 17$ for the moderate-fat diet group for all endpoints except lipoprotein(a). Weight-stable subjects were those with a body weight ± 1.4 kg during the 4-wk weight-maintenance interval ($n = 29$). Comparisons were made within each diet group by using the least-squares means from the mixed model with subject, week, and diet group entered as factors and the P value adjusted for multiple comparisons. Values in the same row with different superscript letters are significantly different, adjusted $P < 0.05$.

[2] Different from baseline, trend for significance ($0.05 <$ adjusted $P < 0.10$).

[3] Data from subjects whose values were <0.05 g/L at all time points were excluded (low-fat diet group: $n = 10$; moderate-fat diet group: $n = 12$); the data were log transformed for analysis.

effects of weight loss and low-fat diets on changes in lipids and lipoproteins (22, 23). HDL cholesterol decreased by 11% in the subjects who consumed a very-low-fat diet, despite an average weight-loss of 4 kg after 12 wk (22). Similar to the findings of the current study, HDL-cholesterol concentrations did not increase when body weight stabilized in the subjects who consumed a very-low-fat diet (22). Also consistent with our results are the findings of Kasim-Karakas et al (23), who showed that HDL-cholesterol concentrations decreased by 15% with a euenergetic, very-low fat diet, a subsequent weight loss of 4.6 kg after an 8-mo intervention failed to result in the return of HDL cholesterol to baseline concentrations. Thus, a low-fat diet results in a decrease in HDL cholesterol, even when weight loss occurs in both short-(22) and long-term (23) studies.

Our results further illustrate the effects of diet on fasting serum triacylglycerol concentrations during weight loss and subsequent weight maintenance. As expected, both diet groups experienced a significant decrease in triacylglycerol concentrations during weight loss. The return of triacylglycerol to baseline concentrations during weight maintenance in the low-fat diet group was not unexpected given the well-known elevating effects of euenergetic, low-fat, high-carbohydrate diets on serum triacylglycerol concentrations [*see* review by Parks and Hellerstein (8)]. However, triacylglycerol concentrations returned to baseline during the consumption of a low-fat diet, despite the maintenance of a lower weight. The rebound response in plasma triacylglycerol concentrations in subjects who consumed the low-fat diet during weight maintenance was most likely due to increased VLDL-triacylglycerol secretion, which was due to increased hepatic fatty acid availability as the result of a decrease in hepatic fatty acid oxidation (24).

After weight maintenance, LDL cholesterol decreased from baseline by 15% in the subjects who consumed the low-fat diet. The 7% decrease in LDL cholesterol in the moderate-fat diet group was not statistically significant. Importantly, in both groups there was a modest increase in LDL cholesterol after the weight-maintenance period. Studies in weight-stable subjects have shown a similar LDL-cholesterol-lowering response to the consumption of low-fat and high-monounsaturated-fat diets when saturated fat and cholesterol are held constant (12, 18–20, 25). In the current study, the response of LDL cholesterol in the moderate-fat diet group, after weight loss and after the weight-maintenance period, could be explained by differences in diet-induced insulin sensitivity. The decrease in insulin sensitivity with a higher-fat diet (26, 27) would attenuate activation of the LDL receptor, which is under insulin regulation (28, 29). The increase in free fatty acid concentrations during weight loss in conjunction with the moderate-fat diet and the increased influx

of free fatty acids into the liver would increase VLDL synthesis, which would lead to an increase in LDL. This, coupled with a reduction in clearance via the LDL receptor, may explain the slightly diminished LDL-cholesterol-lowering response relative to baseline for subjects who consumed the moderate-fat diet.

In the weight-stable subset of subjects, non-HDL cholesterol was reduced by 11% and 10% with the low-fat and moderate-fat diets, respectively. Evidence suggests that serum concentrations of non-HDL cholesterol may be a better predictor of risk of death from CVD than are LDL-cholesterol concentrations (30). Thus, the changes in non-HDL cholesterol in the weight-stable subset suggest that both weight-loss diets lower CVD risk.

The weight-stable subset of subjects was selected to examine the effects of weight maintenance on the study endpoints. The rebound in triacylglycerol concentrations in the low-fat diet group was significant in this smaller subset. However, this procedure also reduced the statistical power to detect sustained reductions in triacylglycerol and LDL-cholesterol concentrations in the moderate-fat diet group. Thus, longer-term studies with more subjects are needed to clarify the effects of weight loss with a moderate fat-diet on triacylglycerol concentrations in weight-stable subjects.

We evaluated lipoprotein ratios that reflect CVD risk (total:HDL cholesterol, LDL:HDL cholesterol, and non-HDL cholesterol:HDL cholesterol) in both diet groups. Decreases in LDL:HDL cholesterol and in non-HDL cholesterol were observed from weeks 1 to 10, which indicates a beneficial effect of the 2 diets on these important markers of CVD risk. The significant decrease in total:HDL cholesterol and in non-HDL cholesterol:HDL cholesterol in the weight-stable subjects who consumed the moderate-fat diet favorably affects CVD risk status. Given the evidence that a 1% decrease in total:HDL cholesterol confers a 1.3% reduction in CVD risk (31), and assuming that the decrease in non-HDL cholesterol:HDL cholesterol confers a similar reduction in risk (31), the 11% decrease in non-HDL cholesterol:HDL cholesterol might elicit a 14% reduction in CVD risk in the moderate-fat diet group.

In summary, our results indicate that a moderate-fat weight-loss diet decreases CVD risk. Moreover, a moderate-fat weight-loss diet may also facilitate long-term adherence (32) and minimize weight fluctuations, which adversely affect CVD risk (2, 33). These findings are all consistent with the objective of implementing a weight-loss program designed to effectively promote dietary behaviors that maintain a reduced body weight. Inclusion of popular food sources of MUFAs, such as peanuts and peanut butter, may promote better adherence to a calorie-reduced diet intended for weight loss. Further studies, especially longer-term studies (34) with a longer weight-maintenance period, are needed to corroborate the efficacy of moderate-fat weight-loss diets with respect to lipid and lipoprotein risk factors and to assess the long-term maintenance of reduced body weight in persons consuming self-selected diets.

Because physical activity is an essential component of a weight-loss program (35, 36), the added benefits conferred by physical activity would be expected to further enhance the beneficial effect of the optimal weight-loss diet on CVD risk. In keeping with the "Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults—The Evidence Report" (4), which recommends a daily intake of <30% of calories from fat for weight reduction, our results advise against a diet that provides appreciably lower than 30% of calories from fat to achieve weight loss. Thus, we support the recommendation of a weight-loss diet that has a moderate total fat content and conforms with current guidelines for saturated fat, to achieve the most desirable CVD risk profile.

PMK-E, VKF, DHM, and TAP were responsible for the study design. VKF and DHM were responsible for the data collection under the supervision of PMK-E. CLP completed the data analysis in collaboration with DTM. CLP and PMK-E wrote the manuscript. None of the authors had any financial or personal interest in the organization sponsoring the research, including advisory board affiliations, during the conduct of this study.

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