

# The Effects of Low-Carbohydrate versus Conventional Weight Loss Diets in Severely Obese Adults: One-Year Follow-up of a Randomized Trial

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**Background:** A previous paper reported the 6-month comparison of weight loss and metabolic changes in obese adults randomly assigned to either a low-carbohydrate diet or a conventional weight loss diet.

**Objective:** To review the 1-year outcomes between these diets.

**Design:** Randomized trial.

**Setting:** Philadelphia Veterans Affairs Medical Center.

**Participants:** 132 obese adults with a body mass index of 35 kg/m<sup>2</sup> or greater; 83% had diabetes or the metabolic syndrome.

**Intervention:** Participants received counseling to either restrict carbohydrate intake to <30 g per day (low-carbohydrate diet) or to restrict caloric intake by 500 calories per day with <30% of calories from fat (conventional diet).

**Measurements:** Changes in weight, lipid levels, glycemic control, and insulin sensitivity.

**Results:** By 1 year, mean ( $\pm$ SD) weight change for persons on the low-carbohydrate diet was  $-5.1 \pm 8.7$  kg compared with  $-3.1 \pm 8.4$  kg for persons on the conventional diet. Differences between groups were not significant ( $-1.9$  kg [95% CI,  $-4.9$  to

$1.0$  kg];  $P = 0.20$ ). For persons on the low-carbohydrate diet, triglyceride levels decreased more ( $P = 0.044$ ) and high-density lipoprotein cholesterol levels decreased less ( $P = 0.025$ ). As seen in the small group of persons with diabetes ( $n = 54$ ) and after adjustment for covariates, hemoglobin A<sub>1c</sub> levels improved more for persons on the low-carbohydrate diet. These more favorable metabolic responses to a low-carbohydrate diet remained significant after adjustment for weight loss differences. Changes in other lipids or insulin sensitivity did not differ between groups.

**Limitations:** These findings are limited by a high dropout rate (34%) and by suboptimal dietary adherence of the enrolled persons.

**Conclusion:** Participants on a low-carbohydrate diet had more favorable overall outcomes at 1 year than did those on a conventional diet. Weight loss was similar between groups, but effects on atherogenic dyslipidemia and glycemic control were still more favorable with a low-carbohydrate diet after adjustment for differences in weight loss.

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The prevalence of obesity and its associated metabolic abnormalities has increased markedly over the past 2 decades (1, 2). Although guidelines to follow a high-complex carbohydrate, low-fat, energy-deficient diet to achieve weight loss are generally accepted (3), considerable public interest has focused on low-carbohydrate diets (4). We recently reported that persons with severe obesity lost more weight and had greater improvements in triglyceride levels, insulin sensitivity, and glycemic control after 6 months of a low-carbohydrate diet as compared with a conventional weight loss diet based on calorie and fat restriction (5). However, these findings were preliminary because of the short duration of that study (6). A simultaneously published study by Foster and colleagues suggested that persons on a low-carbohydrate diet tended to regain weight by 1 year (7). These findings were limited, however, because few participants completed the study and because the study used a self-help approach, which is less effective than direct counseling for maintaining weight loss (8). Foster and colleagues also excluded persons with diabetes, which is highly prevalent in the obese population.

During the development of this study, we decided to analyze and report preliminary results at 6 months and final results at 1 year. We thought that the short-term

results would be important, given the high-risk nature of our study sample, but that long-term outcomes would provide more information about the sustainability of any diet-related outcomes. We now report our findings 1 year after randomization to a low-carbohydrate diet versus a low-fat weight loss diet (conventional diet) in severely obese adults with a high prevalence of diabetes or the metabolic syndrome.

## METHODS

### Study Participants

The study design has been previously described (5). Participants were recruited from the outpatient practices of the Philadelphia Veterans Affairs Medical Center and included persons 18 years of age and older with a body mass index (BMI) of 35 kg/m<sup>2</sup> or greater. The exclusion criteria were a serum creatinine level greater than 133  $\mu$ mol/L ( $>1.5$  mg/dL), hepatic disease, severe life-limiting medical illness, inability to self-monitor glucose levels, or active use of a weight loss program or weight loss medication. Between May 2001 and November 2001, 132 persons were randomly assigned to either a low-carbohydrate diet ( $n = 64$ ) or a conventional diet ( $n = 68$ ). The Institutional Re-

view Committee at the Philadelphia Veterans Affairs Medical Center approved the study, and all participants provided written informed consent.

### Interventions

Diet groups met in weekly counseling sessions for 4 weeks, followed by 11 monthly sessions. Participants on the low-carbohydrate diet were instructed only to reduce carbohydrate intake to less than 30 g per day. Participants on the conventional diet were instructed to reduce caloric intake by 500 calories per day, with less than 30% of calories derived from fat, in accordance with the National Heart, Lung, and Blood Institute guidelines (3).

### Outcome Measures

We collected data, including weight (single calibrated scale, SR Instruments, Inc., Tonawanda, New York), medical history (self-reported), and blood pressure, at baseline, 6 months, and 1 year. Fasting blood specimens were obtained for glucose, hemoglobin A<sub>1c</sub>, and serum lipid levels (Synchron LX20, Beckman Coulter, Inc., Fullerton, California). Low-density lipoprotein (LDL) cholesterol level was calculated by using the Friedewald formula (9). We defined the presence of diabetes by a historical fasting blood glucose level greater than 6.94 mmol/L (>125 mg/dL) or use of antidiabetic medications. The metabolic syndrome was considered present if a participant had 3 or more of the following (10): central obesity, fasting blood glucose level of 6.11 mmol/L (110 mg/dL) or greater, fasting triglyceride level of 1.70 mmol/L (150 mg/dL) or greater, high-density lipoprotein (HDL) cholesterol level less than 1.04 mmol/L (<40 mg/dL) for men or less than 1.30 mmol/L (<50 mg/dL) for women, blood pressure of 130/85 mm Hg or greater, or antihypertensive therapy. We assumed that all participants had central obesity because of the uniform severity of their obesity (BMI range, 35.0 to 79.4 kg/m<sup>2</sup>). Serum insulin was measured by radioimmunoassay (Laboratory Corporation of America Holdings [LabCorp], Burlington, North Carolina). Insulin resistance in nondiabetic persons was estimated by the quantitative insulin sensitivity check (QUICK) index:  $1/[(\log(\text{fasting insulin } (\mu\text{U/mL})) + \log \text{fasting glucose}(\text{mg/dL}))]$ .

### Statistical Analysis

Our primary end point was total weight loss at 1 year. Secondary analyses included the change from baseline in serum lipid levels, insulin sensitivity, and glycemic control.

We estimated that we would need 100 persons (50 per group), assuming a 2-sided type I error of 5%, for the study to have 80% power to detect a 5-kg greater mean weight loss in the low-carbohydrate group than in the conventional diet group. These calculations were based on an anticipated maximum weight loss by 6 months, with weight stabilization in both diet groups between 6 months and 1 year. To compensate for an anticipated dropout rate of 25%, we set our enrollment target at 135 persons. Randomization was performed by using a pre-established algo-

### Context

In 2003, the authors reported that severely obese adults lost more weight and had better serum lipid patterns after 6 months of a low-carbohydrate diet rather than a conventional low-fat diet.

### Contribution

After 1 year, these same patients still had more favorable triglyceride and high-density lipoprotein cholesterol levels on the low-carbohydrate diet than on the conventional diet. However, weight loss and the other metabolic parameters were similar in the 2 diet groups.

### Cautions

The effect of the modest improvements in high-density lipoprotein cholesterol and triglyceride levels on the development of diabetes and cardiovascular disease is unknown.

—The Editors

rithm generated from a random set of numbers that was constructed and held in a separate center and concealed from those enrolling persons during randomization. We used stratified randomization, with blocking within strata, to ensure assignment of approximately equal numbers of women, diabetic persons, and severely obese persons (BMI  $\geq$  40 kg/m<sup>2</sup>) to each study group.

Changes in weight, dietary intake, and metabolic data were compared between the 2 diets by random-coefficient analysis (11). This type of analysis was selected to allow for a variable number of observations for participants and to take into account that the repeated observations of the outcome variables over time for individuals were correlated. The random-coefficient analysis model takes these correlations into account by allowing the intercept to vary randomly among persons. We used a restricted maximum likelihood analysis, which assumed that changes were distributed according to a bivariate normal distribution and that data were missing at random. The outcome variables were changes from baseline in weight, dietary macronutrient consumption, and metabolic measurements. For all of these analyses, the covariates included an indicator variable for time (6 months and 1 year), diet group, and a diet group by time interaction term. This diet group by time interaction term was kept in the model, regardless of its statistical significance ( $P = 0.063$  for the weight loss analysis). Separate analyses to adjust for baseline differences between diet groups were also made by entering the following covariates to each of these models: age; race (white or African American); sex; baseline BMI; baseline caloric intake; and the presence or absence of hypertension, use of lipid-lowering therapy, diabetes, active smoking, and sleep apnea (12). All variables were assessed for normality before entry into the analyses. Triglyceride, insulin, and glucose

Table 1. Baseline Characteristics of Study Participants\*

Variable	Low-Carbohydrate Diet			Conventional Diet		
	All Persons in the Study (n = 64)	Persons Who Completed the Study (n = 44)	Persons Who Dropped Out of the Study (n = 20)	All Persons in the Study (n = 68)	Persons Who Completed the Study (n = 43)	Persons Who Dropped Out of the Study (n = 25)
Age, y†	53 ± 9	55 ± 9	48 ± 9	54 ± 9	55 ± 9	50 ± 10
BMI, kg/m <sup>2</sup>	42.9 ± 6.6	43.6 ± 6.9	41.3 ± 5.8	42.9 ± 7.7	42.3 ± 5.9	44.0 ± 10.2
Weight, kg	130 ± 23	132 ± 23	126 ± 24	132 ± 27	129 ± 20	137 ± 36
Systolic blood pressure, mm Hg	133 ± 15	133 ± 16	133 ± 14	135 ± 16	139 ± 16	127 ± 13
Diastolic blood pressure, mm Hg	78 ± 11	77 ± 11	81 ± 10	80 ± 9	82 ± 9	76 ± 8
Race, %‡						
White	42	48	30	34	28	44
African American	55	48	70	63	70	52
Hispanic	3	5	0	3	2	4
Sex, %§						
Female	20	18	30	15	19	8
Male	80	82	70	85	81	92
Metabolic syndrome (without diabetes), %	44	46	40	40	42	36
Diabetes mellitus, %	42	41	45	40	37	44
Medications for diabetes, %						
Sulfonylureas	11	9	15	16	16	16
Metformin	17	18	15	13	12	16
Peroxisome proliferator-activated receptor-γ agonist	2	2	0	2	2	0
Insulin	9	7	15	6	5	8
Hypertension, %¶	72	75	65	57	63	48
Antihypertensive drugs, %	64	68	55	57	60	55
Hyperlipidemia, %	51	49	55	50	49	52
Medications for hyperlipidemia, %						
Statin	42	44	41	37	35	41
Gemfibrozil	3	5	0	2	0	0
Niacin	0	0	0	2	2	0
Coronary artery disease, %	16	16	15	16	9	28
Depression, %	33	34	30	34	33	36
Cigarette smoking, %	20	16	30	22	19	28
Sleep apnea, %**	27	34	10	21	23	16

\* Values expressed with a plus/minus sign are the mean ± SD. Participants were considered to have hyperlipidemia if they reported a total cholesterol level greater than 5.18 mmol/L (>200 mg/dL) or were actively using lipid-lowering therapy. *P* values were determined by chi-square analysis for categorical variables, by the unpaired *t*-test for continuous variables, and by logistic regression for interaction terms. BMI = body mass index.

† *P* = 0.001 for younger age predicting a greater likelihood of dropping out of the study.

‡ *P* > 0.2 for baseline differences in race between diet groups; *P* = 0.162 for an interaction between diet and race on the number of persons who dropped out at 1 year. § *P* = 0.120 for an interaction between diet and sex on the number of persons who dropped out at 1 year.

|| Includes 2 persons who developed diabetes during the first few weeks after study enrollment.

¶ *P* = 0.082 for a difference in the prevalence of hypertension between diet groups.

\*\* *P* = 0.053 for the ability of the presence of sleep apnea to predict a greater likelihood of remaining in the study.

levels were skewed and thus were log-transformed before the analyses. Baseline differences between diet groups were compared by chi-square analysis for dichotomous variables and by the unpaired *t*-test for continuous variables. All *P* values are 2-sided, and a *P* value of 0.05 was considered statistically significant. Analyses were performed with SPSS statistical software, version 11.1 (SPSS, Inc., Chicago, Illinois).

### Missing Data

Of the 132 enrolled persons, follow-up was done at 6 months for 79 persons and at 1 year for 87 persons. For measurements at 6 months, we retrieved weights on an additional 16 persons on the low-carbohydrate diet and 23 persons on the conventional diet (total, 39 persons at a mean [±SD] of 6.6 ± 1.2 months). For measurements at 1 year, we retrieved weights on 18 persons on the low-carbohydrate diet and 21 persons on the conventional diet

(total, 39 persons at a mean [±SD] of 13.5 ± 3.2 months). Thus, we had 6-month weights on 118 of 132 persons (89%) and 1-year weights on 126 of 132 persons (96%). Of the 18 persons who missed the 6-month visit but returned for the 1-year visit (6 in the low-carbohydrate group and 12 in the conventional diet group), all but 2 had 6-month weights retrieved from medical records. Of the 6 persons for whom no 1-year weights were available, 2 were in the low-carbohydrate group and 4 in the conventional diet group. The weights retrieved from medical records were obtained on scales that were different from those used for the study and were probably obtained in a nonuniform manner with regard to clothing.

We used several approaches to handle the 45 participants with missing data for diet recall and metabolic measurements. For the primary analysis by random-coefficient analysis, we assumed data were missing at random. To

verify this assumption, we performed sensitivity analyses based on comparisons of baseline characteristics and weight loss differences between those who dropped out and those who completed the study. We also performed 2 additional sensitivity analyses: The first analysis included only persons who completed the study, and the second analysis included all persons, with the baseline data carried forward for those persons who dropped out.

### Role of the Funding Source

The funding source had no role in the design, conduct, or reporting of the study or in the decision to submit the manuscript for publication.

## RESULTS

### Baseline Characteristics

Participants were well matched between diet groups regarding baseline characteristics, although the low-carbohydrate group had more hypertensive and white persons (Table 1). Both groups had a high prevalence of diabetes or the metabolic syndrome (Table 1). Twenty persons on the low-carbohydrate diet and 25 on the conventional diet dropped out by 1 year. These persons were younger and had a lower prevalence of sleep apnea but were not otherwise significantly different from those who completed the study (Table 1). Differences in baseline lipid values ( $P > 0.2$  for all comparisons), diet composition ( $P \geq 0.149$  for all comparisons), glycemic control indices ( $P \geq 0.158$  for all comparisons), and insulin sensitivity ( $P > 0.2$ ) between

those who dropped out of the study and those who completed the study were not significant.

### Dietary Intake Assessment

Table 2 shows the dietary recall data. Caloric intake decreased more by 1 year in the low-carbohydrate group than in the conventional diet group, although the difference between diet groups was not statistically significant. The low-carbohydrate group reduced carbohydrate intake by 52%, reduced fiber intake by 42%, increased total fat intake by 31%, increased dietary cholesterol intake by 32%, and reduced sodium intake by 21% relative to baseline. However, only the reductions in carbohydrate intake and sodium intake were greater than observed in the conventional diet group.

### Weight Loss

Participants on the low-carbohydrate diet maintained most of their 6-month weight loss, whereas those on a conventional diet continued to lose weight throughout the year. The final 1-year weight change (mean  $\pm$  SD) was  $-5.1 \pm 8.7$  kg in the low-carbohydrate group and  $-3.1 \pm 8.4$  kg in the conventional diet group (Figure). The difference in weight loss between the 2 diet groups was not significant ( $-2.0$  kg [CI,  $-4.9$  kg to  $1.0$  kg];  $P = 0.195$  before and  $P > 0.2$  after adjustment for baseline variables). The difference in weight loss between the 2 diet groups between 6 months and 1 year was not statistically significant ( $P = 0.063$ ). Persons on the low-carbohydrate diet who dropped out lost less weight than those who com-

Table 2. Changes in Dietary Composition between Baseline and 1 Year for the 2 Diets\*

Variable	Baseline (n = 87)	1 Year (n = 87)	Change (n = 87)	Mean Difference (95% CI)†	P Value‡
<b>Calories</b>				$-354$ ( $-881$ to $172$ )	0.183
Conventional diet	$1919 \pm 940$	$1822 \pm 1008$	$-97 \pm 1067$		
Low-carbohydrate diet	$1972 \pm 1046$	$1462 \pm 776$	$-510 \pm 1187$		
<b>Protein, g</b>				$-15$ ( $-39$ to $9$ )	$>0.2$
Conventional diet	$67 \pm 34$	$74 \pm 50$	$7 \pm 56$		
Low-carbohydrate diet	$84 \pm 48$	$73 \pm 34$	$-11 \pm 56$		
<b>Carbohydrate, g</b>				$-98$ ( $-179$ to $-40$ )	0.011
Conventional diet	$252 \pm 139$	$230 \pm 150$	$-22 \pm 157$		
Low-carbohydrate diet	$251 \pm 155$	$120 \pm 93$	$-131 \pm 168$		
<b>Fat, g</b>				$28$ ( $-14$ to $70$ )	0.194
Conventional diet	$74 \pm 54$	$69 \pm 48$	$-6 \pm 55$		
Low-carbohydrate diet	$72 \pm 50$	$93 \pm 117$	$22 \pm 127$		
<b>Fiber, g</b>				$-4$ ( $-10$ to $1$ )	0.113
Conventional diet	$13 \pm 11$	$12 \pm 12$	$-1 \pm 14$		
Low-carbohydrate diet	$12 \pm 9$	$7 \pm 6$	$-5 \pm 10$		
<b>Saturated fat, g</b>				$1$ ( $-8$ to $10$ )	$>0.2$
Conventional diet	$21 \pm 18$	$17 \pm 15$	$-4 \pm 17$		
Low-carbohydrate diet	$21 \pm 19$	$19 \pm 20$	$-2 \pm 23$		
<b>Dietary cholesterol, g</b>				$145$ ( $-25$ to $314$ )	0.093
Conventional diet	$276 \pm 248$	$250 \pm 260$	$-26 \pm 359$		
Low-carbohydrate diet	$273 \pm 264$	$361 \pm 289$	$88 \pm 362$		
<b>Dietary sodium, mg</b>				$-1086$ ( $-2171$ to $-1$ )	0.050
Conventional diet	$2994 \pm 1723$	$3444 \pm 2422$	$451 \pm 2761$		
Low-carbohydrate diet	$3408 \pm 2395$	$2775 \pm 1726$	$-633 \pm 2435$		

\* The values for dietary macronutrient data are given as the mean ( $\pm$ SD) g per day and are based on 24-hour dietary recall from the 87 persons who completed the study.

† The mean difference in 1-year change and 95% CIs are for the low-carbohydrate group relative to the conventional diet group and are obtained by random-coefficient analysis.

‡ The  $P$  values are for comparison of the change from baseline to 1 year between diet groups by random-coefficient analysis. All participants are included and the values are not adjusted for baseline variables.

Table 3. Change in Serum Lipids, Glycemic Indices, Creatinine Levels, and Uric Acid Levels at 1 Year\*

Variable	Baseline (n = 87)	1 Year (n = 87)	Change (n = 87)	Mean Difference (95% CI)†	P Value‡	Adjusted P Value§
<b>Triglyceride level, mmol/L (mg/dL)</b>				-0.62 (-1.09 to -0.15) [-55 (-96 to -13)]	0.044	0.041
Conventional diet	1.83 ± 0.88 (162 ± 78)	1.88 ± 1.15 (166 ± 102)	0.05 ± 0.96 (4 ± 85)			
Low-carbohydrate diet	2.27 ± 2.31 (201 ± 204)	1.63 ± 1.09 (144 ± 96)	-0.65 ± 1.78 (-58 ± 158)			
<b>Cholesterol level, mmol/L (mg/dL)</b>				0.31 (-0.10 to 0.73) [12 (-4 to 28)]	0.143	0.133
Conventional diet	5.03 ± 0.75 (194 ± 29)	4.84 ± 0.88 (187 ± 34)	-0.21 ± 0.91 (-8 ± 35)			
Low-carbohydrate diet	4.71 ± 1.24 (182 ± 48)	4.87 ± 1.14 (188 ± 44)	0.16 ± 1.11 (6 ± 43)			
<b>HDL cholesterol level, mmol/L (mg/dL)</b>				0.08 (0.01 to 0.16) [3 (0 to 6)]	0.028	0.014
Conventional diet	1.06 ± 0.23 (41 ± 9)	0.93 ± 0.21 (36 ± 8)	-0.13 ± 0.16 (-5 ± 6)			
Low-carbohydrate diet	1.06 ± 0.26 (41 ± 10)	1.04 ± 0.23 (40 ± 9)	-0.03 ± 0.18 (-1 ± 7)			
<b>LDL cholesterol level, mmol/L (mg/dL)¶</b>				0.23 (-0.13 to 0.57) [9 (-5 to 22)]	0.191	0.341
Conventional diet	3.13 ± 0.73 (121 ± 28)	3.06 ± 0.70 (118 ± 27)	-0.10 ± 0.75 (-4 ± 29)			
Low-carbohydrate diet	2.90 ± 0.83 (112 ± 32)	3.11 ± 1.01 (120 ± 39)	0.18 ± 0.91 (7 ± 35)			
<b>Glucose level for persons without diabetes, mmol/L (mg/dL) (n = 78)</b>				-0.06 (-0.39 to 0.33) [-1 (-7 to 6)]	0.693	0.948
Conventional diet	5.66 ± 0.72 (100 ± 11)	5.72 ± 0.61 (103 ± 11)	0.17 ± 0.67 (3 ± 12)			
Low-carbohydrate diet	5.61 ± 0.72 (99 ± 14)	5.66 ± 0.56 (102 ± 10)	0.17 ± 0.61 (3 ± 11)			
<b>Glucose level for persons with diabetes, mmol/L (mg/dL) (n = 54)</b>				-0.28 (-2.33 to 1.72) [-5 (-42 to 31)]	0.800	0.674
Conventional diet	8.55 ± 2.78 (154 ± 50)	7.44 ± 3.44 (134 ± 62)	-1.17 ± 3.66 (-21 ± 66)			
Low-carbohydrate diet	9.21 ± 3.66 (166 ± 66)	7.66 ± 3.39 (138 ± 61)	-1.55 ± 2.16 (-28 ± 39)			
<b>HBA<sub>1c</sub> level for persons with diabetes, % (n = 54)</b>				-0.7 (-1.6 to 0.2)	0.102	0.019
Conventional diet	7.3 ± 1.1	7.2 ± 1.9	-0.1 ± 1.6			
Low-carbohydrate diet	7.4 ± 1.6	6.6 ± 1.4	-0.7 ± 1.0			
<b>Insulin level for persons without diabetes, pmol/L (n = 78)</b>				-49 (-195 to 97)	0.162	0.255
Conventional diet	160 ± 299	174 ± 236	14 ± 354			
Low-carbohydrate diet	153 ± 139	104 ± 49	-49 ± 139			
<b>Insulin level in persons with diabetes (n = 54)</b>				0 (-125 to 125)	0.917	0.458
Conventional diet	229 ± 174	201 ± 125	-28 ± 139			
Low-carbohydrate diet	292 ± 333	257 ± 236	-35 ± 236			
<b>Insulin sensitivity in persons without diabetes¶¶</b>				0.01 (-0.01 to 0.03)	0.234	0.308
Conventional diet	0.32 ± 0.03	0.31 ± 0.03	-0.01 ± 0.04			
Low-carbohydrate diet	0.31 ± 0.03	0.32 ± 0.02	0.01 ± 0.03			
<b>Serum creatinine level, mmol/L</b>				1.8 (-3.5 to 7.1)	0.462	0.321
Conventional diet	89.2 ± 20.3	90.1 ± 20.3	0.9 ± 10.6			
Low-carbohydrate diet	94.4 ± 16.8	96.6 ± 19.5	2.7 ± 14.1			
<b>Blood urea nitrogen level, mmol/L</b>				1.0 (0.3 to 1.7)	0.007	0.002
Conventional diet	5.4 ± 2.1	5.0 ± 1.8	-0.5 ± 1.8			
Low-carbohydrate diet	5.7 ± 1.4	6.1 ± 1.8	0.4 ± 1.4			
<b>Uric acid level, mmol/L</b>				30 (0 to 60)	0.050	0.146
Conventional diet	399 ± 83	387 ± 77	-12 ± 71			
Low-carbohydrate diet	381 ± 83	399 ± 89	17 ± 71			

Continued on following page

Table 3—Continued

Blood pressure, mm Hg						
Systolic				-1 (-8 to 6)	0.780	0.208
Conventional diet	139 ± 16	142 ± 18	2 ± 15			
Low-carbohydrate diet	133 ± 16	134 ± 20	1 ± 19			
Diastolic				2 (-4 to 7)	0.502	0.997
Conventional diet	82 ± 9	83 ± 10	1 ± 10			
Low-carbohydrate diet	77 ± 11	80 ± 14	3 ± 15			

\* Values are given as the mean (±SD) for the 87 persons who completed the study. HBA<sub>1c</sub> = hemoglobin A<sub>1c</sub>; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

† The mean difference in 1-year change and 95% CIs are for the low-carbohydrate diet group relative to the conventional diet group and are obtained by random-coefficient analysis.

‡ The *P* values are for comparison of the change from baseline to 1 year between diet groups by random-coefficient analysis.

§ Adjusted *P* values are obtained by random-coefficient analysis; the included covariates are age, race, sex, baseline body mass index, baseline caloric intake, and the presence or absence of hypertension, lipid-lowering therapy use, diabetes, active smoking, and sleep apnea.

|| LDL cholesterol was not calculated in 2 persons in the low-carbohydrate diet group because of triglyceride levels above 4.52 mmol/L (400 mg/dL).

¶ Determined by the quantitative insulin sensitivity check index:  $1/[(\text{fasting insulin } (\mu\text{U/mL}) + (\log \text{ fasting glucose } (\text{mg/dL}))]$ .

pleted the study (change,  $-0.2 \pm 7.6$  kg vs.  $-7.3 \pm 8.3$  kg, respectively; mean difference,  $-7.1$  kg [CI,  $-11.6$  kg to  $-2.8$  kg];  $P = 0.003$ ). In contrast, weight loss was not significantly different for those on the conventional diet, whether they dropped out or completed the study (change,  $-2.2 \pm 9.5$  kg vs.  $-3.7 \pm 7.7$ , respectively; mean difference,  $-1.5$  kg [CI,  $-5.7$  kg to  $2.7$  kg];  $P > 0.2$ ). Nevertheless, the difference in weight loss between the 2 diet groups for those who dropped out of the study was not significant ( $P > 0.2$ ).

### Serum Lipids

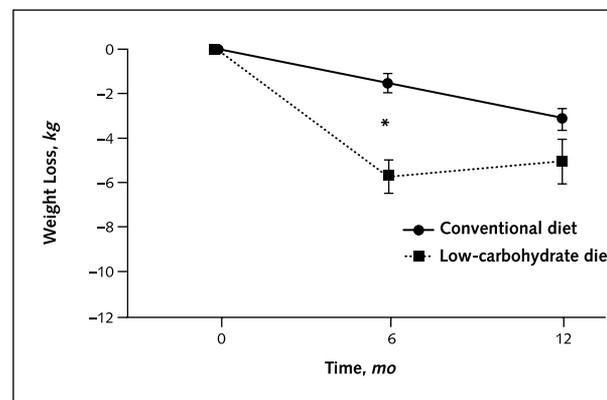
Changes in total and LDL cholesterol were not significantly different between groups (Table 3). Triglyceride levels decreased more in the low-carbohydrate group than in the conventional diet group ( $P = 0.044$  before and  $P = 0.041$  after adjustment for baseline variables) (Table 3). A separate sensitivity analysis that included only the 87 persons who completed the study confirmed the significance of this finding (adjusted  $P = 0.016$ ), as did the sensitivity analysis in which baseline values were carried forward for missing data (adjusted  $P = 0.001$ ). Assignment to the low-carbohydrate group ( $P = 0.003$ ) and greater weight loss ( $P = 0.004$ ) were each independent predictors of a decrease in triglyceride concentration, suggesting a direct effect of the low-carbohydrate diet on triglyceride reduction.

The HDL cholesterol concentration decreased more in the conventional diet group than in the low-carbohydrate group by 1 year ( $P = 0.025$  before and  $P = 0.014$  after adjustment for baseline variables) (Table 3). A separate sensitivity analysis that included only the 87 persons who completed the study confirmed the significance of this finding (adjusted  $P = 0.004$ ), as did the analysis using baseline values carried forward for missing data (adjusted  $P = 0.011$ ). The difference in mean HDL cholesterol response between diet groups remained significant after adjustment for both baseline variables and weight loss ( $P = 0.028$ ), suggesting direct diet-related effects on HDL cholesterol.

### Glycemic Control and Insulin Sensitivity

The difference in the response of glucose and insulin sensitivity between diet groups by 1 year was not significant (Table 3). Despite this, the hemoglobin A<sub>1c</sub> level in the small group of persons with diabetes ( $n = 54$ ) decreased more in the low-carbohydrate group, after adjustment for baseline differences (Table 3). This difference remained significant after weight loss amount was added to the model ( $P = 0.019$ ), suggesting a direct effect of the low-carbohydrate diet on glycemic control. However, the significance of the difference in the response of hemoglobin A<sub>1c</sub> was not confirmed by an analysis that included only the persons who completed the study (adjusted  $P = 0.080$ ) or when baseline values were carried forward for missing persons (adjusted  $P = 0.18$ ). Two persons on the low-carbohydrate diet and 4 on the conventional diet developed diabetes at 1 year ( $P > 0.2$ ).

Figure. Comparison of mean weight loss in kg between participants on the conventional diet and participants on the low-carbohydrate diet at 6 months ( $n = 118$ ) and at 1 year ( $n = 126$ ).



\*  $P = 0.003$  for comparisons between diet groups by random-coefficient analysis. The difference in weight loss was not significant between the 2 diet groups by 1 year ( $P = 0.195$  before and  $P > 0.2$  after adjustment for baseline variables, by random-coefficient analysis). Error bars represent SDs.

### Adverse Reactions

As shown in Table 3, changes in serum creatinine concentration did not significantly differ between groups. However, blood urea nitrogen level increased more in the low-carbohydrate diet group. Changes in uric acid level were not clinically significant.

One person on the low-carbohydrate diet was hospitalized with noncardiac chest pain during the third month of the study. Two persons in the low-carbohydrate group died, including one who died of complications of hyperosmolar coma 5 months into the study and another who had severe ischemic cardiomyopathy and died suddenly 10 months after study enrollment. Laboratory values obtained 14 days before this person's death showed no electrolyte abnormalities.

### DISCUSSION

To our knowledge, this is the largest and longest study to date to compare weight and metabolic responses in persons with a high prevalence of diabetes or the metabolic syndrome receiving intensive counseling on either a low-carbohydrate diet or a conventional diet. We found no significant difference in overall weight loss between persons on these 2 diets. In contrast to the findings by Foster and colleagues (7), persons on the low-carbohydrate diet maintained most of their initial weight loss, whereas those on the conventional diet continued to lose weight. Our different findings may be due to the more intensive diet counseling used in our study. We cannot exclude that a larger study might have demonstrated a statistically significant difference in weight loss between diets. Our enrollment targets were based on a maximum anticipated weight loss by 6 months and assumed weight stabilization thereafter. Given that weight loss continued beyond 6 months in the conventional diet group, we would have needed a sample size of approximately 284 persons per group to show a difference between groups at 1 year, assuming preservation of the observed changes.

Although it has been speculated that a low-carbohydrate diet would facilitate weight loss by promoting the metabolism of adipose tissue (13), our data suggest that weight loss differences may be explained by lower caloric intake on a low-carbohydrate diet. If true, this may be attributable to the simplicity of a low-carbohydrate diet or to greater effects on satiety. Of note, persons on the low-carbohydrate diet who dropped out of the study were less likely to lose weight, whereas those assigned to the conventional diet lost a similar amount of weight whether or not they remained in the study. This observation, together with the difference between diets in weight loss beyond 6 months, raises the possibility that a low-carbohydrate diet is less sustainable than a conventional diet. The low-carbohydrate diet followed in our study had healthy (lower sodium intake) and unhealthy (higher nonsaturated fat and cholesterol levels and lower fiber intake) aspects. The dif-

ference in sodium intake between groups was statistically significant and could represent less consumption of pre-packaged, low-fat but high-salt foods in the low-carbohydrate group.

Despite modest and comparable overall weight loss, the responses of triglycerides and HDL cholesterol to the low-carbohydrate diet were more favorable than to the conventional diet. These findings are consistent with previous studies (7, 14–17) and may be related to diminished very-low-density lipoprotein triglyceride production by the liver in response to decreased carbohydrate substrate delivery, as well as to improvements in insulin sensitivity. The greater preservation of HDL cholesterol on the low-carbohydrate diet may be a secondary effect of the greater decrease in triglycerides via cholesterol ester transferase or through downregulation of hepatic scavenger receptor B1 levels (18). The expression of these receptors, which bind HDL cholesterol and facilitate reverse cholesterol transport to the liver, may be modulated by dietary fats (18).

We also found that the hemoglobin A<sub>1c</sub> levels in the small group of persons with diabetes improved more on the low-carbohydrate diet, although this difference was not significant in our sensitivity analyses. Nevertheless, the amount of improvement in hemoglobin A<sub>1c</sub> in the low-carbohydrate group has a clinically significant effect on micro- and macrovascular complications of diabetes (19).

Our study has several important limitations. Overall weight loss was modest and the overall dropout rate was high. We tried to minimize any biasing effect by extracting 1-year weights for persons who dropped out. Although these weights were not measured in a standardized fashion, any random measurement errors would bias results toward the null. Second, most persons did not meet their dietary targets (<30 g of carbohydrate daily in the low-carbohydrate group and reduction of 500 calories per day in the conventional diet). Meeting these targets would probably have yielded different results. Last, there were some differences between the persons who completed the study and those who dropped out, such as greater weight loss in the former. Nevertheless, the observed differences in responses of triglyceride, HDL cholesterol, and hemoglobin A<sub>1c</sub> levels between diets were independent of differences in weight loss.

In summary, we found similar weight loss in persons randomly assigned to a low-carbohydrate diet or a conventional diet by 1 year. Despite modest overall weight loss in both diet groups, assignment to the low-carbohydrate group had a direct and more favorable effect on triglyceride level, HDL cholesterol level, and glycemic control in the smaller subgroup of patients with diabetes. These findings give further evidence that restriction of carbohydrates in obese persons, who may be overconsuming carbohydrates at baseline, may have favorable metabolic effects. Caution is still needed, however, in recommending a low-carbohydrate diet, as important concerns remain. Most important, future studies will need to evaluate whether a low-carbo-

hydrate diet has more favorable effects on the development of diabetes and on cardiovascular outcomes.

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