

# Effects of Low-Carbohydrate vs Low-Fat Diets on Weight Loss and Cardiovascular Risk Factors

## A Meta-analysis of Randomized Controlled Trials

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**Background:** Low-carbohydrate diets have become increasingly popular for weight loss. However, evidence from individual trials about benefits and risks of these diets to achieve weight loss and modify cardiovascular risk factors is preliminary.

**Methods:** We used the Cochrane Collaboration search strategy to identify trials comparing the effects of low-carbohydrate diets without restriction of energy intake vs low-fat diets in individuals with a body mass index (calculated as weight in kilograms divided by the square of height in meters) of at least 25. Included trials had to report changes in body weight in intention-to-treat analysis and to have a follow-up of at least 6 months. Two reviewers independently assessed trial eligibility and quality of randomized controlled trials.

**Results:** Five trials including a total of 447 individuals fulfilled our inclusion criteria. After 6 months, individuals assigned to low-carbohydrate diets had lost more weight than individuals randomized to low-fat diets (weighted mean difference, -3.3 kg; 95% confidence interval [CI], -5.3 to -1.4 kg). This difference was no longer obvious after 12 months (weighted mean difference, -1.0 kg; 95% CI, -3.5 to 1.5 kg). There were no differences in blood pressure. Tri-

glyceride and high-density lipoprotein cholesterol values changed more favorably in individuals assigned to low-carbohydrate diets (after 6 months, for triglycerides, weighted mean difference, -22.1 mg/dL [-0.25 mmol/L]; 95% CI, -38.1 to -5.3 mg/dL [-0.43 to -0.06 mmol/L]; and for high-density lipoprotein cholesterol, weighted mean difference, 4.6 mg/dL [0.12 mmol/L]; 95% CI, 1.5-8.1 mg/dL [0.04-0.21 mmol/L]), but total cholesterol and low-density lipoprotein cholesterol values changed more favorably in individuals assigned to low-fat diets (weighted mean difference in low-density lipoprotein cholesterol after 6 months, 5.4 mg/dL [0.14 mmol/L]; 95% CI, 1.2-10.1 mg/dL [0.03-0.26 mmol/L]).

**Conclusions:** Low-carbohydrate, non-energy-restricted diets appear to be at least as effective as low-fat, energy-restricted diets in inducing weight loss for up to 1 year. However, potential favorable changes in triglyceride and high-density lipoprotein cholesterol values should be weighed against potential unfavorable changes in low-density lipoprotein cholesterol values when low-carbohydrate diets to induce weight loss are considered.

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**I**N THE PAST 4 DECADES, THE PREVALENCE of obesity among adults aged 20 to 74 years in the United States increased from 13% to 31%.<sup>1</sup> In the United States, obesity results in an estimated 325 000 deaths annually<sup>2</sup> and accounts for about 5.5% of total direct health care costs.<sup>3,4</sup> At any given time, approximately 45% of women and 30% of men in the United States are attempting to lose weight.<sup>5</sup> Numerous diets have been proposed to promote weight loss.<sup>6</sup> Weight loss from certain diets may lead to prevention of type 2 diabetes and improved control of hypertension<sup>7</sup> and may reduce cardiovascular morbidity and mortality. In a recent meta-analysis of randomized controlled trials, little evidence was found to support the use of diets other than low-fat diets for weight reduction.<sup>7</sup> However, there is a lack

of data from well-controlled trials about the most effective dietary approaches to achieve meaningful and long-term weight loss in overweight individuals. Although fat- and energy-restricted diets are generally recommended for these individuals,<sup>8,9</sup> low-carbohydrate, high-protein diets are one of the most popular alternative weight loss approaches.<sup>10</sup> Low-carbohydrate diets derive a large proportion of energy intake from protein and fat, and there is concern for the potentially detrimental impact of these diets on blood lipid levels and on cardiovascular risk.<sup>11</sup> Results from individual clinical trials and uncontrolled studies suggest that there is insufficient evidence to make recommendations for or against the use of low-carbohydrate diets.<sup>12</sup>

In this meta-analysis, we compare the effects of low-carbohydrate diets without en-

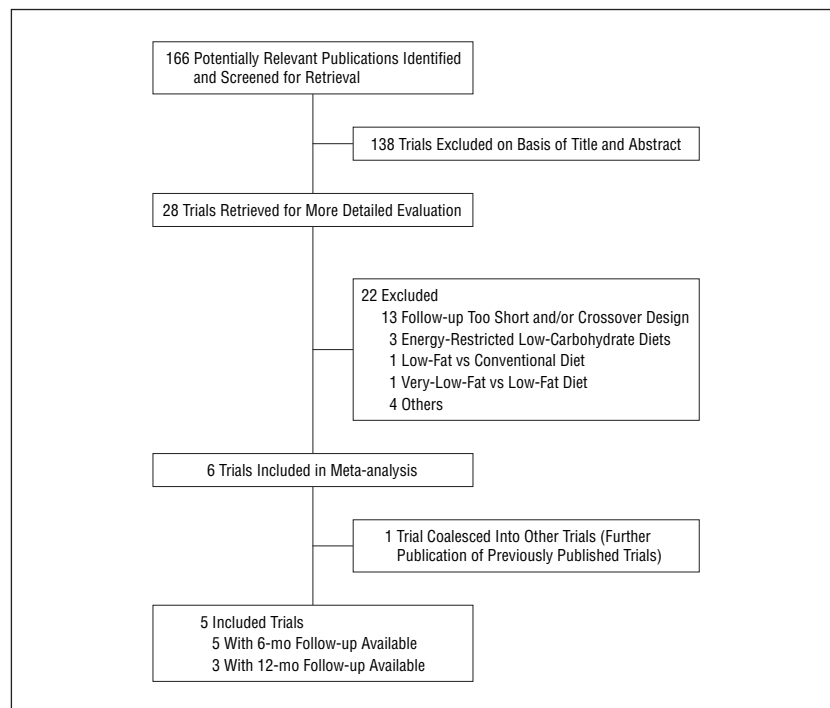


Figure 1. Flow diagram of systematic review.

ergy restriction vs energy-restricted low-fat diets on weight loss, blood pressure, and lipid values in randomized controlled trials with diet interventions for at least 6 months.

## METHODS

### LITERATURE SEARCH

We used the Cochrane Collaboration search strategy<sup>13</sup> and, together with a professional librarian, searched MEDLINE, EMBASE, PASCAL, GLOBAL HEALTH, HEALTH, Web of Science, and the Cochrane Library from January 1, 1980, to February 28, 2005, to identify all randomized controlled trials that compared low-carbohydrate with low-fat diets. We additionally reviewed UptoDate version 2005 and Clinical Evidence Concise 2004 (issue 12), contacted experts in the field, and searched reference lists of identified publications for citations of additional relevant articles. We contacted original trial investigators for additional information where needed.

### TRIAL SELECTION AND DATA ABSTRACTION

To be included in this meta-analysis, trials were required to use a randomized controlled design comparing the effects of a low-carbohydrate diet (defined as a diet allowing a maximum intake of 60 g of carbohydrates per day) without energy intake restriction vs a

low-fat diet (defined as a diet allowing a maximum of 30% of the daily energy intake from fat) with energy intake restriction in individuals with a body mass index (calculated as weight in kilograms divided by the square of height in meters) of at least 25. Included trials had to report changes in body weight by using an intention-to-treat analysis, to have a follow-up of at least 6 months, and to include individuals 16 years and older. We excluded trials with crossover or sequential designs.

Two investigators (A.J.N. and A.N.) independently assessed trial eligibility and quality. Disagreement was resolved by consensus. Data from eligible trials were extracted in duplicate. We assessed the quality of included trials with respect to concealed treatment allocation, blinded outcome assessment, loss to follow-up, and full description of losses to follow-up and withdrawals.<sup>14</sup> The nature of the trials comparing diets required an open intervention with no blinding of trial participants and investigators.

The main end point was the weighted mean difference in weight loss from baseline to 6 and 12 months of follow-up between the 2 groups. Secondary end points were the attrition rates on diets and the weighted mean differences in percentage change of body weight, systolic and diastolic blood pressure, blood lipid levels (total cholesterol, high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], and triglycerides), fasting glucose level, fasting insulin level, and quality of life.

## STATISTICAL ANALYSIS

We pooled treatment effects across trials and calculated weighted mean differences for outcome measures in the low-carbohydrate and the low-fat diet groups by means of a random effects model.<sup>15</sup> We investigated the presence of publication bias by means of funnel plots.<sup>16</sup> We tested for heterogeneity with the Cochran Q test and measured inconsistency ( $I^2$ ; the percentage of total variance across studies that is due to heterogeneity rather than chance) of treatment effects across trials.<sup>17</sup> Sensitivity analyses were conducted to explore heterogeneity. We planned to conduct sensitivity analyses comparing trials with blinded vs unblinded outcome assessment, and trials with low-fat vs very-low-fat diets as a comparison with the low-carbohydrate diets. All statistical analyses were performed with Stata 8.2 software (Stata Corp, College Station, Tex).

## RESULTS

Six published articles fulfilled our inclusion criteria (Figure 1).<sup>18-23</sup> Five of them described trials that included a total of 447 individuals (222 on low-carbohydrate diets and 225 on low-fat diets) and reported 6-month follow-up data. The sixth article<sup>21</sup> reported on an extended 12-month follow-up from 1 of the other 5 articles.<sup>20</sup> Twelve-month follow-up data were available from only 3 trials,<sup>19,21,23</sup> including 137 individuals on low-carbohydrate diets and 138 individuals on low-fat diets. Table 1 shows the characteristics of the 5 trials; Table 2 summarizes the patient data.

Four of the included trials compared the effects of low-carbohydrate diets vs energy-restricted low-fat diets allowing for up to 30% of daily energy intake from fat. One trial compared a low-carbohydrate diet with a very-low-fat diet containing only 10% of energy from fat.<sup>23</sup> There was no trial with a follow-up of more than 12 months. The small number of trials with small numbers of individuals precluded a sensitive exploration of publication bias, although the funnel plot did not indicate evidence of such a bias.

All subjects in the trials were free-living individuals who bought and/or prepared their own food.

**Table 1. General Characteristics of Trials Comparing Low-Carbohydrate vs Low-Fat Diets**

Source	Inclusion Criteria	Method for Missing Data	Concealed Random Allocation	Blinded Outcome Assessor	Interventions
Brehm et al, <sup>18</sup> 2003	Women, BMI 30-35, stable weight during preceding 6 mo	Last follow-up value carried forward* + baseline value carried forward	Yes	No	LC: Maximum 20 g/d of carbohydrates for first 2 wk; increase to 40-60 g/d thereafter if urinary ketones continued to indicate ketosis; no restriction of fat or proteins LF: Energy-restricted (based on body size and calculated by Harris-Benedict equation), <sup>18</sup> maximum 30% of energy from fat, recommended intake of 55% of energy from carbohydrates and 15% from protein
Foster et al, <sup>19</sup> 2003	None specified	Last follow-up value carried forward* + baseline value carried forward	Yes	No	LC: Maximum 20 g/d of carbohydrates for first 2 wk, then gradual increase until desired weight stabilized; no restriction of fat or proteins LF: High-carbohydrate, low-fat, low-energy diet (1200-1500 kcal/d for women and 1500-1800 kcal/d for men); approximately 60% of energy from carbohydrates, 25% from fat, and 15% from protein
Samaha et al, <sup>20</sup> 2003/ Stern et al, <sup>21</sup> 2004	BMI ≥35	Last follow-up value carried forward* + baseline value carried forward	Yes	No	LC: Restriction of carbohydrate intake to <30 g/d, no restriction of total fat intake; recommendation of vegetables and fruits with high ratios of fiber to carbohydrate LF: Restriction to ≤30% of total energy intake from fat, energy restriction to create deficit of 500 kcal/d
Yancy et al, <sup>22</sup> 2004	BMI 30-60, elevated lipid levels, no serious medical condition	Linear mixed-effects model	Yes	No	LC: Restriction of carbohydrate intake to <20 g/d (with weekly addition of 5 g/wk when halfway to body weight goal), unlimited amounts of animal foods and eggs, 4 oz of hard cheese, 2 cups of salad vegetables, and 1 cup of low-carbohydrate vegetables daily LF: <30% of daily energy intake from fat, <10% of daily energy intake from saturated fat, and <300 mg/d of cholesterol; recommended energy intake 500-1000 kcal less than participants' calculated energy intake necessary for weight maintenance
Dansinger et al, <sup>23</sup> 2005	BMI 27-42, ≥1 additional cardiac risk factor	Baseline value carried forward	Yes	No	LC: Restriction of carbohydrates to <20 g/d with gradual increase to 50 g/d LF: Vegetarian diet containing 10% of energy from fat (Ornish diet)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); LC, low-carbohydrate diet; LF, low-fat diet.  
\*Method used for primary analysis.

Mean ages of included individuals ranged from 42 to 49 years. Most trials included predominantly women and healthy individuals. Only 1 trial<sup>20</sup> included extremely obese individuals, with a mean body mass index of 43 and a prevalence of diabetes of 39% (Table 2). One trial<sup>22</sup> reported intention-to-treat data using a linear mixed-effects model,

and another trial<sup>23</sup> used the baseline-value-carried-forward method to account for missing data. The 3 remaining trials<sup>18-20</sup> presented intention-to-treat analyses using both the last-value and the baseline-carried-forward methods. In this meta-analysis, we report results using these individual trials' data based on the last-value-carried-forward method.

There was no qualitative change in outcome when data from these trials were reanalyzed by the baseline-value-carried-forward method. Changes in body weight are shown in **Table 3**, blood pressure in **Table 4**, and lipid values in **Tables 5, 6, 7, and 8** in individual trials comparing low-carbohydrate with low-fat diets.

**Table 2. Patient Characteristics in Trials Comparing Low-Carbohydrate vs Low-Fat Diets**

Source	Diet	N	Age, Mean (SD), y	Sex, No. (%) M	Race, No. (%) White	BMI, Mean (SD)	Follow-up, mo	Completion Rate on Diets at End of Trial, %
Brehm et al, <sup>18</sup> 2003	LC	26	43 (7)	0	22 (85)	34 (2)	6	85
	LF	27	42 (9)	0	18 (67)	34 (2)	6	74
Foster et al, <sup>19</sup> 2003	LC	33	44 (9)	12 (36)	26 (79)	34 (4)	12	61
	LF	30	44 (7)	8 (27)	22 (73)	34 (3)	12	57
Samaha et al, <sup>20</sup> 2003/Stern et al, <sup>21</sup> 2004	LC	64	43 (7)	51 (80)	27 (42)	43 (7)	12	69
	LF	68	43 (8)	58 (85)	23 (34)	43 (8)	12	63
Yancy et al, <sup>22</sup> 2004	LC	59	44 (10)	15 (25)	44 (75)	35 (5)	6	76
	LF	60	46 (9)	13 (22)	47 (78)	34 (5)	6	57
Dansinger et al, <sup>23</sup> 2005	LC	40	47 (12)	19 (47)	32 (80)	35 (4)	12	52
	LF	40	49 (12)	23 (57)	32 (80)	35 (4)	12	50

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); LC, low-carbohydrate diet; LF, low-fat diet.

**Table 3. Changes in Body Weight in Individual Trials Comparing Low-Carbohydrate vs Low-Fat Diets**

Trial	Follow-up, mo	Body Weight, Mean (SD), kg			
		Baseline		Difference	
		LC	LF	LC	LF
Brehm et al, <sup>18</sup> 2003	6	90 (8)	92 (8)	-7.2 (5)	-3.2 (4)
	6	99 (20)	98 (16)	-6.9 (7)	-3.2 (6)
Foster et al, <sup>19</sup> 2003	12	NA	NA	-7.2 (7)	-4.4 (8)
	6	130 (23)	132 (27)	-5.8 (9)	-1.9 (4)
Samaha et al, <sup>20</sup> 2003/Stern et al, <sup>21</sup> 2004	12	NA	NA	-5.1 (9)	-3.1 (8)
	6	98 (15)	97 (19)	-12.0 (7)	-6.5 (7)
Yancy et al, <sup>22</sup> 2004	6	100 (14)	103 (15)	-3.2 (5)	-3.6 (7)
	12	NA	NA	-2.1 (5)	-3.3 (7)

Abbreviations: LC, low-carbohydrate diet; LF, low-fat diet; NA, no data available for intention-to-treat analysis.

### QUALITY OF TRIALS

All trials used concealed treatment allocation. Because of the nature of the trials, blinding of participants was impossible. None of the trials used blinded outcome assessment for the primary outcome of change in body weight. Only 1 trial<sup>22</sup> fully described the reasons for losses to follow-up (Table 1).

### WEIGHT LOSS

After 6 months, individuals assigned to low-carbohydrate diets had lost more weight than individuals randomized to low-fat diets (weighted mean difference, -3.3 kg; 95% confidence interval [CI], -5.3 to -1.4 kg;  $P = .02$  for the test of heterogeneity;  $I^2 = 65\%$ ; 95% uncertainty interval [UI], 7%-87%) (Figure 2). Heterogeneity was mainly due to the fact that the only trial assigning subjects in the low-fat arm to the Ornish diet allowed

a maximum of 10% of the daily energy intake from fat,<sup>23</sup> whereas all other trials allowed 30% of the daily energy intake from fat in subjects randomized to low-fat diets. When this trial was excluded in a sensitivity analysis, the weighted mean difference for subjects randomized to low-carbohydrate vs low-fat diets was -4.3 kg (95% CI, -5.6 to -3.0;  $P = .77$  for the test of heterogeneity;  $I^2 = 0\%$ ; 95% UI, 0%-85%). After 12 months there was no significant difference in weight loss between individuals in the 3 trials<sup>19,21,23</sup> randomized to low-carbohydrate and low-fat diets (weighted mean difference, -1.0 kg; 95% CI, -3.5 to 1.5;  $P = .15$  for the test of heterogeneity;  $I^2 = 48\%$ ; 95% UI, 0%-85%).

The summary estimates of weighted mean differences in percentage change in body weight in individuals randomized to low-car-

bohydrate vs low-fat diets were as follows: after 6 months, -3.4%; 95% CI, -6.0% to -0.7%;  $P < .001$  for the test of heterogeneity;  $I^2 = 91\%$ ; 95% UI, 83%-96%; and after 12 months (3 trials), -0.9%; 95% CI, -3.1 to 1.3;  $P = .15$  for the test of heterogeneity;  $I^2 = 47\%$ ; 95% UI, 0%-84%.

### COMPLETION RATES ON DIETS

After 6 months, individuals randomized to low-carbohydrate diets were more likely to complete the trial than were individuals randomized to low-fat diets (156 [70%] of 222 individuals randomized to low-carbohydrate diets vs 129 [57%] of 225 individuals randomized to low-fat diets; odds ratio, 1.8; 95% CI, 1.2-2.6). After 12 months, this difference was no longer significant (84 [62%] of 135 individuals vs 72 [54%] of 134 individuals; odds ratio, 1.4; 95% CI, 0.9-2.3).

### BLOOD PRESSURE

There was a trend toward lower systolic and diastolic blood pressure in individuals randomized to low-carbohydrate diets after 6 months (weighted mean difference in systolic blood pressure, -2.4 mm Hg; 95% CI, -4.9 to 0.1 mm Hg;  $P = .76$  for the test of heterogeneity;  $I^2 = 0\%$ ; 95% UI, 0%-79%; weighted mean difference in diastolic blood pressure, -1.8 mm Hg; 95% CI, -3.7 to 0.1 mm Hg;  $P = .30$  for the test of heterogeneity;  $I^2 = 17\%$ ; 95% UI, 0%-83%). However, this trend was no longer detectable after 12 months (Figure 3).

**Table 4. Changes in Blood Pressure in Individual Trials Comparing Low-Carbohydrate vs Low-Fat Diets**

Source	Follow-up, mo	Blood Pressure, Mean (SD), mm Hg							
		Systolic				Diastolic			
		Baseline		Difference		Baseline		Difference	
		LC	LF	LC	LF	LC	LF	LC	LF
Brehm et al, <sup>18</sup> 2003	6	115 (15)	114 (12)	-1.8 (16)	-1.0 (11)	78 (12)	75 (10)	-4.8 (12)	-0.7 (6)
Foster et al, <sup>19</sup> 2003	6	121 (11)	123 (14)	-3.9 (14)	2.0 (15)	75 (9)	78 (11)	-4.1 (10)	-3.8 (11)
	12	NA	NA	-1.9 (15)	3.6 (20)	NA	NA	-4.6 (12)	-5.2 (13)
Samaha et al, <sup>20</sup> 2003/ Stern et al, <sup>21</sup> 2004	6	133 (15)	135 (16)	-2.0 (19)	-2.0 (15)	78 (11)	80 (9)	-1.0 (15)	-2.0 (10)
	12	NA	NA	1.0 (19)	2.0 (15)	NA	NA	3.0 (15)	1.0 (10)
Yancy et al, <sup>22</sup> 2004	6	134 (16)	133 (16)	-9.6 (14)	-7.5 (16)	82 (9)	82 (8)	-6.0 (8)	-5.2 (9)
Dansinger et al, <sup>23</sup> 2005	6	129 (17)	133 (17)	-3.7 (10)	-0.6 (9)	77 (9)	76 (9)	-4.0 (7)	-0.3 (6)
	12	NA	NA	0.2 (12)	0.5 (8)	NA	NA	-1.4 (8)	0.2 (5)

Abbreviations: LC, low-carbohydrate diet; LF, low-fat diet; NA, no data available for intention-to-treat analysis.

### LIPID VALUES

Intention-to-treat data for lipid values were available from 4 of 5 trials.<sup>19,20,22,23</sup> Summary estimates of weighted mean differences at 6 months were not in favor of low-carbohydrate diets for total cholesterol values (8.9 mg/dL [0.23 mmol/L]; 95% CI, 3.1-14.3 mg/dL [0.08-0.37 mmol/L];  $P = .48$  for the test of heterogeneity;  $I^2 = 0\%$ ; 95% UI, 0%-85%) (**Figure 4**), nor for LDL-C values (5.4 mg/dL [0.14 mmol/L]; 95% CI, 1.2-10.1 mg/dL [0.03-0.26 mmol/L];  $P = .66$  for the test of heterogeneity;  $I^2 = 0\%$ ; 95% UI, 0%-85%) (**Figure 5**). At 12 months, the summary estimates of the weighted mean change for total cholesterol level (10.1 mg/dL [0.26 mmol/L]; 95% CI, 3.5-16.2 mg/dL [0.09-0.42 mmol/L];  $P = .63$  for the test of heterogeneity;  $I^2 = 0\%$ ; 95% UI, 0%-90%) and LDL-C level (7.7 mg/dL [0.20 mmol/L]; 95% CI, 1.9-13.9 mg/dL [0.05-0.36 mmol/L];  $P = .80$  for the test of heterogeneity;  $I^2 = 0\%$ ; 95% UI, 0%-90%) were basically unchanged when compared with the 6-month data.

Contrarily, summary estimates of weighted mean differences after 6 months in HDL-C (**Figure 6**) and triglyceride (**Figure 7**) values were in favor of low-carbohydrate diets (for HDL-C, 4.6 mg/dL [0.12 mmol/L]; 95% CI, 1.5-8.1 mg/dL [0.04-0.21 mmol/L];  $P = .01$  for the test of heterogeneity;  $I^2 = 75\%$ ; 95% UI, 29%-91%; and for triglyceride, -22.1 mg/dL [-0.25 mmol/L]; 95% CI, -38.1 to -5.3 mg/dL [-0.43 to -0.06 mmol/L];  $P = .13$  for the test of het-

**Table 5. Changes in Total Cholesterol Values in Individual Trials Comparing Low-Carbohydrate vs Low-Fat Diets**

Source	Follow-up, mo	Total Cholesterol, Mean (SD), mg/dL			
		Baseline		Difference	
		LC	LF	LC	LF
Foster et al, <sup>19</sup> 2003	6	201 (35)	193 (31)	6.6 (23)	-8.1 (23)
	12	NA	NA	0.4 (27)	-10.8 (19)
Samaha et al, <sup>20</sup> 2003/ Stern et al, <sup>21</sup> 2004	6	182 (50)	193 (31)	1.9 (35)	-1.2 (31)
	12	NA	NA	6.2 (43)	-8.1 (35)
Yancy et al, <sup>22</sup> 2004	6	244 (35)	240 (35)	-8.1 (35)	-13.5 (39)
Dansinger et al, <sup>23</sup> 2005	6	213 (31)	213 (35)	-0.8 (19)	-11.6 (27)
	12	NA	NA	-4.3 (23)	-10.8 (19)

Abbreviations: LC, low-carbohydrate diet; LF, low-fat diet; NA, no data available for intention-to-treat analysis.

SI conversion factor: To convert cholesterol values to millimoles per liter, multiply by 0.0259.

**Table 6. Changes in LDL-C Values in Individual Trials Comparing Low-Carbohydrate vs Low-Fat Diets**

Source	Follow-up, mo	LDL-C, Mean (SD), mg/dL			
		Baseline		Difference	
		LC	LF	LC	LF
Foster et al, <sup>19</sup> 2003	6	128 (31)	120 (31)	4.6 (19)	-3.1 (27)
	12	NA	NA	0.8 (27)	-7.0 (19)
Samaha et al, <sup>20</sup> 2003/ Stern et al, <sup>21</sup> 2004	6	112 (35)	120 (27)	5.0 (23)	3.1 (19)
	12	NA	NA	7.0 (35)	-3.9 (31)
Yancy et al, <sup>22</sup> 2004	6	159 (27)	147 (31)	1.5 (35)	-7.3 (39)
Dansinger et al, <sup>23</sup> 2005	6	135 (31)	135 (39)	-2.7 (15)	-10.4 (23)
	12	NA	NA	-7.0 (23)	-12.8 (19)

Abbreviations: LC, low-carbohydrate diet; LDL-C, low-density lipoprotein cholesterol; LF, low-fat diet; NA, no data available for intention-to-treat analysis.

SI conversion factor: To convert cholesterol values to millimoles per liter, multiply by 0.0259.

erogeneity;  $I^2 = 48\%$ ; 95% UI, 0%-83%). At 12 months, summary estimates of weighted mean differences for HDL-C and triglycerides, respectively, were as follows: 3.1 mg/dL

(0.08 mmol/L) (95% CI, -0.8 to 7.0 mg/dL [-0.02 to 0.18 mmol/L];  $P = .01$  for heterogeneity;  $I^2 = 79\%$ ; 95% UI, 31%-93%); and -31.0 mg/dL (-0.35 mmol/L) (95% CI, -59.3 to -2.7

mg/dL [-0.67 to -0.03 mmol/L];  $P=.09$  for the test of heterogeneity;  $I^2=59\%$ ; 95% UI, 0%-88%).

## GLUCOSE AND INSULIN VALUES

Intention-to-treat data for changes in glucose and insulin values were available from 3 trials, but meth-

odologic differences in assessment of glucose and insulin values precluded a pooled analysis of these measures. In one trial there was no difference between the 2 groups, either in the area under the glucose curve or in the area under the insulin curve after a glucose tolerance test.<sup>19</sup> Similarly, in the one trial comparing a low-carbohydrate with a

very-low-fat diet, there was no difference in fasting glucose or insulin values between the 2 groups.<sup>23</sup> In the last trial,<sup>20</sup> fasting glucose values were lowered more efficiently in individuals on the low-carbohydrate diet than on the low-fat diet after 6 months ( $-10.8 \pm 23.4$  mg/dL [ $-0.6 \pm 1.3$  mmol/L] vs  $-1.8 \pm 21.6$  mg/dL [ $-0.1 \pm 1.2$  mmol/L];  $P=.02$ ), but this effect was no longer detectable after 12 months. In the same trial, there was no difference in insulin levels between the 2 groups after 12 months. In the subgroup of patients with diabetes in this trial, hemoglobin A<sub>1c</sub> values changed more favorably in individuals on the low-carbohydrate diet than on the low-fat diet at 12 months ( $-0.7\% \pm 1.0\%$  vs  $-0.1\% \pm 1.6\%$ ;  $P=.02$ ; after adjustment for weight loss).

**Table 7. Changes in HDL-C Values in Individual Trials Comparing Low-Carbohydrate vs Low-Fat Diets**

Source	Follow-up, mo	HDL-C, Mean (SD), mg/dL			
		Baseline		Difference	
		LC	LF	LC	LF
Foster et al, <sup>19</sup> 2003	6	46 (12)	50 (12)	9.3 (12)	2.3 (8)
	12	NA	NA	8.5 (12)	1.5 (8)
Samaha et al, <sup>20</sup> 2003/ Stern et al, <sup>21</sup> 2004	6	43 (12)	43 (12)	0 (4)	-1.2 (8)
	12	NA	NA	-1.2 (8)	-1.2 (8)
Yancy et al, <sup>22</sup> 2004	6	54 (15)	54 (15)	5.4 (12)	-1.5 (12)
Dansinger et al, <sup>23</sup> 2005	6	46 (15)	46 (4)	3.9 (8)	-1.5 (8)
	12	NA	NA	3.5 (8)	-0.4 (8)

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LC, low-carbohydrate diet; LF, low-fat diet; NA, no data available for intention-to-treat analysis.

SI conversion factor: To convert cholesterol values to millimoles per liter, multiply by 0.0259.

**Table 8. Changes in Triglyceride Values in Individual Trials Comparing Low-Carbohydrate vs Low-Fat Diets**

Source	Follow-up, mo	Triglycerides, Mean (SD), mg/dL			
		Baseline		Difference	
		LC	LF	LC	LF
Foster et al, <sup>19</sup> 2003	6	133 (115)	124 (80)	-26.6 (44)	-15.9 (27)
	12	NA	NA	-37.2 (35)	-1.8 (62)
Samaha et al, <sup>20</sup> 2003/ Stern et al, <sup>21</sup> 2004	6	186 (177)	177 (124)	-38.1 (80)	-7.1 (53)
	12	NA	NA	-57.6 (159)	4.4 (89)
Yancy et al, <sup>22</sup> 2004	6	159 (106)	195 (106)	-74.4 (80)	-27.5 (89)
Dansinger et al, <sup>23</sup> 2005	6	151 (97)	168 (133)	-10.6 (44)	-2.7 (71)
	12	NA	NA	-1.8 (80)	5.3 (35)

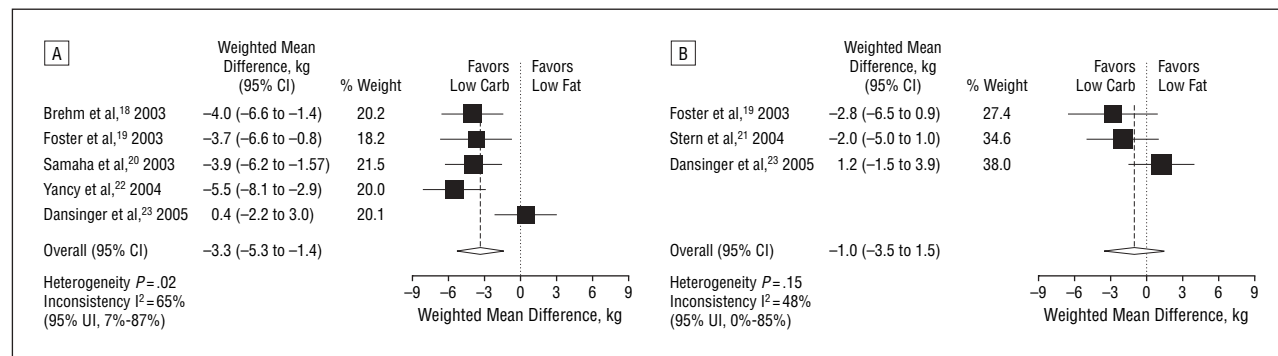
Abbreviations: LC, low-carbohydrate diet; LF, low-fat diet; NA, no data available for intention-to-treat analysis.

SI conversion factor: To convert triglyceride values to millimoles per liter, multiply by 0.0113.

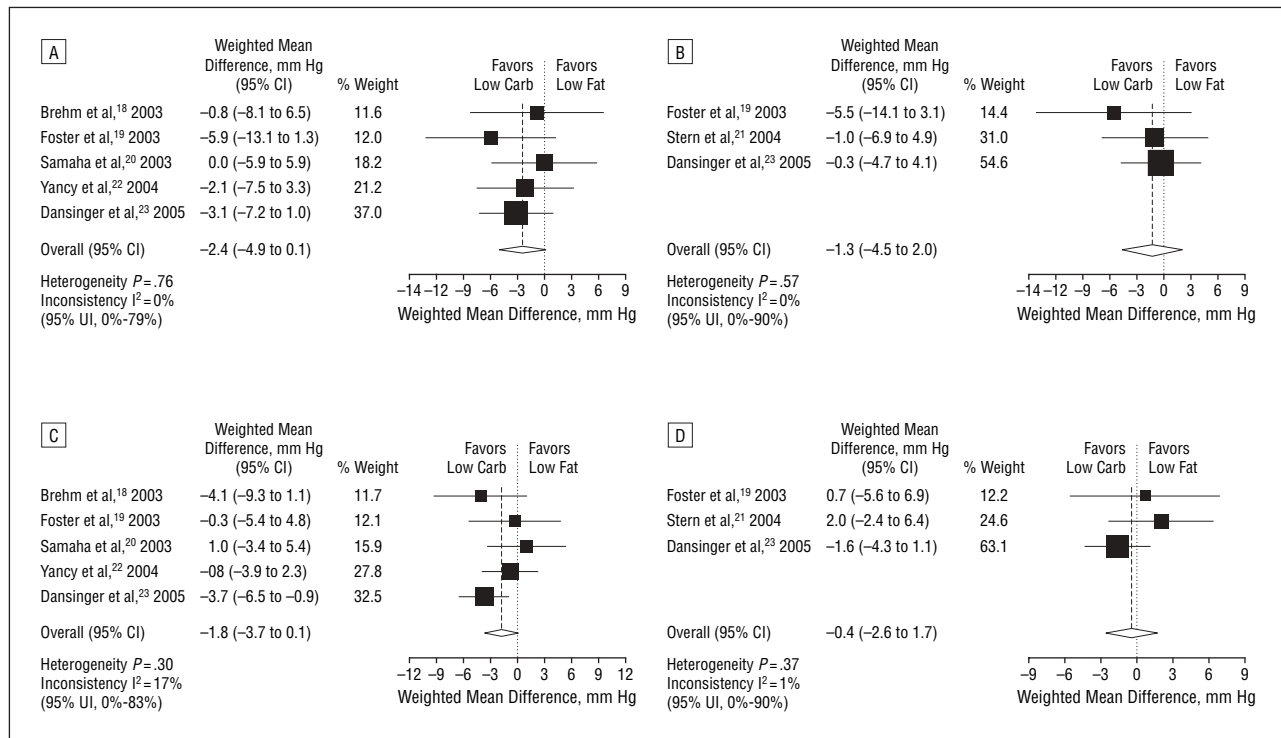
## COMMENT

In this meta-analysis of randomized controlled trials comparing the effects of low-carbohydrate vs low-fat diets, low-carbohydrate diets were more effective in inducing weight loss after 6 months, but this effect was no longer obvious after 12 months of follow-up. There was no clear benefit of either diet when their effects on cardiovascular risk factors were examined. Changes in blood pressure were not different between the 2 groups. Whereas total and LDL-C levels decreased more in individuals randomized to low-fat diets, HDL-C and triglyceride values changed more favorably in individuals randomized to low-carbohydrate diets.

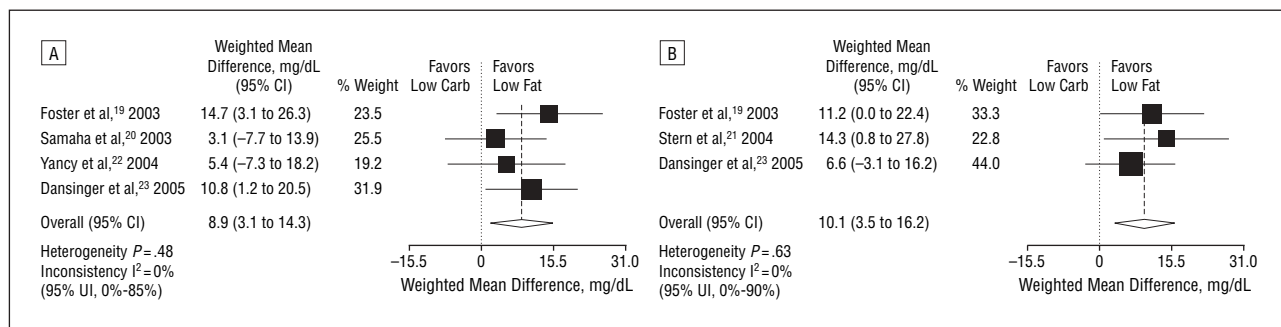
This study has several strengths and limitations. We conducted an



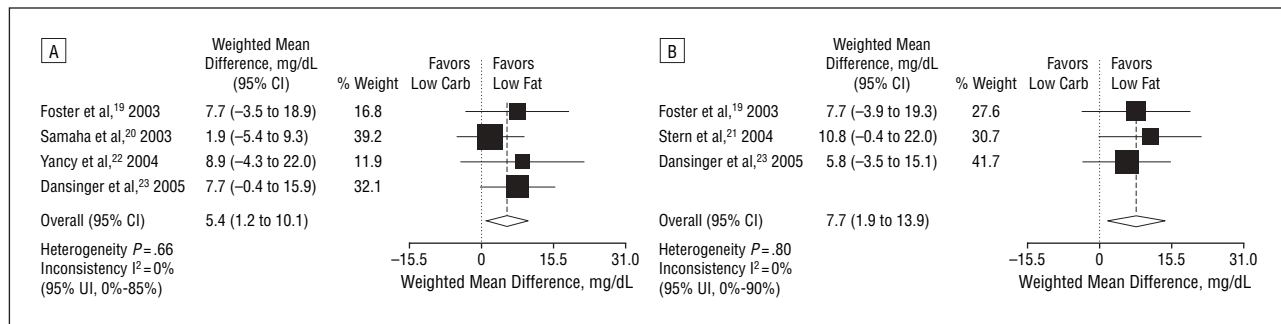
**Figure 2.** Weighted mean differences in weight loss after 6 (A) and 12 (B) months of follow-up. Carb indicates carbohydrates; CI, confidence interval; UI, uncertainty interval.



**Figure 3.** Weighted mean differences in systolic and diastolic blood pressure (BP) after 6 and 12 months of follow-up. A, Systolic BP, 6 months; B, systolic BP, 12 months; C, diastolic BP, 6 months; and D, diastolic BP, 12 months. Carb indicates carbohydrates; CI, confidence interval; UI, uncertainty interval.



**Figure 4.** Weighted mean differences in total cholesterol level after 6 (A) and 12 (B) months of follow-up. Carb indicates carbohydrates; CI, confidence interval; UI, uncertainty interval. To convert cholesterol levels to millimoles per liter, multiply by 0.0259.



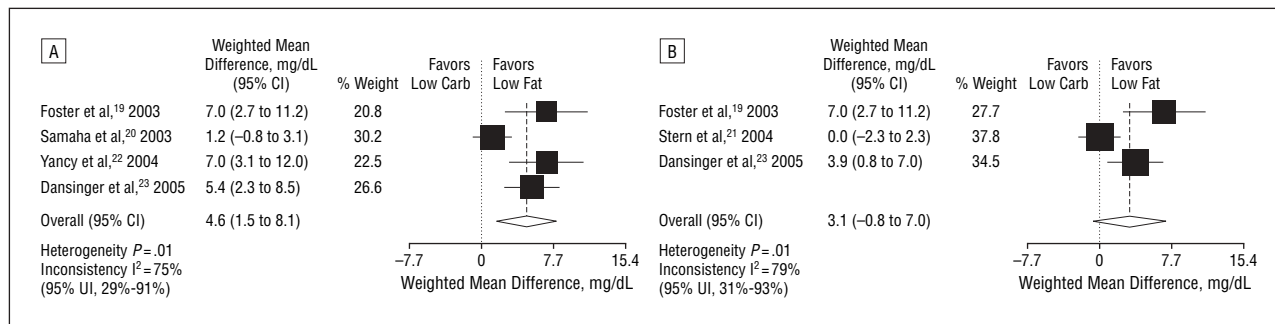
**Figure 5.** Weighted mean differences in low-density lipoprotein cholesterol level after 6 (A) and 12 (B) months of follow-up. Carb indicates carbohydrates; CI, confidence interval; UI, uncertainty interval. To convert cholesterol levels to millimoles per liter, multiply by 0.0259.

extensive literature search to retrieve all relevant eligible trials. Although formal testing did not indicate any publication bias, such a bias cannot be definitely ruled out because of the small number of the

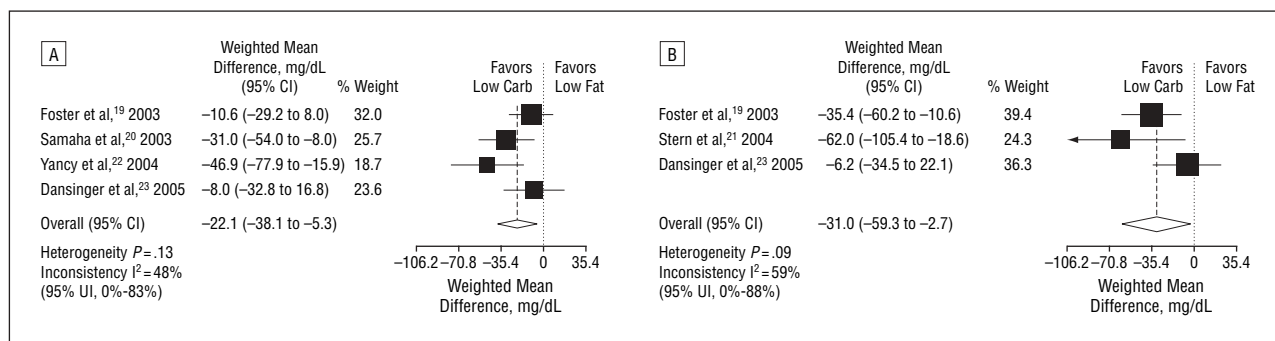
trials included and the low power of any test to detect publication bias.

The quality of the included trials was moderate. Whereas most trials used concealed treatment allocation, losses to follow-up were

quite substantial. No trial reported blinded outcome assessment. Therefore, we were not able to conduct sensitivity analyses comparing trials with blinded outcome assessment vs trials without it, as



**Figure 6.** Weighted mean differences in high-density lipoprotein level after 6 (A) and 12 (B) months of follow-up. Carb indicates carbohydrates; CI, confidence interval; UI, uncertainty interval. To convert cholesterol levels to millimoles per liter, multiply by 0.0259.



**Figure 7.** Weighted mean differences in triglyceride level after 6 (A) and 12 (B) months of follow-up. Carb indicates carbohydrates; CI, confidence interval; UI, uncertainty interval. To convert triglyceride levels to millimoles per liter, multiply by 0.0113.

originally planned. The absence of blinded outcome assessment is a flaw that potentially limits the validity of individual trials.

Dropout rates were substantial. After 1 year of follow-up, between 31% and 48% of individuals randomized to low-carbohydrate diets, and between 37% and 50% of individuals randomized to low-fat diets, had dropped out of the trials. To account for missing data, original trials conducted intention-to-treat analyses, most of them using either the baseline or the last-value-carried-forward method. Both methods are problematic, as one cannot necessarily assume that individuals dropping out of a dietary intervention trial will return to their baseline body weight or maintain their body weight achieved at the time of dropout. However, the results based on various methods of analysis were consistent and thus may strengthen the credibility of our findings. Future trials, however, should aim at obtaining a complete evaluation of body weight and cardiovascular risk factors in all participating individuals irrespective of complete or incomplete adherence to allocated diet.<sup>24</sup>

There was evidence of heterogeneity concerning the main outcome of weight loss after 6 months. The small number of trials included in this meta-analysis and the absence of trials using blinded outcome assessment precluded formal exploration of heterogeneity. Nonetheless, heterogeneity was likely to be due to the one trial that compared a low-carbohydrate diet with a very-low-fat diet, as opposed to a low-fat diet as in other trials.<sup>23</sup> Results were not qualitatively different when the analysis was repeated after exclusion of that trial.

Follow-up in the trials was too short to look at cardiovascular morbidity or mortality. Hence, outcomes were limited to surrogate markers such as body weight and cardiovascular risk factors. Even for the surrogate markers chosen, follow-up durations were rather short. Most trials included younger individuals with severe overweight and obesity. Therefore, our results cannot be generalized to more senior individuals or to individuals with moderate overweight. In addition, no trial reported assessment of quality of life for individuals on either diet. Clearly, there is a need for longer-

term trials in individuals with wider ranges of age and overweight and addressing not only weight loss and cardiovascular risk factors but also cardiovascular morbidity, mortality, and quality of life.

A recent systematic review<sup>12</sup> looking at the efficacy and safety of low-carbohydrate diets concluded that, at that time, there was insufficient evidence to make recommendations for or against the use of low-carbohydrate diets. That review included highly heterogeneous trials with respect to design and carbohydrate content. The review did not include any randomized controlled trial comparing the effects of a low-carbohydrate diet without energy restriction vs a low-fat diet during a minimum of 6 months. On the basis of our results from a meta-analysis of 6 randomized controlled trials published subsequent to the systematic review, we believe there is still insufficient evidence to make recommendations for or against the use of low-carbohydrate diets to induce weight loss, especially for durations longer than 6 months. The differences in weight loss between low-carbohydrate and low-fat diets after 12 months were minor and not clinically relevant. In our opinion, the un-

favorable changes in LDL-C levels caution against the conclusion that low-carbohydrate diets can be generally recommended to promote weight loss. No trials of low-carbohydrate diets have been performed that are powered for clinical end points (eg, myocardial infarction or death). It is therefore uncertain whether the beneficial effects of these diets on HDL-C and triglyceride levels outweigh the unfavorable changes in LDL-C level. In contrast, trials of reduced-fat diets, in conjunction with other lifestyle modifications such as increased physical activity, have demonstrated long-term maintenance of weight reduction and delayed onset of diabetes.<sup>25,26</sup> Furthermore, randomized controlled trials have also demonstrated the benefits of the Mediterranean diet on secondary prevention of cardiovascular disease.<sup>6</sup>

We conclude that low-carbohydrate diets appear to be at least as effective as low-fat diets in inducing weight loss for a duration of up to 1 year. Low-carbohydrate diets are associated with unfavorable changes in total cholesterol and LDL-C levels, but favorable changes in triglyceride and probably HDL-C values. In the absence of evidence that low-carbohydrate diets reduce cardiovascular morbidity and mortality, such diets currently cannot be recommended for prevention of cardiovascular disease.

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ticipate in the study; the participation rate is similar to that in other community-based studies in China.<sup>2</sup>

Having grown up and lived for 21 years in Yingshang County, where the study villages are situated, and continuing to work in rural health research for many years in China (R.C. and X.Q.), we do not think that the “power” of the village leaders and the shadow of the Cultural Revolution would still influence our rural elderly health investigation in terms of reporting bias. The Cultural Revolution has passed and the economic reforms started more than a quarter of a century ago.<sup>3</sup> Village leaders, now selected by rural citizens themselves, need to show acceptable behavior to achieve their position. Because the community we studied is much deprived and is lacking in health care and medication, the participants warmly welcomed our health survey and developed a close collaboration with the medically based interview team. They were eager to tell the interviewers their symptoms in the clinical interviews (the Chinese version of the Geriatric Mental State examination has been used in other Chinese older populations<sup>4</sup>). The validated depression diagnosis by the local Chinese psychiatrists, the  $\kappa$  value of which is similar to that in other

studies,<sup>5</sup> has supported our estimation of a low prevalence of depression in older people in rural China.

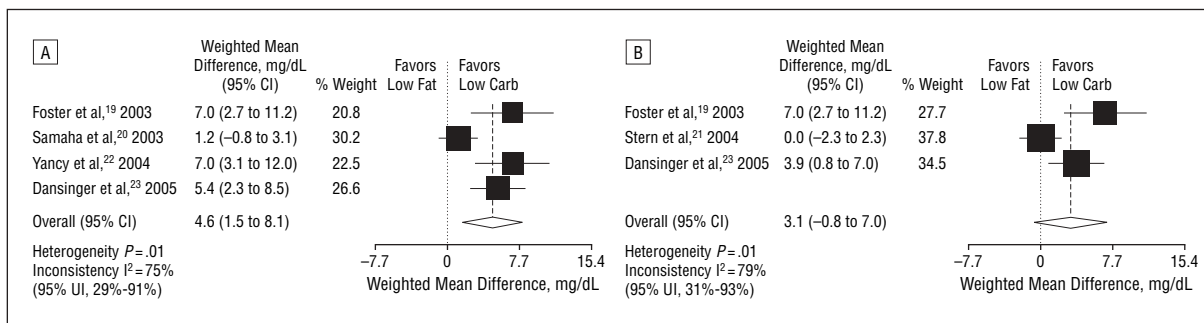
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### Correction

**Error in Figure.** In the Original Investigation by Nordmann et al titled “Effects of Low-Carbohydrate vs Low-Fat Diets on Weight Loss and Cardiovascular Risk Factors: A Meta-analysis of Randomized Controlled Trials,” published in the February 13 issue of the ARCHIVES (2006;166:285-293), an error occurred in **Figure 6** on page 292. The graph labels “Favors Low Fat” and “Favors Low Carb” should have been reversed in both parts A and B of that figure. The corrected Figure 6 is reproduced here with its legend.



**Figure 6.** Weighted mean differences in high-density lipoprotein level after 6 (A) and 12 (B) months of follow-up. Carb indicates carbohydrates; CI, confidence interval; UI, uncertainty interval. To convert cholesterol levels to millimoles per liter, multiply by 0.0259.