Low-Fat Dietary Pattern and Weight Change Over 7 Years

The Women's Health Initiative Dietary Modification Trial

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Context Obesity in the United States has increased dramatically during the past several decades. There is debate about optimum calorie balance for prevention of weight gain, and proponents of some low-carbohydrate diet regimens have suggested that the increasing obesity may be attributed, in part, to low-fat, high-carbohydrate diets.

Objectives To report data on body weight in a long-term, low-fat diet trial for which the primary end points were breast and colorectal cancer and to examine the relationships between weight changes and changes in dietary components.

Design, Setting, and Participants Randomized intervention trial of 48 835 postmenopausal women in the United States who were of diverse backgrounds and ethnicities and participated in the Women's Health Initiative Dietary Modification Trial; 40% (19 541) were randomized to the intervention and 60% (29 294) to a control group. Study enrollment was between 1993 and 1998, and this analysis includes a mean follow-up of 7.5 years (through August 31, 2004).

Interventions The intervention included group and individual sessions to promote a decrease in fat intake and increases in vegetable, fruit, and grain consumption and did not include weight loss or caloric restriction goals. The control group received diet-related education materials.

Main Outcome Measure Change in body weight from baseline to follow-up.

Results Women in the intervention group lost weight in the first year (mean of 2.2 kg, $P<.001$) and maintained lower weight than control women during an average 7.5 years of follow-up (difference, 1.9 kg, $P<.001$ at 1 year and 0.4 kg, $P=.01$ at 7.5 years). No tendency toward weight gain was observed in intervention group women overall or when stratified by age, ethnicity, or body mass index. Weight loss was greatest among women in either group who decreased their percentage of energy from fat. A similar but lesser trend was observed with increases in vegetable and fruit servings, and a nonsignificant trend toward weight loss occurred with increasing intake of fiber.

Conclusion A low-fat eating pattern does not result in weight gain in postmenopausal women.

Clinical Trial Registration ClinicalTrials.gov, NCT00000611.

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THE PREVALENCE OF OBESITY IN the United States has increased dramatically during the past several decades.[1,2] Although the cause of obesity is undoubtedly multifactorial, much attention has been paid to possible effects of dietary macronutrient composition.[3-7] A number of popular diet books[8-10] have suggested that increasing obesity may be attributed to the diets recommended for chronic disease prevention by various national health organizations.[11-13] Specifically, these organizations recommend diets that are lower in total and saturated fat and high in carbohydrates from vegetables, fruits, and whole grains or fiber-rich foods. Proponents of the popular alternative diets[8-10] have claimed that the higher proportion of

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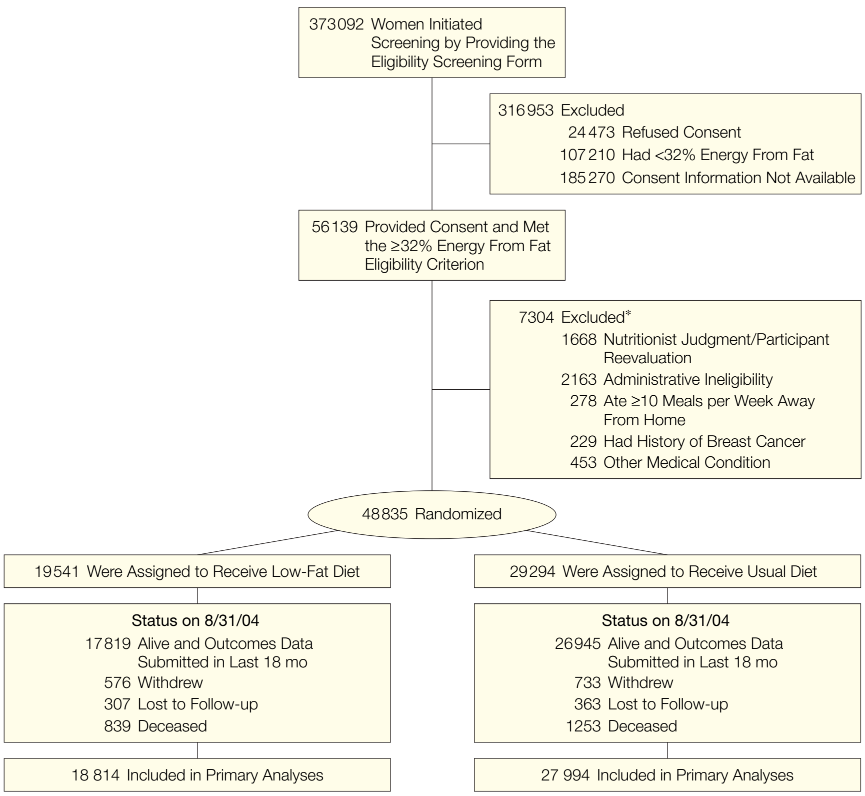
Figure 1. Participant Flow in the Dietary Modification Component of the Women's Health Initiative



*Categories are presented for which exclusions are known. More than 1 reason could be given for exclusion.

carbohydrates in the standard diets may promote weight gain.

Three recent studies reported that individuals assigned to a hypocaloric low-carbohydrate diet (with high protein and fat content) lost more weight during a 6-month period than did those assigned to reduced-fat (25%-33%) diets[14-16]; however, in the study that was extended to 1 year, no differences in weight loss were demonstrated between the low-carbohydrate and low-fat diet groups after 12 months.[14] Furthermore, in the Women's Health Initiative (WHI) Feasibility Study, women in the low-fat intervention group after 6 months lost weight compared with the usual diet control group.[17] A recent comparison of 4 low-fat and high-fat diets showed that weight changes did not differ at 1 year,[7] but an 18-month comparison of a low-fat and Mediterranean-style diet showed poorer adherence to the low-fat diet.[18] No published data are available on the longer-term effects on body weight of the reduced-fat, higher-carbohydrate diets that are recommended.

The WHI Dietary Modification Trial was designed to examine the long-term benefits and risks of a dietary pattern low in fat, with increased vegetable, fruit, and grain intake, on breast and colorectal cancers and cardiovascular disease in postmenopausal women.[19] Between 1993 and 1998, 48 835 postmenopausal women were randomly assigned to either a low-fat dietary intervention or self-selected dietary control group.[20] This report includes anthropometric and nutrient data through August 31, 2004, with a mean follow-up of 7.5 years. The intervention aimed to change diet patterns but did not encourage weight loss or caloric reduction. The trial, therefore, provided a unique opportunity to examine the long-term effects of an ad libitum reduced-fat dietary pattern on body weight. In this article, we report longitudinal data on body weight in the intervention and control groups during follow-up and examine the relationships between weight changes and specific changes in dietary components and macronutrient composition.

METHODS

Details of the study design and recruitment methods for the WHI Dietary Modification Trial have been published.[20,21] Briefly, 48 835 women, nearly 20% of whom were ethnic minorities, between the ages of 50 and 79 years were randomly assigned to the intervention (40%, n=19 541) or control groups (60%, n=29 294) (FIGURE 1). Exclusions after consent were (1) being unable or unwilling to complete a 4-day food record (after a prerandomization trial run-in), (2) changes in eligibility since the initial screening visit, and (3) a combination of nutritionist judgment and participant reevaluation of interest. The third criterion involved a review between the nutritionist and participant about adherence, willingness to be randomized to intervention or control, and willingness to attend sessions and self-monitor if randomized to intervention. Ethnicity was classified by self-report, using options outlined on the personal data form completed by all participants at baseline.

Eligibility criteria included being 50 to 79 years of age, postmenopausal, and consuming a diet at baseline with fat intake of at least 32% of daily total calories as evaluated by a food frequency questionnaire (FFQ); this latter criterion eliminated approximately 50% of individuals screened.[22] Major exclusions included previous breast cancer, cancers other than nonmelanoma skin cancer in the last 10 years, medical conditions with predicted survival less than 3 years, and adherence concerns such as alcoholism. All women provided informed consent before randomization into the trial, and the study was approved by the institutional review boards at the Fred Hutchinson Cancer Institute and all 40 clinical centers.

Women assigned to the control group received a copy of the *Dietary Guidelines for Americans*[23,24] as well as other diet- and health-related educational materials, but otherwise had no contact with study dietitians. In contrast, women randomized to dietary intervention were assigned to groups of 8 to 15 participants for a series of sessions structured to promote dietary and behavioral changes that would result in reducing total dietary fat to 20% and increasing intake of vegetables and fruit to 5 or more servings and grains (whole grains encouraged) to 6 or more servings daily. Participants were informed that the diet was not intended to promote weight loss and were encouraged to maintain usual energy intake by replacing fat calories with calories from other sources, mainly carbohydrate. Details of the intervention have been published.[22] Eighteen group sessions were scheduled during the first 12 months, after which the session frequency was reduced to 4 per year for the duration of the trial. Individual contacts were completed in person or by telephone or mail for women who could not attend the sessions. Group activities were supplemented throughout the course of the study by an intervention protocol consisting of 3 individual interviews that used reflective listening techniques that were validated in a pilot study at 3 centers,[25] targeted message campaigns, and personalized feedback.

The participants were asked to self-monitor dietary fat, fruit and vegetable, and grain intake throughout the study.[21] Independent of the dietary intervention, women in both groups were contacted by telephone every 6 months by clinic staff and scheduled to complete annual clinic visits, during which height, weight, and waist and hip circumference were measured. Physical activity was assessed at baseline and years 1, 3, 6, and 9; questions assessed walking and sports, and hours of activity per week were calculated for each participant. Physical activity was expressed as metabolic equivalents (METs) per week for the analyses.

Diet was monitored with the self-administered WHI FFQ,[21] which was designed specifically for the study. All participants completed an FFQ at baseline and 1 year; thereafter, one third of the participants completed the FFQ each year in a rotating sample so that each participant was asked to complete an FFQ every 3 years. Completion rates were 100% at baseline and thereafter averaged 81% through year 8. Data on diet during follow-up were computed from FFQs obtained during years 5 through 7. Trained clinic staff, who were responsible for anthropometric assessments and administration of FFQs, were blinded to treatment assignments to the extent practical. The dietary intervention staff did not conduct clinical assessments, and clinic staff were not permitted to participate in any intervention activities; participants were instructed not to discuss nutrition activities with clinic staff. Body weight was measured using standardized methods on beam scales at the WHI clinics at baseline and annually throughout the study. Weight measurements during follow-up were unavailable for 727 intervention and 1300 control group women.

For this report, primary analyses using generalized estimating equation methods[26,27] compared weight change from baseline for all participants to estimate mean weight change across follow-up time, adjusted for various characteristics (age, race/ethnicity, and body mass index [BMI] at baseline and change in both dietary intake and physical activity patterns). These estimating methods allow flexibility in the shape of the distribution of weight change at each follow-up year and allow correlations among the weight changes for a given woman at various follow-up times.

Proportions with missing follow-up data for weight (3.7% and 4.4%) and FFQ (20% and 22%) were similar in intervention and control groups. To address the issue of missing data, the inverse selection probability weighted method was used.[28] Secondary analyses examined the relationship between weight change from baseline and various aspects of dietary patterns during follow-up, using a linear regression model for the mean weight change. Aspects examined included changes in percentage of energy from fat, fruit and vegetable consumption, and fiber intake, with a focus on the ability of these data to provide an explanation for weight-change data. Secondary analyses also were performed, adjusting for energy intake by including total kilocalories at baseline in the model to confirm the strength of any associations found between weight change and change in nutrient intake. To monitor potential weight-loss confounders, analyses were evaluated for women who reported having diabetes at baseline (n=2948), women who reported no diabetes at baseline or follow-up (n=42 859), or women who reported no malignancy at baseline or follow-up (n=42 003). All analyses were performed with SAS statistical software, version 9.1.3 (SAS Institute Inc, Cary, NC). All tests used an a priori defined .05 level of significance.

RESULTS

As of August 31, 2004, 2092 (4.3% control and 4.3% intervention) participants were deceased, 1309 had stopped follow-up (2.5% control and 2.9% intervention), and 670 (1.2% control and 1.6% intervention) were lost to follow-up. Mean follow-up was 7.5 years. Dropout rates (sum of stopped or lost to follow-up) were slightly higher in younger (50-59 years) women (4.7%) and in nonwhite women (6.1%).

Baseline characteristics of the study participants by intervention group are summarized in **TABLE 1**. The cohort was ethnically diverse, with a mean (SD) age of 62.3 (6.9) years, and included a range of education and income levels. No significant differences were found between the groups for any of the demographic and clinical measures presented. The groups reflect the characteristics of the general population of postmenopausal women throughout the United States, except the women in this trial had somewhat higher income and education and lower smoking rates.[17] Forty-four percent of the women were taking postmenopausal hormone therapy at baseline, and the proportion decreased during the years of follow-up. Compared with whites, the other racial and ethnic groups were younger, and black, Hispanic, and American Indian women had higher BMIs and lower levels of education and income. Diabetes prevalence was higher among black, Hispanic, and American Indian women than among white or Asian/Pacific Islander women (data not shown).

In comparing nutrient intakes at last follow-up visit and baseline (TABLE 2), only minor (nonsignificant) changes were observed in the average intake and dietary pattern in the control group. Those randomized to the diet intervention reported significant changes in all of the dietary components included in the intervention. Percentage of energy from total, saturated, and unsaturated fat was significantly lower, and percentage of energy from carbohydrate was significantly higher compared with that of control group women during follow-up. Intake of fiber, vegetables and fruits, total grains, and whole grains also increased significantly from baseline in the intervention group while remaining stable in the control group. Black and Hispanic women decreased fat intake slightly less (6.6% and 5.6%) than did the group as a whole (8.3%), and Hispanic women showed somewhat lower increases in fiber than did the group as a whole (1.5. vs 2.5 g/d).

FIGURE 2 shows change in weight in both groups throughout the study period. Mean weight decreased significantly in the intervention group from baseline to year 1 by 2.2 kg ($P<.001$) and was 2.2 kg less than the control group change from baseline at year 1. This difference from baseline between control and intervention groups diminished over time, but a significant difference in weight was maintained through year 9 (0.5 kg, $P=.01$); this diminution in the difference between groups was similar if women who died, dropped out, or were lost to follow-up were removed from the analysis (data not shown). There was no evidence of weight gain over the baseline value among women in the intervention group at any follow-up point.

Changes in body weight during the study are shown by racial/ethnic group in Figure 2. In all racial and ethnic groups, initial weight loss occurred in the intervention group. Decreases in weight from baseline in the intervention vs control group during the course of the study remained significantly different in all years for white women, in year 1 for black women, in years 2 and 5 for Hispanic women, and in years 1, 3, 4, and 6 for American Indian women; in Asian/Pacific Islander women, the differences were not significant. All anthropometric data for each ethnic group and the total cohort are included in TABLE 3.

Table 1. Baseline Characteristics of the Women's Health Initiative Dietary Modification Trial Intervention and Control Groups

	No. (%)		
	Intervention (n = 19 541)	Control (n = 29 294)	*P* Value*
Age at screening	19 541	29 294	
Mean (SD), y	62.3 (6.9)	62.3 (6.9)	.99
Race/ethnicity			
White	15 869 (81.2)	23 890 (81.6)	.76
Black	2137 (10.9)	3129 (10.7)	
Hispanic	755 (3.9)	1099 (3.8)	
American Indian	88 (0.5)	115 (0.4)	
Asian/Pacific Islander	433 (2.2)	674 (2.3)	
Unknown	259 (1.3)	387 (1.3)	
Education			
Grade school	210 (1.1)	366 (1.3)	.27
Some high school	632 (3.3)	1007 (3.5)	
High school diploma/GED	3425 (17.6)	5093 (17.5)	
School after high school	7711 (39.7)	11 597 (39.8)	
College degree or higher	7445 (38.3)	11 042 (37.9)	
Family income, $			
<10 000	683 (3.7)	1100 (4.0)	.40
10 000-19 999	2091 (11.4)	3203 (11.6)	
20 000-34 999	4501 (24.4)	6814 (24.7)	
35 000-49 999	3954 (21.5)	5868 (21.3)	
50 000-74 999	3887 (21.1)	5662 (20.5)	
≥75 000	3293 (17.9)	4948 (17.9)	
Height	19 479	29 205	
Mean (SD), cm	162.2 (6.4)	162.1 (6.6)	.12
Weight	19 523	29 271	
Mean (SD), kg†	76.8 (16.7)	76.7 (16.5)	.38
Body mass index	19 454	29 157	
Mean (SD)‡	29.1 (5.9)	29.1 (5.9)	.58
Waist circumference	19 486	29 224	
Mean (SD), cm	89.0 (13.9)	89.0 (13.7)	.84
Current smoker	1273 (6.6)	1977 (6.8)	.33
History of diabetes	1165 (6.0)	1783 (6.1)	.57
History of cancer	853 (4.4)	1286 (4.4)	.89
Current hormone therapy use at baseline	8640 (44.2)	12 972 (44.3)	.86

Abbreviation: GED, general equivalency diploma.
*P values from 2-sample *t* tests for continuous variables or from χ^2 tests for categorical variables.
†Tested on the log scale.
‡Measured as weight in kilograms divided by height in meters squared.

Stratification of the cohort by age (FIGURE 3) revealed different weight-change trends throughout the study period in the control group, with more weight gain demonstrated among women aged 50 to 59 years (mean, 1.2 kg), relative to those aged 60 to 69 years at baseline (mean, −0.4 kg) and a tendency toward weight loss in those aged 70 to 79 years (mean, −2.2 kg). Mean weight change from baseline was significantly different (ie, lower) in the intervention group than in the control group through year 7 for women aged 70 to 79 years and through year 8 for the 2 younger age strata. Because of the trend toward weight loss in the older control women, analyses also were performed by eliminating the older age group; mean weight-change differences between control and intervention were 2.2 kg at year 1 and 0.6 kg at year 9 (data not shown). Stratification by baseline BMI showed that although the normal-weight (BMI <25) women in the control group tended to gain more weight (mean, 1.4 kg) than the obese women (BMI ≥30), the differences in weight change between the intervention and

Table 2. Baseline and Final Nutrient Intakes in Intervention and Control Groups*

	Intervention		Control			
	No.	Mean (SD)	No.	Mean (SD)	Difference (SE)	*P* Value†
Total energy, kcal						
Baseline	19 517	1788.1 (703.8)	29 273	1789.2 (703.3)	1.1 (6.5)	.86
Follow-up	14 246	1445.9 (510.1)	22 083	1564.0 (594.9)	118.0 (6.1)	<.001
Change	14 246	−361.4 (653.8)	22 083	−240.8 (643.6)	120.7 (7.0)	<.001
Energy from fat, %						
Baseline	19 517	38.8 (5.0)	29 273	38.8 (5.0)	0.01 (0.05)	.84
Follow-up	14 246	29.8 (8.3)	22 083	38.1 (7.2)	8.3 (0.1)	<.001
Change	14 246	−8.8 (8.5)	22 083	−0.6 (7.2)	8.2 (0.1)	<.001
Energy from saturated fat, %						
Baseline	19 517	13.6 (2.6)	29 273	13.6 (2.5)	0.02 (0.02)	.41
Follow-up	14 246	10.1 (3.3)	22 083	13.2 (3.2)	3.1 (0.04)	<.001
Change	14 246	−3.4 (3.6)	22 083	−0.3 (3.2)	3.1 (0.04)	<.001
Energy from carbohydrates, %						
Baseline	19 517	44.5 (6.2)	29 273	44.5 (6.2)	0.02 (0.1)	.73
Follow-up	14 246	52.7 (9.8)	22 083	44.7 (8.5)	−8.0 (0.1)	<.001
Change	14 246	8.2 (9.6)	22 083	0.2 (8.3)	8.0 (0.1)	<.001
Fiber, g						
Baseline	19 517	14.4 (6.0)	29 273	14.4 (6.0)	0.05 (0.1)	.44
Follow-up	14 246	16.9 (7.1)	22 083	14.4 (6.1)	−2.5 (0.1)	<.001
Change	14 246	2.2 (7.0)	22 083	−0.2 (5.9)	2.4 (0.1)	<.001
Fruits and vegetables, servings/d						
Baseline	19 428	3.6 (1.8)	29 170	3.6 (1.8)	0.01 (0.02)	.67
Follow-up	14 183	5.0 (2.4)	22 020	3.9 (2.0)	−1.2 (0.02)	<.001
Change	14 183	1.4 (2.3)	22 020	0.2 (1.9)	−1.2 (0.02)	<.001
Grains, servings/d						
Baseline	19 428	4.7 (2.5)	29 170	4.8 (2.5)	0.02 (0.02)	.45
Follow-up	14 183	4.1 (2.2)	22 020	3.8 (2.0)	−0.4 (0.02)	<.001
Change	14 183	−0.7 (2.7)	22 020	−1.1 (2.5)	−0.4 (0.03)	<.001
Whole grains, servings/d						
Baseline	19 428	1.1 (0.8)	29 170	1.1 (0.8)	0.002 (0.01)	.88
Follow-up	14 183	1.2 (0.8)	22 020	1.0 (0.7)	−0.2 (0.01)	<.001
Change	14 183	0.1 (0.9)	22 020	−0.1 (0.8)	−0.2 (0.01)	<.001
Non–whole grains, servings/d						
Baseline	19 428	3.6 (2.1)	29 170	3.6 (2.1)	0.02 (0.02)	.33
Follow-up	14 183	2.9 (1.7)	22 020	2.7 (1.6)	−0.17 (0.02)	<.001
Change	14 183	−0.7 (2.2)	22 020	−0.9 (2.0)	−0.2 (0.02)	<.001
Physical activity, METs/wk						
Baseline	17 507	10.0 (11.7)	26 254	10.1 (12.0)	0.1 (0.1)	.44
Year 1	9962	11.4 (12.8)	14 822	11.1 (12.7)	−0.3 (0.2)	.13
Change	9962	1.1 (10.4)	14 822	0.9 (10.5)	−0.2 (0.1)	.07

Abbreviation: MET, metabolic equivalents.
*Change = follow-up − baseline. Follow-up values were computed from food frequency questionnaires (FFQs) taken between years 5 and 7. Completion rates for FFQs for years 5 through 7 were 86.8%, 86.6%, and 70.5%, respectively.
†*P* values are from 2-sample *t* tests.

control groups were similar across BMI groups (FIGURE 4).

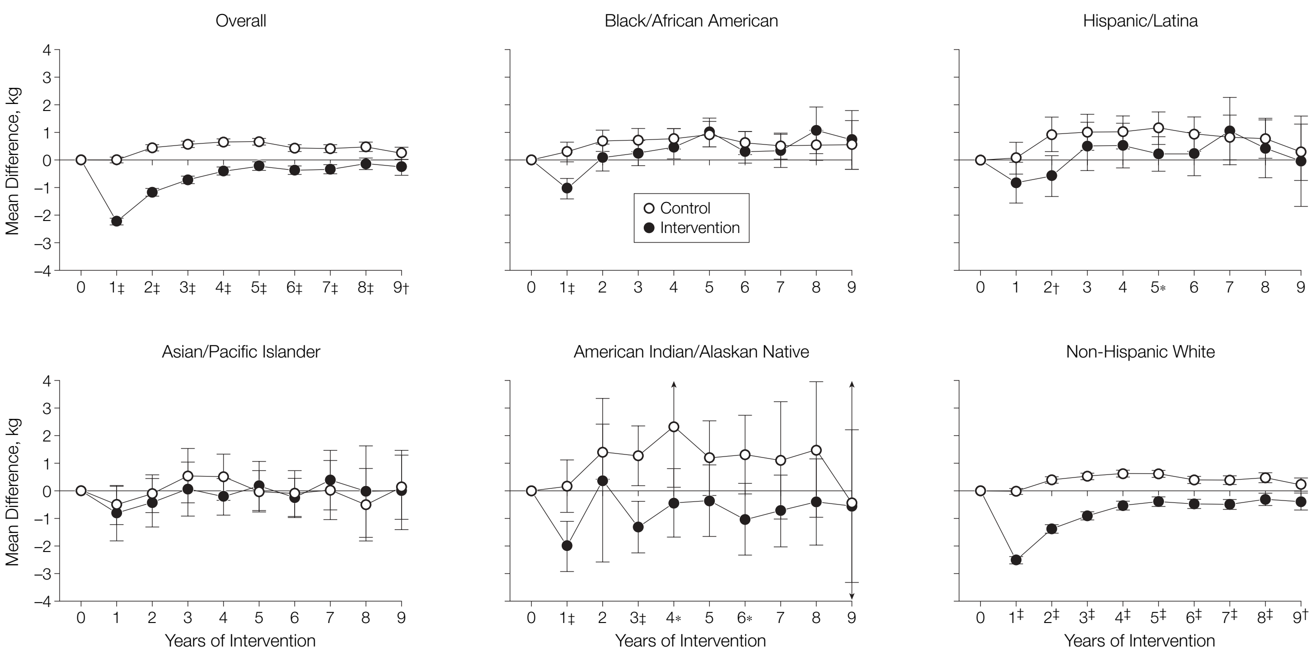
In comparing quintiles of change in percentage of energy intake from fat at follow-up compared with baseline for the participants, a clear relationship was observed between a change in percentage of fat and weight change in the intervention and control groups; those women with the greatest reduction in fat intake had the largest weight loss (FIGURE 5) (*P* for trend <.001 in both the intervention and control groups in models with and without adjustment for baseline energy intake). Those in the fifth quintile, who had at least a 3% increase in fat intake, showed an average weight gain.

Similar analyses for changes in intake of vegetables and fruits showed a trend in both groups for more weight loss with increasing servings of vegetables and fruits, except for the first quintile of individuals, who had reduced vegetable and fruit servings (*P* for trend=.005 and .02 for intervention; *P*=.02 and .03 for control for both models, respectively). A similar analysis for change in fiber intake showed a significant trend for increasing weight loss in the intervention group with increasing fiber (*P*=.002 and .10, respectively), which was not demonstrated in the control group (*P*=.24 and .52, respectively). Analyses examining weight change with changing percentage of energy from carbohydrates showed a trend toward decreasing weight in those with the greatest percentage of increases in carbohydrate intake (*P*<.001 for both intervention and control groups); no significant trends were observed with changes in protein intake for intervention women; however, there was a statistically significant trend for control women (*P*<.001).

In a multivariate model that included age, BMI, race and ethnicity, and changes from baseline to follow-up in percentage of energy from fat, vegetables and fruits, and fiber, weight-change differences between the intervention and control groups were significant (*P*=.001) and were significantly related to reduction in percentage of energy as fat (*P*<.001) and increased total fiber intake (*P*=.001) (TABLE 4). Results from the multivariate modeling using the inverse selection probability weighted method to address the issue of missing data yielded slight differences at the fourth decimal place for a few parameter estimates and *P* values.

Data on change in physical activity data were available for approximately one third of the participants. When change in physical activity was included in the multivariate model, weight-change differences between the intervention and control groups during the study period remained significant (*P*=.001). We examined changes over time in waist circumference, and slight increases occurred in both the intervention group and the control group (Table 3); waist increases were less in the intervention group (*P*=.04).

Figure 2. Change in Body Weight by Group and Ethnicity



Error bars indicate 95% confidence intervals.
**P*≤.05 and >.01 for control group minus intervention group difference.
†*P*≤.01 and >.001 for control group minus intervention group difference.
‡*P*≤.001 for control group minus intervention group difference.

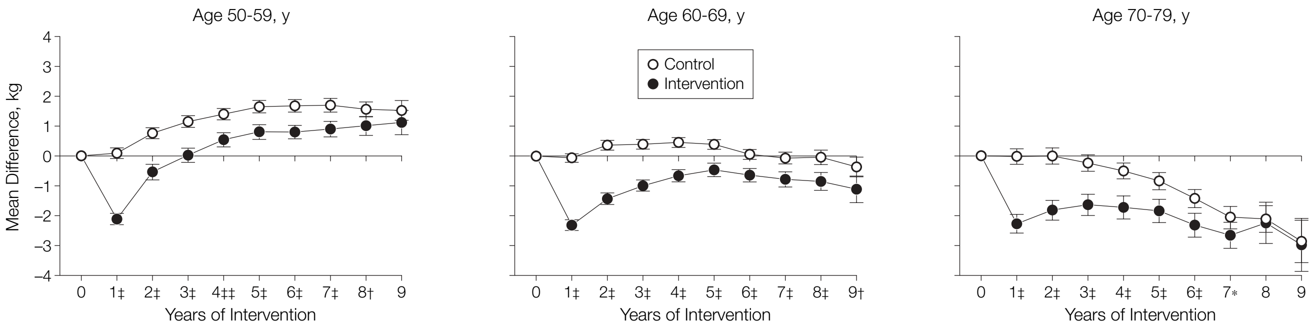
Analyses that excluded women who had a malignancy at baseline (n= 2139) or developed a malignancy during the study (n= 4258) did not substantially alter the pattern of weight change (data not shown). Finally, analyses were conducted in individuals who reported diabetes at baseline (n= 2948), and the same

Table 3. Anthropometric Measures by Race/Ethnicity*

	Intervention		Control		Difference (SE)	*P* Value	Intervention		Control		Difference (SE)	*P* Value
	No.	Mean (SD)	No.	Mean (SD)			No.	Mean (SD)	No.	Mean (SD)		
	Non-Hispanic White						**Black/African American**					
Weight, kg												
Baseline	15 855	76.1 (16.1)	23 868	76.1 (15.9)	−0.03 (0.2)	>.99	2136	85.2 (18.1)	3129	85.1 (18.4)	−0.2 (0.5)	.66
Follow-up	13 400	74.8 (16.5)	20 650	75.4 (16.4)	0.6 (0.2)	<.001	1697	85.0 (19.3)	2523	85.0 (18.7)	−0.1 (0.6)	.91
Change	13 400	−1.0 (10.0)	20 650	−0.2 (10.1)	0.8 (0.1)	<.001	1697	0.2 (11.3)	2523	0.2 (11.2)	0.1 (0.4)	.85
BMI												
Baseline	15 805	28.8 (5.7)	23 782	28.8 (5.7)	0.01 (0.1)	.78	2124	32.1 (6.4)	3118	32.0 (6.5)	−0.1 (0.2)	.70
Follow-up	13 350	28.6 (5.9)	20 564	28.8 (5.7)	0.2 (0.1)	<.001	1684	32.2 (6.7)	2507	32.3 (6.7)	0.03 (0.2)	.77
Change	13 350	−0.01 (3.2)	20 564	0.3 (3.1)	0.3 (0.03)	<.001	1684	0.2 (3.4)	2507	0.4 (3.3)	0.2 (0.1)	.12
Waist circumference, cm												
Baseline	15 830	88.6 (13.8)	23 823	88.7 (13.6)	0.1 (0.1)	.38	2130	93.6 (13.8)	3121	93.5 (13.7)	−0.1 (0.4)	.93
Follow-up	4541	89.7 (14.4)	7045	90.2 (14.1)	0.5 (0.3)	.03	879	94.4 (14.1)	1261	94.7 (14.4)	0.3 (0.6)	.65
Change	4541	1.6 (8.6)	7045	1.9 (8.8)	0.3 (0.2)	.06	879	1.5 (9.9)	1261	2.0 (9.4)	0.5 (0.4)	.27
WHR												
Baseline	15 824	0.82 (0.1)	23 812	0.82 (0.1)	0 (0.001)	.53	2128	0.83 (0.1)	3117	0.82 (0.1)	−0.002 (0.002)	.51
Follow-up	4519	0.83 (0.1)	7022	0.83 (0.1)	0.001 (0.002)	.44	873	0.84 (0.1)	1257	0.84 (0.1)	−0.003 (0.004)	.35
Change	4519	0.02 (0.1)	7022	0.02 (0.1)	0.001 (0.002)	.48	873	0.02 (0.1)	1257	0.02 (0.1)	−0.0002 (0.003)	.96
	Hispanic/Latina						**American Indian/Alaskan Native**					
Weight, kg												
Baseline	754	75.2 (16.0)	1099	73.6 (15.2)	−1.5 (0.7)	.04	87	77.8 (14.4)	115	80.8 (16.9)	2.9 (2.3)	.23
Follow-up	560	75.4 (16.6)	870	73.4 (15.0)	−2.0 (0.8)	.03	66	75.5 (14.4)	88	84.0 (16.9)	8.5 (2.6)	<.001
Change	560	0.2 (9.8)	870	0.5 (8.9)	0.3 (0.5)	.57	66	−0.9 (5.4)	88	0.6 (8.4)	1.5 (1.2)	.19
BMI												
Baseline	749	30.1 (5.7)	1094	29.6 (5.6)	−0.5 (0.3)	.08	87	29.9 (5.5)	115	30.7 (6.2)	0.8 (0.8)	.37
Follow-up	557	30.5 (6.1)	864	29.8 (5.5)	−0.7 (0.3)	.06	65	29.2 (5.3)	88	32.2 (6.2)	3.0 (1.0)	.002
Change	557	0.4 (2.8)	864	0.4 (2.9)	−0.001 (0.2)	>.99	65	−0.1 (2.1)	88	0.7 (3.4)	0.8 (0.5)	.09
Waist circumference, cm												
Baseline	748	89.2 (13.3)	1097	88.3 (13.5)	−0.9 (0.6)	.11	87	92.5 (14.5)	115	94.6 (16.8)	2.1 (2.3)	.37
Follow-up	302	90.6 (12.6)	502	90.1 (12.4)	−0.5 (0.9)	.62	30	90.5 (11.3)	41	96.0 (15.8)	5.5 (3.4)	.13
Change	302	2.0 (7.5)	502	1.2 (9.7)	−0.7 (0.7)	.24	30	0.6 (7.6)	41	4.2 (7.5)	3.5 (1.8)	.06
WHR												
Baseline	747	0.82 (0.1)	1097	0.82 (0.1)	0.001 (0.004)	.81	87	0.84 (0.1)	115	0.86 (0.1)	0.02 (0.02)	.25
Follow-up	300	0.84 (0.1)	500	0.84 (0.1)	−0.01 (0.01)	.17	30	0.83 (0.1)	41	0.85 (0.1)	0.02 (0.02)	.43
Change	300	0.02 (0.1)	500	0.01 (0.1)	−0.01 (0.01)	.01	30	0.01 (0.04)	41	0.02 (0.1)	0.002 (0.01)	.87
	Asian/Pacific Islander						**Total**					
Weight, kg												
Baseline	433	63.4 (13.2)	674	63.3 (14.3)	−0.1 (0.9)	.76	19 524	76.8 (16.6)	29 272	76.7 (16.5)	−0.1 (0.2)	.36
Follow-up	380	63.0 (13.5)	609	62.9 (13.1)	−0.1 (0.9)	.99	16 297	75.7 (17.1)	25 056	76.1 (16.9)	0.4 (0.2)	.01
Change	380	−0.2 (8.6)	609	−0.4 (10.4)	−0.3 (0.6)	.67	16 297	−0.8 (10.1)	25 056	−0.1 (10.1)	0.7 (0.1)	<.001
BMI												
Baseline	433	26.2 (4.9)	670	26.0 (4.9)	−0.2 (0.3)	.50	19 457	29.1 (5.9)	29 164	29.1 (5.9)	−0.03 (0.1)	.57
Follow-up	380	26.1 (4.8)	605	26.1 (4.8)	−0.04 (0.3)	.94	16 230	29.0 (6.1)	24 943	29.2 (5.9)	0.2 (0.1)	<.001
Change	380	0.1 (2.8)	605	0.1 (2.9)	0.1 (0.2)	.67	16 230	0.03 (3.2)	24 943	0.3 (3.1)	0.3 (0.03)	<.001
Waist circumference, cm												
Baseline	431	81.5 (10.9)	673	81.0 (11.1)	−0.4 (0.7)	.51	19 485	89.0 (13.9)	29 216	89.0 (13.7)	0.003 (0.1)	.85
Follow-up	303	83.4 (12.3)	493	82.8 (11.9)	−0.6 (0.9)	.51	6154	90.1 (14.4)	9517	90.4 (14.2)	0.3 (0.2)	.12
Change	303	1.5 (5.9)	493	1.8 (6.1)	0.2 (0.4)	.58	6154	1.6 (8.6)	9517	1.9 (8.8)	0.3 (0.1)	.04
WHR												
Baseline	431	0.82 (0.1)	673	0.82 (0.1)	−0.001 (0.004)	.82	19 475	0.82 (0.1)	29 200	0.82 (0.1)	0.0002 (0.001)	.67
Follow-up	303	0.84 (0.1)	492	0.84 (0.1)	−0.01 (0.01)	.31	6123	0.83 (0.1)	9487	0.83 (0.1)	−0.0003 (0.002)	.98
Change	303	0.01 (0.1)	492	0.01 (0.1)	−0.0002 (0.004)	.97	6123	0.02 (0.1)	9487	0.02 (0.1)	0.0003 (0.001)	.85

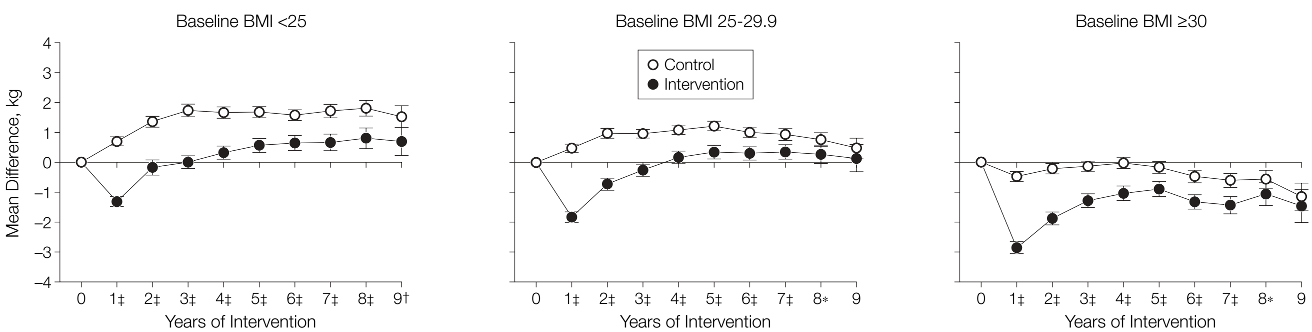
Abbreviations: BMI, body mass index, measured as weight in kilograms divided by height in meters squared; WHR, waist-hip ratio.
* Difference = control − intervention. Change = follow-up − baseline.

Figure 3. Differences (From Baseline) in Body Weight by Group and Age at Screening



Error bars indicate 95% confidence intervals. Numbers at baseline for intervention and control were 50-59 years, 7206 and 10 797; 60-69 years, 9086 and 13 626; 70-79 years, 3249 and 4871.
**P*≤.05 and ≥.01 for control group minus intervention group difference.
†*P*≤.01 and >.001 for control group minus intervention group difference.
‡*P*≤.001 for control group minus intervention group difference.

Figure 4. Differences (From Baseline) in Body Weight by Group and Body Mass Index (BMI) at Screening



Error bars indicate 95% confidence intervals. Numbers at baseline for intervention and control were BMI <25, 5072 and 7585; BMI 25-29.9, 6940 and 10 446; and BMI ≥30, 7442 and 11 126, respectively. BMI was calculated as weight in kilograms divided by height in meters squared.
**P*≤.05 and ≥.01 for control group minus intervention group difference.
†*P*≤.01 and >.001 for control group minus intervention group difference.
‡*P*≤.001 for control group minus intervention group difference.

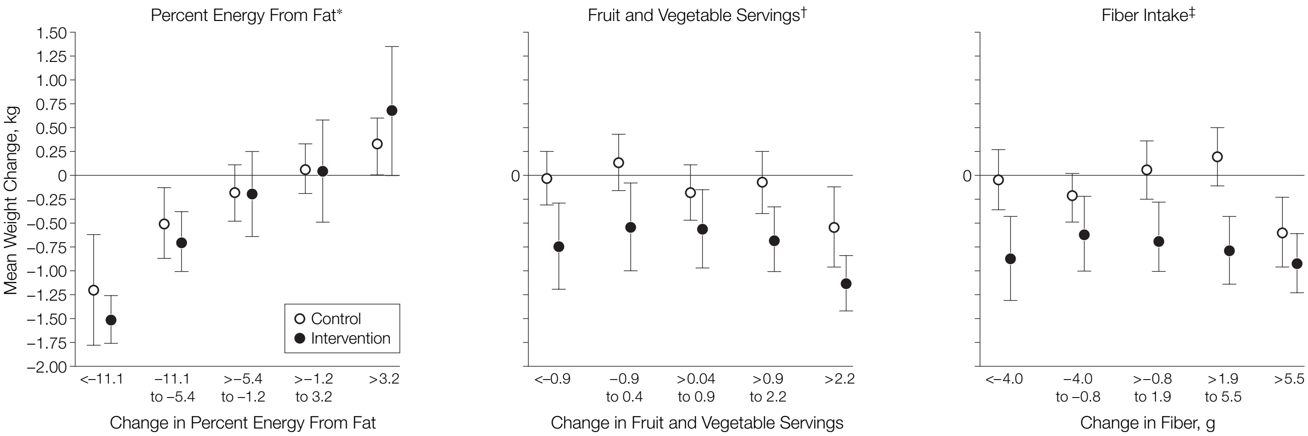
pattern of lower weight in the intervention group was observed (data not shown).

COMMENT

The WHI Dietary Modification Trial provides a unique opportunity to evaluate whether the adoption and maintenance of a lower-fat eating pattern that incorporates higher carbohydrate intake in the form of vegetables, fruits, and grains is associated with weight change, particularly in the absence of any focus on weight loss or total calorie reduction. Results show that after losing 2.2 kg in the first year, women in the intervention group maintained a modest weight loss, compared with the control group, during an average 7.5 years of follow-up and showed no increase from their baseline weight at any point during the study. Weights in the intervention group were lower than those of the control group, who followed their usual eating pattern during the follow-up period, suggesting that a low-fat dietary pattern may help attenuate the tendency for weight gain commonly observed in postmenopausal women.

Some modest weight loss was observed in all ethnic groups during the initial years of the intervention; despite attenuation of the differences in weight between the intervention and control groups as the study progressed, there was no evidence of adverse effects on weight in the intervention women in any ethnic group. The difference in magnitude of response among ethnic groups is difficult to interpret, given that nonwhites are represented in much smaller numbers and may not be representative of specific ethnic populations. Stratification by initial body weight showed no differences in the effect of this dietary pattern among obese, overweight, or normal-weight women. Stratified analyses by age showed that the weight of women in the intervention group remained significantly lower than the weight of women in the control group in all age strata. In the control group, the younger (50-59 years) women tended to gain the most weight,

Figure 5. Mean Weight Change (Baseline to Follow-up) by Quintiles of Change in Nutrient Intake



Error bars indicate 95% confidence intervals.
*P for trend in both groups <.001; R^2 = 0.007 for intervention group, 0.002 for control group.
†P for trend = .005 for intervention group, .02 for control group; R^2 = 0.002 for intervention group, 0.0004 for control group.
‡P for trend = .002 for intervention group, .24 for control group; R^2 = 0.002 for intervention group, 0.0002 for control group.

whereas older (70-79 years) women tended to lose weight throughout the course of the trial. Overall, the weight gain in the control group during the 9 years was less than published trends, probably because of the older age and stable trial cohort.

Because the intervention involved a combination of dietary changes, we sought to determine which of these might be related to the weight changes and weight differences that were observed. Weight loss from baseline through the follow-up period was greatest among women who had the greatest decrease in percentage of energy from fat; the small number of women who increased percentage of energy from fat during the study showed weight increases. Similarly, there was a trend for greater weight loss in the participants who made the largest increase in their numbers of vegetable and fruit servings consumed daily. A nonsignificant trend was observed toward weight loss with increasing fiber intake. Although analyses were conducted on the whole study cohort, including individuals with chronic disease at baseline or follow-up, removing those with a diagnosis of malignancy from the analysis did not significantly change the results. We also performed analyses separately in women who reported diabetes at baseline, and the patterns were similar.

Recommendations from several national organizations have focused on overall health benefits of dietary change (eg, reduction in cardiovascular disease or cancer), rather than weight control, and have emphasized reducing saturated and total fat and increasing complex carbohydrate intake. Proponents of recent popular diet regimens[8-10] have suggested that these dietary recommendations have contributed to the weight gain that has occurred in the United States during the past 4 decades.

Overall, this large randomized trial demonstrates that dietary recommendations for reducing fat and replacing it with vegetables, fruits, and grains do not increase body weight, which implies that guidelines that restrict fat intake and advocate increases in complex carbohydrates have not been a contributing factor to the weight gain that has been occurring in the United States throughout the past several decades.

Three additional studies support weight-loss effects of ad libitum low-fat dietary intake. A study that included reduced fat intake in postmenopausal women after breast cancer diagnosis showed similar results, with small losses in weight.[29] In the Polyp Prevention Trial, intervention-control reductions in body weight were observed in men and women after 4 years of a low-fat, high-fiber dietary intervention,[30] and in the WHI Feasibility Study, weight loss was observed after 6 months.[17]

Table 4. Low-Fat Dietary Pattern and Weight Change Over Time: Results From a Multivariate-Adjusted Model

	Average Rate of Change (SE)	P Value
Age at screening, y		
50-59	2.47 (0.07)	<.001
60-69	0.26 (0.06)	<.001
70-79	Reference	
Race/ethnicity		
White	Reference	
Black	4.16 (0.21)	<.001
Hispanic	−2.59 (0.25)	<.001
American Indian	1.17 (0.61)	.05
Asian/Pacific Islander	−5.39 (0.25)	<.001
Unknown	0.93 (0.38)	.02
Body mass index*		
<25	−18.10 (0.08)	<.001
25-29.9	−6.83 (0.07)	<.001
30-34.9	4.63 (0.09)	<.001
≥35	Reference	
Energy from fat, % (follow-up – baseline)	0.08 (0.01)	<.001
Fruits and vegetables, servings/d (follow-up – baseline)	0.06 (0.03)	.06
Fiber, g (follow-up – baseline)	−0.03 (0.01)	.001
Visit year	0.08 (0.01)	<.001
Intervention vs control	−0.37 (0.11)	.001

*Measured as weight in kilograms divided by height in meters squared.

Most governmental and disease-specific organizations[11-13] now recommend a dietary pattern balanced in macronutrients, with fat between 20% and 35% of calories and total carbohydrates between 45% and 65% of energy intake as the optimum diet, coupled with energy restrictions when weight loss is indicated.[23] Because this trial was not designed to evaluate relative effectiveness of diet composition on caloric reduction or weight loss or maintenance, it cannot definitively establish an optimum fat intake, but rather it provides evidence that restricting fat intake does not lead to weight gain. Thus, it is likely that weight-loss diets throughout a relatively wide range of fat intake may be effective as long as calorie intake is restricted.

The strengths of this study are its randomized design, long-term follow-up, large numbers of participants, diversity of ethnicity and socioeconomic status, and high retention rates. An important limitation of these analyses is that only postmenopausal women aged 50 to 79 years were studied; however, there is no reason to assume that these findings cannot be extrapolated to younger individuals and both sexes, although studies in other groups are needed to support any extrapolations. The exclusion of women reporting more than 32% fat intake at baseline resulted in a truncated sample, with average fat intake in the intervention group being reduced from 39% at baseline to 25% at year 1 and 30% at years 5 through 7, and carbohydrate intake increasing to 57% and 53% at year 1 and years 5 through 7. Because trends showed that weight loss correlated with fat reduction, it is likely these data can be extrapolated to persons who achieve lower fat and higher carbohydrate intake.

An important issue is that food intake was based on an FFQ; major limitations include bias caused by self-report[31] and the need to recall food intake throughout a 3-month period. In addition, the database available for the analyses in this article did not allow the separation of carbohydrate intake into the percentage of sugar or simple vs complex carbohydrate. Finally, although data were adjusted for energy intake, the FFQ is not sufficiently reliable to allow evaluation of the potential effects of changes in caloric intake; in addition, our validation study suggested that baseline percentage of energy from fat may be overestimated by 2% to 3% because of the use of the FFQ in eligibility screening.[20,32] An ongoing nutrient biomarker study using doubly labeled water in a subset of the women will allow calibration of energy consumption from the FFQ and thus provide a reliable way to assess the magnitude of differences between the control and intervention groups.

In summary, the results of this long-term trial of diverse postmenopausal women demonstrate that long-term recommendations to achieve a diet lower in total and saturated fat with increased consumption of fruits, vegetables, and whole grains, and without focus on weight loss, do not cause weight gain. Long-term effects of this dietary pattern on other health outcomes will be available after confirmation of end points and data analyses are completed, and long-term weight-loss studies designed to compare hypocaloric diets of varying macronutrient intake will be needed to establish the relative merits of different weight-loss regimens.

Author Contributions: Dr Howard had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Howard, Manson, Stefanick, Snetselaar, Tinker, Vitolins, Prentice.

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Drafting of the manuscript: Howard, Stefanick, Frank, Thomson, Tinker, Vitolins.

Critical revision of the manuscript for important intellectual content: Howard, Manson, Stefanick, Beresford, Jones, Rodabough, Snetselaar, Thomson, Tinker, Prentice.

Statistical analysis: Frank, Rodabough, Prentice.

Obtained funding: Howard, Manson, Stefanick, Beresford, Snetselaar, Prentice.

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Study supervision: Howard, Manson, Beresford, Thomson.

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Role of the Sponsor: The funding organization, the National Heart, Lung, and Blood Institute, has representation on the steering committee, which governed the design and conduct of the study, the interpretation of the data, and preparation and approval of the article. The National Heart, Lung, and Blood Institute Project Office reviewed the article.

Independent Statistical Analyses: All statistical analyses for the study were performed by statisticians at the Fred Hutchinson Cancer Research Center, Division of Public Health Sciences, under the direction of the principal investigator of the Coordinating Center, Ross Prentice, PhD.

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