Effects of Apolipoprotein E Genotype on Dietary-Induced Changes in High-Density Lipoprotein Cholesterol in Obese Postmenopausal Women

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Lipid responses to a dietary intervention are highly variable between individuals. Part of this variation may be accounted for by individual differences in lipid-regulating genes that interact with diet to induce changes in lipoprotein metabolism. This study determined whether apolipoprotein E (APOE) genotype affects lipid responses to a low-fat, low-cholesterol diet in obese, postmenopausal women. Body weight and lipoprotein lipid responses to a 10-week, dietary intervention (American Heart Association [AHA] Step I) were compared in 61 women with the APOE 2/3 and APOE 3/3 genotype (APOE4-) and 18 women with the APOE 3/4 genotype (APOE4+) of a similar age, body composition, and maximal aerobic capacity. Body weight decreased by 2% in both groups, but changes in body weight correlated only with changes in low-density lipoprotein-cholesterol (LDL-C) ($r = .27$, $P < .05$). The dietary intervention decreased total cholesterol and LDL-C to a similar degree in both genotype groups. However, APOE4- women decreased high-density lipoprotein-cholesterol (HDL-C) by 17% ± 11% and increased triglycerides by 20% ± 41% in response to the diet, while APOE4+ women had a smaller decrease in HDL-C (-8% ± 12%) and no change in plasma triglyceride. These group differences were significant for HDL-C ($P < .01$) and approached significance for triglycerides ($P = .08$). Moreover, APOE4- women decreased HDL_2-C by 32% ± 45%, while APOE4+ women increased HDL_2-C by 12% ± 62% ($P < .01$ between groups). It may be prudent to genotype older women before initiating low-fat diet therapy, as those with the APOE4 allele benefit the most, while the lipid profile could worsen in women without the APOE4 allele.

CORONARY HEART DISEASE (CHD) is a major cause of morbidity and mortality in older women.[1] In general, plasma concentrations of total cholesterol, triglycerides, and low-density lipoprotein-cholesterol (LDL-C) increase, while high-density lipoprotein-cholesterol (HDL-C) concentrations decrease with age and menopause.[2-4] In women, low plasma HDL-C and high triglyceride concentrations impart a greater risk of CHD than high total and LDL-C.[5-10] Therefore, interventions designed to lower lipoprotein lipid risk factors for CHD in older women should focus on lowering triglycerides, total cholesterol, and LDL-C, while raising HDL-C concentration.

The National Cholesterol Education Program (NCEP) and the American Heart Association (AHA) currently recommend lowering dietary intake of fat (< 30%), saturated fat (< 10%), and cholesterol (< 300 mg/d) to improve lipid concentrations and reduce CHD risk.[11,12] However, there is controversy over whether these moderately low-fat diets should be advocated universally.[13-15] In general, adoption of a low-fat diet is effective for reducing LDL-C, but it also lowers HDL-C and increases plasma triglyceride concentrations,[16,17] and this effect may be more evident in women.[14,18] As a result, a reduction in plasma HDL-C, along with an elevation in triglyceride concentration, could potentially increase, rather than decrease, CHD risk in certain women.

Lipid responses to a dietary intervention are highly variable between individuals. Part of this variation may be accounted for by individual differences in lipid-regulating genes that interact with diet to induce changes in lipoprotein metabolism.[19] The Apolipoprotein E (APOE) gene codes for a major protein constituent of chylomicrons and very–low-density lipoproteins (VLDL) remnants, which mediate their binding and uptake by hepatic LDL receptors to facilitate their catabolism by the liver.[20,21] APOE is also present on HDL-C and plays a role in reverse cholesterol transport.[21] APOE is a polymorphic protein with 3 major isoforms (APOE2, APOE3, and APOE4) under the control of 3 independent codominant alleles, with frequencies of approximately 8%, 77%, and 15%, respectively, in Caucasian populations.[22,23] Genetic variation in the APOE gene accounts for 5% to 15% of the variance in total cholesterol and LDL-C within populations, with individuals heterozygous and homozygous for the APOE4 allele having the highest concentrations of plasma total cholesterol and LDL-C.[22,24] In addition, women, but not men, with the APOE4 allele tend to have lower HDL-C concentrations than women without this allele.[24-27]

Several previous studies examined APOE gene-diet interactions on lipid concentrations, but results of these studies are inconsistent, especially with regard to changes in HDL-C (reviewed in Ordovas[19]). The discrepant results among studies are likely due to differences in the age, race, gender, and obesity status of the subjects studied. In particular, there appears to be a gene-sex interaction on the effects of APOE genotype on lipid responses to dietary manipulation, with most studies finding a significant diet by APOE gene interaction in men, but not

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premenopausal women.[28] Previous results are also confounded by differences between studies in the interventions used, resulting in variation in the amount of weight loss and the magnitude of reduction in total dietary fat, as well as specific types of fat. Therefore, we conducted a secondary, retrospective analyses of data collected for a weight loss study to assess whether APOE genotype affected lipid responses to a 10-week, weight-maintaining, AHA Step I diet in a homogenous sample of obese, but otherwise healthy, Caucasian, postmenopausal women.

MATERIALS AND METHODS

Caucasian, middle-aged and older (50 to 65 years) women were recruited by newspaper advertisement for participation in a weight loss study, which began with a 10-week period of weight stabilization on the AHA Step 1 diet. This study reports the effects of the APOE genotype in women who completed the initial AHA dietary intervention. Women were first screened by telephone and those who reported being overweight or obese (body mass index [BMI] $>$ 25 to 45 kg/m^2), postmenopausal (no menstruation for at least 1 year), sedentary ($<$ 20 minutes of exercise 2 days per week), weight-stable ($<$ 2.0 kg weight change in the last year), nonsmoking, and not on medications affecting lipid or glucose metabolism, including hormone replacement therapy, were scheduled for further medical screening.

After providing written, informed consent to participate in the study according to the guidelines of the University of Maryland Institutional Review Board for Human Research, the women underwent a medical evaluation to determine their eligibility for the study. This screening evaluation included a medical history, physical examination, fasting blood profile, and 12-lead resting electrocardiogram (ECG) to exclude subjects with evidence of CHD, diabetes (fasting blood glucose $>$ 7.0 mmol/L or 2-hour blood glucose $>$ 11.1 mmol/L),[29] cancer, liver, renal or hematologic disease, or other medical disorders. A total of 88 women met the study eligibility criteria and were enrolled in the AHA Step I diet instruction class. Eight of these women dropped out during the 10-week diet intervention due to personal reasons, such as relocation, new employment opportunities, increasing family responsibilities, or health problems unrelated to the study. Thus, data are reported on 80 women who completed the entire study.

Study Design

All women underwent baseline testing before meeting in a weekly group session with a registered dietitian for 10 weeks of instruction in the principles of the AHA Step 1 diet. This diet was composed of 50% to 55% carbohydrate, 15% to 20% protein, 20 to 30 g of fiber and less than 30% fat with less than 300 mg/d cholesterol and 3 g/d sodium.[12] The women were asked to remain sedentary and weight stable and to follow this diet throughout the 10 weeks. Body weight was measured weekly, and women who started to lose weight were counseled not to decrease caloric intake and to maintain their initial body weight during the intervention. On average, the women attended 90% of these weekly meetings, and dietary compliance was monitored by weekly review of American Diabetic Association exchange records by the dietitian or diet technician. Following the AHA diet intervention, body weight, dietary intake, and lipoprotein lipid concentrations were measured again.

Body composition, fat distribution, and maximal aerobic capacity (measured only at baseline). Height (cm) and weight (kg) were measured and BMI was calculated as kg/m^2. Waist-to-hip ratio (WHR) was measured in duplicate and calculated as the ratio of the minimal waist circumference to the circumference of the maximal gluteal protuberance. Lean mass and adipose tissue mass were measured using dual energy x-ray absorptiometry (DXA, Model DPX-L; Lunar Radiation Corp, Madison, WI). $\dot{V}O_2$max was measured on a motor-driven treadmill (Quinton, Bothell, WA) during a progressive exercise test to voluntary exhaustion as previously described.[30] A valid $\dot{V}O_2$max was obtained when at least 2 of these 3 criteria were met: (1) maximal heart rate greater than 90% of age-predicted maximal heart rate (220 bpm-age), (2) respiratory exchange ratio of at least 1.10, and (3) plateau in $\dot{V}O_2$ ($<$ 200 mL/min change) with increasing work rate.

Dietary intake. Dietary intake was measured from food diaries recorded for 7 consecutive days before and after the AHA dietary intervention. The women were given detailed instructions to record all consumed foods and beverages and were provided with a food scale to weigh food portions. The food records were reviewed individually with each woman by a registered dietitian to ensure accuracy and completeness. Women who did not record a detailed description of a food item (ie, portion size, method of preparation, use of condiments, etc) were personally asked to recall the details before the item was entered into the analysis program (NUTRITIONIST IV, San Bruno, CA).

Lipoprotein lipids. Venous blood samples for the measurement of lipoprotein lipid concentrations were collected in chilled tubes containing 1 mg of EDTA/mL of blood after a 12-hour fast on 2 different days both before and after the AHA diet. Plasma was separated by centrifugation at 4°C and total cholesterol and triglyceride concentrations were measured by enzymatic methods as previously described.[31] Because no subject had a plasma triglyceride concentration greater than 4.52 mmol/L (400 mg/dL), LDL-C was calculated by the Friedewald equation. In our laboratory, the interassay and intra-assay coefficients of variation for the measurement of total cholesterol is 6.2% and 1.5%; triglycerides, 7.6% and 2.6%; HDL-C, 9.2% and 2.7%; and LDL-C, 7.6% and 2.75, respectively. The average value for each measurement period was used in the statistical analyses.

APOE genotyping. DNA was isolated (QIAamp Blood Kit; QIAGEN, Valencia, CA) from peripheral lymphocytes in blood drawn on the day of each subject's initial lipid measurement. The APOE genotype was determined as previously described.[32]

Statistics

All data were analyzed using the Statview program for Macintosh (Abacus Concepts, Berkeley, CA). Descriptive statistics were calculated for all variables, and all data were tested for normal distribution using the Shapiro-Wilk test for normality. Triglyceride concentrations were not normally distributed, and the natural logarithm transformed this variable to a normal distribution before data analyses. Comparisons were made within and between groups of women with and without at least 1 copy of the APOE4 allele. Changes in body weight, dietary intake, and lipoprotein lipids in response to the AHA diet were determined using a paired *t* test within genotype groups. Student's *t* test was used to test for statistically significant differences between groups at baseline and for changes in response to the AHA diet. We used χ^2 analysis to assess the probability of group differences in the number of women with undesirable HDL-C concentrations (ie, $<$ 1.16 mmol/L) before and after the AHA dietary intervention. Regression analysis was used to calculate correlation coefficients between changes in lipoprotein lipids and changes in body weight, as well as the initial lipoprotein lipid level. All data are presented as mean $\pm$ standard deviation (SD), and the level of significance was set at $P < .05$ for all analyses.

RESULTS

The frequency of each APOE genotype in this sample of 80 Caucasian, postmenopausal women was as follows: APOE 2/2 = 1; APOE 2/3 = 14; APOE 2/4 = 1; APOE 3/3 = 46; APOE 3/4 = 18, and APOE 4/4 = 0. This is consistent with literature reports of frequency estimates of 10% to 15% for the APOE4 allele in Caucasian populations.[22] The subject with the

Table 1. Baseline Characteristics of Postmenopausal Women With and Without the APOE4 Allele

	APOE4+ (n = 18)	*APOE4−* (n = 61)
Age (yr)	60 ± 5	60 ± 5
BMI (kg/m^2)	31.9 ± 3.3	32.6 ± 4.3
Fat mass (kg)	37.4 ± 7.7	39.4 ± 9.1
Lean mass (kg)	40.4 ± 4.0	40.9 ± 4.7
Waist (cm)	93.4 ± 8.1	96.8 ± 10.6
Hip (cm)	113.6 ± 7.0	117.3 ± 11.9
WHR	0.83 ± 0.07	0.83 ± 0.07
$\dot{V}o_2$max (mL/kg/min)	20.5 ± 4.1	19.8 ± 3.2

NOTE. Data are mean ± SD; no group differences.
Abbreviations: BMI, body mass index; WHR, waist-to-hip ratio.

APOE 2/2 genotype was grouped with those of the APOE 2/3 genotype, and the subject with the APOE 2/4 genotype was eliminated from the data analyses. Since there were no significant differences in the lipid responses to the AHA diet between women with the APOE 2/3 genotype and those with the APOE 3/3 genotype, these women were combined (APOE 4-, n = 61) for comparison of lipid responses to women with the APOE4 allele (APOE4+, n = 18). Both genotype groups were of a similar age, BMI, body composition, WHR, and V)$o_2$max (Table 1).

Body weight and dietary intake changes by APOE genotype. There was a small, but significant, decrease in body weight following the AHA Step 1 diet, which was not different between genotype groups (APOE4+ = -2.4% ± 2.2%; APOE4- = -2.1% ± 2.8%; Table 2). Dietary instruction on the AHA Step 1 diet for 10 weeks resulted in a decrease in the percentage of energy consumed as fat and an increase in the percentage of energy consumed as carbohydrate and protein in both groups (Table 2). The percentage of saturated, polyunsaturated, and monounsaturated fat also decreased similarly in both groups. Thus, the dietary instructions were complied with to a similar degree in both genotype groups.

Lipoprotein lipid changes by APOE genotype. At baseline, lipoprotein lipid values were similar between genotype groups, except for HDL-C, which was higher in APOE4- women (Table 3). Women without the APOE4 allele (APOE4-) decreased total cholesterol and LDL-C to a similar degree (-14.8% ± 16.6% and –5.7% ± 12.8%, respectively) as women with the APOE4 allele (APOE4+; -15.2% ± 15.9% and −6.4% ± 11.2%, respectively) (Fig 1). However, APOE4- women decreased HDL-C by 17.0% ± 10.8% and increased triglycerides by 19.6% ± 40.6% in response to the low-fat diet, while APOE4+ women had a smaller decrease in HDL-C (-7.8% ± 12.2%) and no change in plasma triglycerides. These group differences were significant for HDL-C ($P < .01$) and approached significance for triglycerides ($P = .08$). Moreover, women who were APOE4- decreased HDL_2-C by 32.3% ± 44.5%, while women who were APOE4+ increased HDL_2-C by 11.9% ± 62.0% ($P < .01$ between groups). The LDL-C/HDL-C ratio in the APOE4- group increased by 15.5% ± 17.1%, but did not change in women who were APOE4+.

At baseline, the number of women with undesirable HDL-C concentrations (ie, <1.16 mmol/L) was 8 (13%) in the APOE4- group and 5 (28%) in the APOE4+ group (not significant by χ^2 analysis). After the dietary intervention, the total number of women with an HDL-C concentration less than 1.16 mmol/L increased from 13 to 36 women. All women whose HDL-C was below 1.16 mmol/L remained below this level after the intervention. Of the 23 women whose HDL-C dropped to undesirable concentrations with the AHA diet, 18 (83% of the women whose HDL-C dropped below 1.16 mmol/L) were APOE4- and 5 (17%) were APOE4+.

Regression analyses. In all women, changes in LDL-C correlated with changes in body weight during the AHA diet ($r = .27$, $P < .05$), but changes in the other lipoprotein lipids were not related to changes in body weight. Except for total cholesterol, changes in all lipids correlated negatively with the baseline concentration for each lipid (LDL-C, $r = -.43$; triglycerides, $r = -.37$; HDL-C, $r = -.56$; and HDL_2-C, $r = -.56$; $P < .01$). These relationships did not differ between genotype groups.

DISCUSSION

This study was conducted to determine whether the APOE genotype influenced lipoprotein lipid responses to an AHA Step 1 diet in a homogenous population of obese, middle-aged and older, postmenopausal women. The findings indicate that total cholesterol and LDL-C concentrations decreased in response to the dietary intervention, and that the magnitude of

Table 2. Effects of AHA Dietary Instruction on Body Weight and Dietary Intake by APOE Genotype

	APOE4+ (n = 18)		APOE4− (n = 61)	
	Before	After	Before	After
Body weight (kg)	83.9 ± 9.2	81.8 ± 9.8*	86.4 ± 12.82	84.8 ± 12.9†
Total energy	1,746 ± 482	1,580 ± 411†	1,874 ± 510	1,710 ± 281†
Carbohydrate (%)	52 ± 6	57 ± 5†	51 ± 6	58 ± 5*
Protein (%)	15 ± 2	19 ± 3†	16 ± 3	18 ± 3*
Fat (%)	31 ± 7	22 ± 6*	31 ± 6	23 ± 5*
Saturated fat (%)	10 ± 3	6 ± 2*	9 ± 3	6 ± 2*
Polyunsaturated fat (%)	6 ± 2	5 ± 2‡	6 ± 2	4 ± 1‡
Monounsaturated fat (%)	10 ± 3	7 ± 2†	10 ± 2	7 ± 2*
Cholesterol (mg/d)	209 ± 70	157 ± 50	204 ± 73	169 ± 90

NOTE. Data are mean ± SD.
*$P < .0001$, †$P < .01$, ‡$P < .05$ *v* baseline (within group) by paired ± test.

Table 3. Effects of AHA Dietary Instruction on Lipoprotein Lipids by APOE Genotype

	APOE4+ (n = 18)		APOE4− (n = 61)	
	Before	After	Before	After
Triglycerides	1.76 ± 0.71	1.75 ± 0.71	1.47 ± 0.54	1.69 ± 0.61*
Total cholesterol	5.64 ± 0.67	4.78 ± 0.91*	5.69 ± 0.93	4.86 ± 1.19†
LDL-cholesterol	3.54 ± 0.49	3.31 ± 0.57‡	3.51 ± 0.78	3.31 ± 0.80‡
HDL-cholesterol	1.29 ± 0.23	1.21 ± 0.23‡	1.50 ± 0.34§	1.24 ± 0.26†
HDL_2-cholesterol	0.14 ± 0.10	0.15 ± 0.09	0.21 ± 0.16	0.15 ± 0.13†
LDL-C/HDL-C	2.8 ± 0.6	2.8 ± 0.6	2.5 ± 0.9	2.8 ± 0.9†

NOTE. Data are mean ± SD in mmol/L.

*$P < .01$, †$P < .0001$, ‡$P < .05$ *v* baseline (within group) by paired *t* test.

§Signifies baseline differences between groups at $P < .05$ using Student's *t* test.

these changes was not affected by APOE genotype. However, changes in other lipid values did differ between genotype groups. Women with the APOE 2/3 and APOE 3/3 genotype decreased their HDL-C and HDL_2-C concentrations and increased their triglyceride concentrations and their LDL-C/HDL-C ratio, possibly negating their beneficial decrease in total cholesterol and LDL-C concentrations. In contrast, the magnitude of the decrease in HDL-C was much less in women with the APOE4 allele, and they did not decrease HDL_2-C, nor increase triglyceride concentrations in response to the diet. In addition, the diet increased the atherogenic risk ratio of LDL-C/HDL-C in the APOE4- women, but had no effect on this ratio in women who were APOE4+. These effects of APOE genotype on HDL-C, HDL_2-C, and LDL-C/HDL-C were independent of individual differences in these variables at baseline. Thus, in obese, postmenopausal women, there is an interaction between the APOE gene and adoption of a lower fat diet, which results in different HDL-C and triglyceride responses. Since the majority of the general population do not have the APOE4 allele,[22] the consistently reported dietary-induced decreases in HDL-C and HDL_2-C, and increases in triglyceride, with a low-fat diet may be attributed to the greater frequency of the APOE2 and APOE3 alleles in the population.

Currently, there is considerable controversy regarding whether a moderately low-fat diet, such as the AHA Step 1 diet, should be recommended for everyone because of this diet's widely reported overall negative effects on HDL-C and triglyceride concentrations.[13-15] In particular, there is little evidence

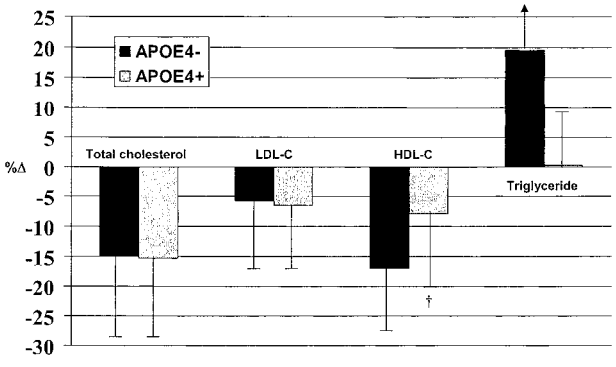

Fig 1. Percent changes in lipoprotein lipids by APOE genotype. The group difference in HDL-C was significant (†$P < .01$).

that a low-fat diet reduces risk of CHD in healthy, older women with a normal lipoprotein lipid profile. Yet, there is strong evidence that, on average, triglyceride concentrations increase and HDL-C concentrations decrease in postmenopausal women placed on a Step 1 low-fat diet.[31,33-36] In addition, decreases in HDL_2-C, the more protective HDL-C subfraction, may be more pronounced than decreases in HDL_3-C with a low-fat diet.[36] Since a low HDL-C concentration is a particularly strong predictor of a higher risk for CHD in women,[5-10] consumption of a low-fat diet may place some women at a higher risk for CHD.

Consistent with findings from prior studies, the average increase in triglycerides was 17%, the average decrease in HDL-C was 15%, and the average decrease in HDL_2-C was 23% among all women in the present study. However, as in other studies, not all women increased their triglyceride and decreased their HDL-C and HDL_2-C concentrations, and individual responses cannot be predicted from general effects seen in large populations. Our findings indicate that a low-fat diet interacts with APOE genotype such that the adverse dietary affects on triglycerides, HDL-C, and HDL_2-C occur to a lesser degree in women with the APOE4 allele. Accordingly, these APOE4+ women may be more likely to reduce their overall CHD risk with a low-fat diet. Indeed, 83% of the women who decreased their HDL-C concentration below 1.16 mmol/L in our study were APOE4-, and only 17% were APOE4+. In population studies, the APOE4 allele is associated with higher total cholesterol, LDL-C, and triglycerides, and with lower HDL-C in women, placing women heterozygous or homozygous for APOE4 at a greater risk of CHD.[22,24-27] Thus, moderately low-fat diets, such as the AHA Step 1 plan, should be more strongly advocated as an effective treatment in this particular subgroup of obese, postmenopausal women.

Results of previous studies examining the effects of APOE genotype on plasma lipid responses to macronutrient and cholesterol dietary modification are variable.[19] Some studies report greater reductions in total cholesterol and LDL-C with a low-fat diet in APOE4+ individuals,[23,37-41] while others report a lack of an APOE-diet interaction, especially in women.[42-45] Our results agree with those studies, which show that APOE genotype does not influence declines in total cholesterol and LDL-C in women in response to dietary reductions in total fat and cholesterol. The previously reported effects of APOE genotype on changes in HDL-C with a low-fat diet are also

variable, but results of 2 studies are consistent with our findings that the APOE 3/4 genotype is associated with a smaller decrease in HDL-C compared with the APOE 2/3 and 3/3 genotypes.[39,41]

The inconsistency in the results of previous studies has been attributed to differences in age, gender, ethnicity, baseline lipid value, obesity, and exercise habits of the subjects, the type of dietary intervention, and/or the retrospective nature of the study. Although the current study was not a prospective intervention trial with equal numbers of each genotype, the results were statistically significant, and the validity of the results is strengthened by accounting for some of these factors. By design, the subjects in the current study were homogenous at baseline with respect to their gender, race, age, lipoprotein lipid profile (except for HDL-C), body composition, and physical fitness. Since we[31] and others[46] found that the decrease in HDL-C in response to a low-fat diet is related to the initial HDL-C concentration, there could be an affect of the different HDL-C concentrations between genotypes at baseline. With respect to the intervention, all women were taught by the same dietitian who used the same curriculum to promote adherence to the AHA Step 1 diet. As a result, there were no differences between genotype groups in the changes in dietary fat, cholesterol, or percentage of a specific type of fat. However, it should be noted that the averages of the reported total fat, saturated fat, and cholesterol intakes at baseline were close to that recommended by the AHA. Nonetheless, according to the self-reported 7-day food records, the women of this study still made dramatic dietary changes in response to the intervention.

In this study, body weight decreased slightly in most women, but the decrease was the same between genotype groups, and there was no influence of changes in body weight on any lipoprotein lipid except LDL-C. Body composition and $\dot{V}O_2$max were not measured after the AHA dietary intervention phase of this study, because this intervention was not designed to elicit changes in body composition or fitness. Although the women did lose a minimal amount of weight, it most likely did not result in significant changes in body composition in these women; and, since it was consistent between genotype groups, most likely did not affect the results. Further studies are needed in which subjects are recruited by APOE genotype and are provided food or fed on a metabolic ward to eliminate misreporting of actual dietary intake and to fully control dietary and body weight changes. This would allow manipulation of diets to determine whether the degree of total fat and/or saturated fat restriction interacts with APOE genotype to alter lipoprotein lipid concentrations.

The results of this study are important for clarifying the role of the APOE gene in lipid responsiveness to the commonly prescribed low-fat, low-cholesterol (AHA or NCEP Step 1) diet in postmenopausal women. These data suggest the need for a controlled, prospective trial with larger numbers of women and equal numbers of each genotype. Understanding the influence of the APOE4 allele on the variability of HDL-C and triglyceride responses to a low-fat diet could potentially lead to a policy for the a priori identification of women who might benefit the most from such a diet to reduce their risk of CHD. Furthermore, identification of women less likely to benefit from low-fat diet therapy due to their genotype will allow them to seek other potentially more effective treatments to reduce their lipid-related risk for CHD.

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