

## Effect of soy protein–containing isoflavones on lipoproteins in postmenopausal women

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### ABSTRACT

**Objective:** Some clinical trials have demonstrated a beneficial effect of dietary soy protein on improving lipoproteins. Research also has documented that serum lipoproteins and some lipoprotein subclasses are altered as a consequence of menopause, resulting in a more atherogenic lipid profile. The purpose of this study was to determine the effects of isolated soy protein–containing isoflavones on lipoproteins and lipoprotein subclasses in both African American and white postmenopausal women with borderline to moderate low-density lipoprotein cholesterol elevations.

**Design:** This was a randomized, double-blind, controlled clinical trial including 216 postmenopausal women. After a 4-week run-in period with a casein protein–based supplement, participants were randomly assigned to continue the casein placebo or receive soy protein–containing isoflavones for a period of 12 weeks.

**Results:** In the soy group, the total cholesterol, low-density lipoprotein cholesterol, and low-density lipoprotein particle number decreased significantly as compared with the placebo group at 6 weeks. Although this decrease continued at 12 weeks in the soy group, the difference from the placebo group was attenuated for total cholesterol and low-density lipoprotein particle number. Multivariate analyses controlling for age, race, change in weight, change in dietary fat intake, and change in kilocalorie energy expenditure revealed that treatment remained a significant independent predictor of change in total cholesterol ( $P = 0.01$ ), low-density lipoprotein cholesterol ( $P = 0.02$ ), and low-density lipoprotein particle number ( $P = 0.002$ ) after 6 weeks of dietary soy.

**Conclusions:** Increased consumption of soy protein replacing animal protein that is high in fat may help improve atherogenic lipid profiles.

**Key Words:** Lipoproteins – Nutrition – Prevention – Postmenopausal women.

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Cardiovascular disease (CVD) remains the leading cause of mortality and morbidity in postmenopausal women.<sup>1</sup> Changes in lipids and lipoproteins at the time of menopause may contribute significantly to the increased risk for the development of CVD over the lifetime of women. Research has documented that serum lipids and lipoproteins are altered as a consequence of menopause, resulting in a more atherogenic lipid profile.<sup>2-8</sup> Evidence also suggests that this may include shifts in atherogenic lipoprotein subclasses.<sup>4,5</sup>

Although the results have been mixed, some clinical trials have demonstrated a beneficial effect of dietary soy protein on plasma lipids and lipoproteins. A 1995 meta-analysis of 38 published controlled clinical trials showed a significant reduction in low-density lipoprotein (LDL) cholesterol of 12.9%, significant lowering of triglycerides by 10.5%, and a nonsignificant increase in high-density lipoprotein (HDL) cholesterol of 2.4%.<sup>9</sup> In a more recent meta-analysis to quantify the effects of soy protein-containing isoflavones on the lipid profile, 23 randomized, controlled trials published from 1995 to 2002 were reviewed.<sup>10</sup> Soy protein with isoflavones was associated with significant decreases in serum total cholesterol (3.77%), LDL cholesterol (5.25%), and triglycerides (7.27%), and significant increases in serum HDL cholesterol (3.03%). The hypocholesterolemic effect was greater in those with higher baseline levels of lipids, but there was only a mild effect in people with moderately elevated cholesterol and no effect in those with mildly elevated or normal cholesterol levels. In addition, there was a dose-response effect based on the amount of isoflavone content of the soy protein, and the reductions were larger in men than in women. The decline in LDL cholesterol or triglyceride weakened as the length of the intervention increased, but longer interventions were associated with a greater improvement in HDL cholesterol.

In the recent American Heart Association Scientific Advisory on Soy Protein, Isoflavones, and Cardiovascular Health, 22 randomized trials of isolated soy protein with isoflavones compared with casein protein, wheat protein, or mixed animal protein were reviewed. LDL cholesterol decreased in most studies with an overall effect of ~3%.<sup>11</sup> Another meta-analysis, in which studies published from 1995 to 2002 were reviewed, showed a similar reduction in LDL cholesterol and no dose effect.<sup>12</sup>

Although there is some evidence to support the positive effect of soy protein-containing isoflavones on serum lipid levels, most studies to date have been small and have included relatively few postmenopausal women and virtually no African American women. Furthermore, no published data exist on the impact of soy protein on the atherogenic lipoprotein subclasses in women. Therefore, the purpose of this study was to determine the effects of isolated soy protein-containing isoflavones on lipids, lipoproteins, and lipoprotein subclasses in both African American and white postmenopausal women with borderline to moderate LDL cholesterol elevations that might increase their lifetime risk of CVD but would not

qualify them for definitive pharmacotherapy under national guidelines.

## METHODS

### Participants

Participants were recruited from the community using a variety of strategies, such as direct mailings of promotional brochures to targeted zip codes, newspaper and radio advertisements, health fairs, and referral from physician practices. African American and white women who had their last menstrual period greater than 12 months ago or a follicle-stimulating hormone greater than 30 mIU/mL if hysterectomized and an LDL cholesterol level between 3.37 and 4.92 nmol/L or triglycerides greater than 1.7 nmol/L were eligible to be included in the study. Because we are addressing the use of soy protein in a primary prevention paradigm, women were excluded if they had a history of CVD or stroke. Women also were excluded from the study if they had any condition that might potentially alter their response to the soy protein or if the use of soy protein might theoretically pose a risk. Such exclusions were triglyceride levels greater than 4.52 nmol/L, a history of diabetes or fasting blood glucose levels greater than 125 mg/dL, older age (older than 79 years), use of hormone therapy or oral contraceptives in the past 6 months, use of lipid-altering medications (antihyperlipidemic drugs, steroids,  $\beta$ -blockers, or thiazide diuretics), consumption of more than two alcoholic drinks per day, or a body mass index (BMI) greater than 39. Additionally, they were excluded for having a history of breast cancer (or for being at high risk for development of breast cancer), uterine cancer, kidney disease, liver disease, thyroid disease, or a chronic gastrointestinal disorder, or for participation in a conflicting clinical trial. Finally, women were excluded if they had a known allergy or hypersensitivity to soy or cow milk or were not willing to avoid soy products for the 4 months of the study. The study was conducted between April 2002 and December 2004. The protocol was approved by the Institutional Review Board, and all participants provided signed informed consent.

### Randomization and blinding

All eligible women participated in a single-blinded, 4-week placebo run-in period. Women who completed the run-in period and reported at least 80% compliance with the product were randomly assigned to the soy protein intervention group or casein protein

placebo group in separate blocks, one for African American women and another for white women. A list of randomization numbers was computer generated, and personnel in the investigational pharmacy, who were not involved in the trial, randomly assigned the participants and dispensed the product with the participant's name and study number attached. Both participants and study personnel were blinded to the group assignment until completion of the study.

### Intervention

The intervention (Revival Soy, Physicians Pharmaceuticals, Inc, Kernersville, NC) consisted of 20 g soy protein containing 160 mg total isoflavones (~96 mg aglycones) in a powder to be mixed with beverages. The intervention was diadzein-rich and contained approximately 63 mg total diadzein, 64 mg total genistein, and 34 mg total glycitein. The placebo (Physicians Pharmaceuticals) contained 20 g whole milk protein, looked identical to the soy, and contained the same nutrients other than isoflavones. The supplement was taken once a day for a total of 12 weeks. A trained dietary counselor counseled all participants on a low-fat diet and on incorporating the supplement into their diet by decreasing their protein intake to compensate for the extra protein in the supplement.

### Measurements

Data were collected in both groups at baseline and at weeks 6 and 12 of the study. Blood was drawn for lipoprotein and lipoprotein subclass analysis after women had fasted for 12 hours overnight. Detailed dietary and physical activity data were collected via interview. Weight was measured on a standardized scale, and a first-voided morning sample of urine was collected to measure isoflavone metabolites to monitor compliance.

### Plasma lipids

Total cholesterol, HDL cholesterol, and triglycerides were measured directly, and LDL cholesterol was calculated using the Friedewald equation:  $\text{LDL cholesterol} = \text{total cholesterol} - \text{HDL cholesterol} - (\text{triglycerides}/5)$ .<sup>13</sup> Plasma samples were analyzed according to Lipid Research Clinics methodology<sup>14</sup> and analyzed at a Clinical Laboratory Improvement Amendments–certified, standardized Quest Laboratory. The coefficients of variation for the measurement of lipids in this laboratory were 1.7% for total cholesterol, 1.3% for triglycerides, and 2.9% for HDL cholesterol.

### Lipoprotein subclasses

LDL particle concentration, LDL particle size, and subclasses of very-low-density lipoprotein, LDL, and HDL were quantified by nuclear magnetic resonance spectroscopy in a Clinical Laboratory Improvement Amendments–approved laboratory (LipoScience, Raleigh, NC). Aliquots of plasma were stored at  $-70^{\circ}\text{C}$  and shipped on dry ice for processing. The quantification of lipoprotein subclasses using proton nuclear magnetic resonance spectroscopy has been fully described and been shown to correspond well with other established methods, such as gradient-gel electrophoresis.<sup>15,16</sup> The coefficients of variation for the lipoprotein subclasses reported by this company range from 0.73% to 3.1%. Direct quantification of six very-low-density lipoprotein, four LDL (including intermediate-density lipoprotein), and five HDL subclasses, as well as average LDL particle size and LDL particle concentration, were provided.

### Dietary intake

Dietary intake was assessed by the Block 1998 Revision of the Health Habits and History Questionnaire food frequency instrument at baseline and again at 6 and 12 weeks.<sup>17,18</sup> Frequency of specific foods was estimated over the prior 6 weeks. Percentage of total calories from fat and saturated fat, milligrams of cholesterol, number of fruits and vegetables, and grams of fiber were calculated. All dietary information was verified and reviewed with the study dietitian. This food frequency assessment method has demonstrated correlations of 0.70 or more with food records, diaries, and 2-day food recall methods.<sup>19,20</sup>

### Physical activity

Changes in levels of physical activity were evaluated with the Stanford 7-Day Physical Activity Recall. This interviewer-administered survey estimates total daily energy expenditure by asking participants to estimate the number of hours spent in sleep and activities, classified into moderate, hard, and very hard activities, over the previous 7 days.<sup>21,22</sup> Light activity is calculated as the remaining time. The amount of time spent in each category is multiplied by the average metabolic equivalent (METs or kcal/kg/h) of each category and summed to calculate energy expenditure in terms of kcal/kg/day. Two-week test-retest reliability was 0.67 for a sample of men and women.<sup>22</sup> It was associated with other measures of physical activity in a community sample, and a 1-year change in estimated daily energy expenditure correlated with change in maximal oxygen uptake, percentage of body fat, HDL

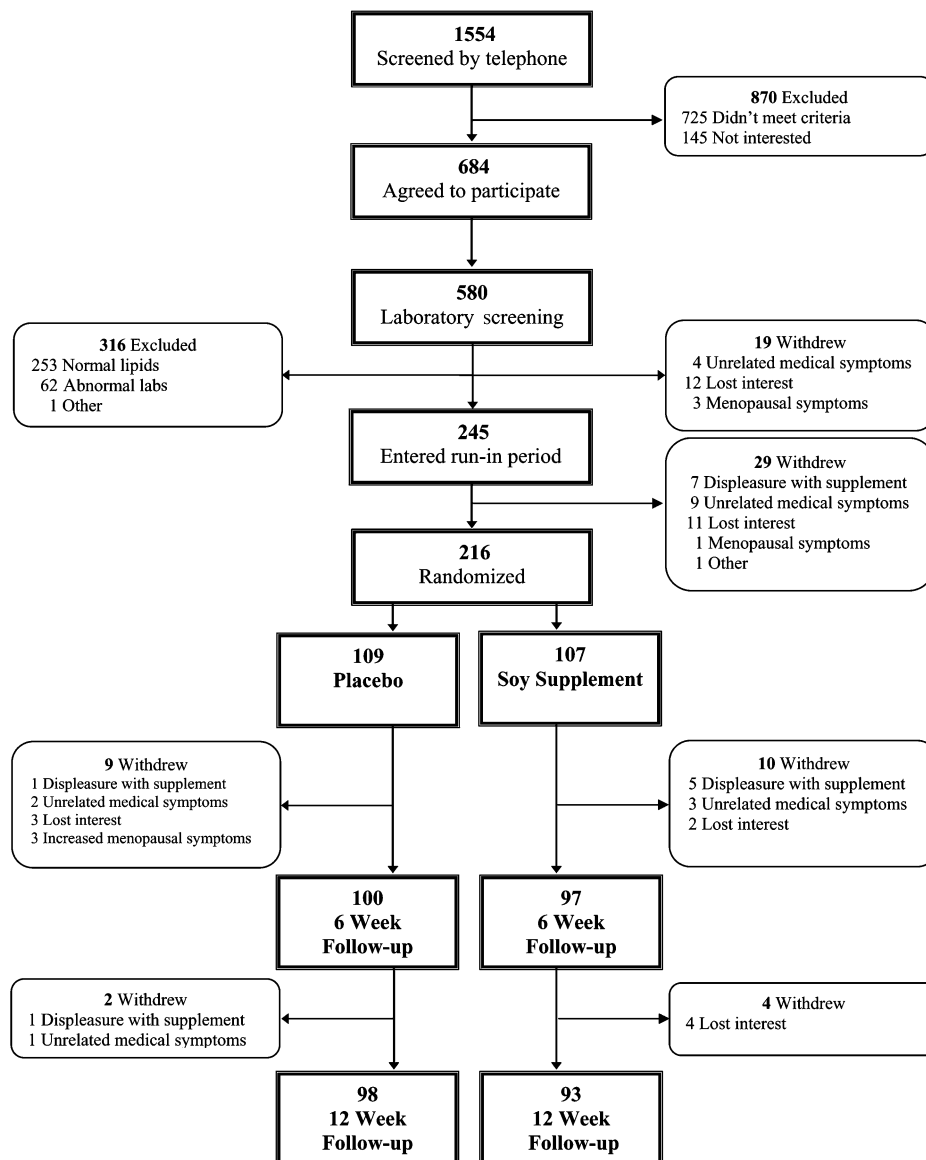


FIG. 1. Participant flow diagram.

cholesterol, and triglyceride levels.<sup>21</sup> The recall correlated with energy expenditure determined from the Caltrac accelerometer in one study ( $r = 0.79$ )<sup>23</sup> but not another ( $r = 0.33$ ).<sup>24</sup> The Stanford 7-Day Physical Activity Recall has been used to assess physical activity in a prospective study of cardiovascular risk factors in a large biracial sample.<sup>25</sup> It also has been used to assess changes in physical activity to assess the effects of physical activity interventions.<sup>26,27</sup>

### Compliance

Compliance was assessed by self-report of the number of packets of product missed, which was then

converted to a percentage of the prescribed packets that were ingested. Self-report was verified by the measurement of changes in levels of the urinary isoflavones of genistein and diadzein from baseline to follow-up. Urinary isoflavones and equol, a metabolite of diadzein, were analyzed using high-performance liquid chromatography (HPLC) with electrochemical detection. Overnight urine samples (~100 mL) were collected from the participants before the start of the soy or placebo supplementation (baseline) and again at the 6- and 12-week follow-ups exams. The instrumentation consists of a CoulArray model 5600 eight-channel electrode HPLC system (ESA, Inc) with

electrochemical detection and including a model 580 ESA solvent pump, a model 540 ESA autosampler with refrigeration, and a thermal chamber to heat the HPLC column. The mean extraction recovery  $\pm$  standard error for the isoflavones was  $96\% \pm 4\%$ . The determination of phytoestrogens in human specimens, including plasma, serum, and urine, using the CoulArray HPLC system with electrochemical detection has been validated and reported in previous studies.<sup>28-32</sup>

### Statistical analysis

Data were analyzed according to the intention-to-treat principle, including all original participants in the groups to which they were randomly assigned. Baseline measures were used for missing outcome data for those who had dropped out at 6 or 12 weeks. The major approach to analysis was multiple linear regression modeling, predicting change in the outcomes and adjusting for age, race, changes in body weight, dietary fat, and kilocalorie energy expenditure. We also examined whether the effect of soy differed across various subgroups, including thresholds for baseline levels of LDL cholesterol ( $<4.14$  and  $\geq 4.14$  nmol/L), BMI ( $<30$  and  $\geq 30$ ), age ( $<56$  and  $\geq 56$  years), and racial groups (African American and white). SAS version 9.1 (SAS Institute, Cary, NC) was used to perform the analyses.

### RESULTS

Participant screening, enrollment, and completion are shown in Figure 1. A total of 216 women (104 African American and 112 white) were randomly assigned to the two treatments. Twenty-five women (14 African American and 11 white) did not complete the trial. Women dropped out of the study because they lost interest ( $n = 9$ ), were displeased with the supplement taste or the gastrointestinal side effects ( $n = 7$ ), had unrelated medical issues ( $n = 6$ ), or wanted to initiate other therapy for bothersome menopausal symptoms ( $n = 3$ ). There was no significant difference in dropout rate between the two groups (11 placebo and 14 soy).

Table 1 shows the baseline characteristics of the participants by intervention group. There were no significant differences between the groups. The average age was 57, and women were on average 10 years postmenopausal. A high percentage of the women were high school graduates with moderate incomes. The average BMI was 28, and only a small percentage of the women were current smokers.

Baseline lipoprotein values were comparable between groups with average levels of total cholesterol and LDL cholesterol that would be categorized as mildly hypercholesterolemic and relatively good HDL cholesterol and triglyceride levels. The average number of LDL particles was increased in both groups. The LDL particle number is the total number of cholesterol-carrying LDL particles in nmol/L. The LDL particle number goal for moderately high-risk patients is less than 1,300 and for high-risk patients is less than 1,000. Testing showed no significant differences in baseline

TABLE 1. Baseline sample characteristics

Characteristic	Placebo (n = 109)	Soy (n = 107)	P
<b>Sociodemographic</b>			
Race, n (%)			0.49
African American	55 (52.88)	49 (47.12)	
White	54 (48.21)	58 (51.79)	
Age, y, mean (SD)	56.49 (4.82)	57.14 (6.31)	0.39
Education, n (%)			0.321
<High school	6 (5.50)	3 (2.80)	
$\geq$ High school	103 (94.50)	104 (97.20)	
Income per year, n (%)			0.851
<\$20,000	8 (7.62)	10 (9.71)	
\$20,000-\$49,999	28 (26.67)	28 (27.18)	
$\geq$ \$50,000	69 (65.71)	65 (63.11)	
Current smoker, n (%)	5 (4.59)	7 (6.54)	0.56
<b>Clinical, mean (SD)</b>			
Years postmenopause	9.06 (8.11)	9.84 (8.44)	0.50
BMI, kg/m <sup>2</sup>	27.73 (4.78)	28.15 (4.57)	0.50
<b>Lipoproteins, mean (SD)<sup>a</sup></b>			
Total cholesterol, mg/dL	220.89 (24.77)	224.30 (26.43)	0.33
LDL cholesterol, mg/dL	139.32 (22.25)	141.98 (22.10)	0.38
HDL cholesterol, mg/dL	58.95 (12.19)	60.16 (14.24)	0.50
Triglycerides, mg/dL	113.05 (53.14)	110.94 (45.21)	0.75
<b>Lipoprotein subclasses, mean (SD)</b>			
LDL particle number, nmol/L	1,378.41 (300.12)	1,406.85 (251.54)	0.45
LDL size, nm	21.17 (0.64)	21.19 (0.63)	0.82
Large HDL, mg/dL	28.13 (13.82)	29.00 (15.30)	0.66
Large VLDL, mg/dL	13.78 (27.92)	14.06 (21.89)	0.94
<b>Dietary intake, mean (SD)</b>			
Total fat, g	87.75 (33.89)	89.34 (33.71)	0.73
Saturated fat, g	23.33 (9.65)	23.83 (9.58)	0.70
Total calories from fat, %	35.50 (6.37)	36.08 (6.93)	0.52
<b>Physical activity, mean (SD)</b>			
kcal/d	2,546.03 (506.08)	2,586.68 (416.23)	0.52
kcal/kg/d	34.28 (2.14)	34.41 (1.90)	0.65

BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; VLDL, very low-density lipoprotein.

<sup>a</sup>To convert total cholesterol, LDL cholesterol, and HDL cholesterol to SI units, multiply by 0.0259; to convert triglycerides to SI units, multiply by 0.0113.

TABLE 2. Lipoproteins at baseline and follow-up by group

Variable	Baseline		6 weeks		12 weeks	
	Placebo	Soy	Placebo	Soy	Placebo	Soy
Lipoproteins, mg/dL, mean (SD) <sup>a</sup>						
Total cholesterol	220.89 (24.77)	224.30 (26.43)	224.35 (25.45)	221.43 (25.03)	222.10 (27.65)	222.17 (26.57)
LDL cholesterol	139.32 (22.25)	141.98 (22.10)	141.27 (22.27)	137.63 (20.17)	139.56 (23.72)	137.27 (21.34)
HDL cholesterol	58.95 (12.19)	60.16 (14.24)	60.55 (11.92)	62.22 (14.10)	60.35 (12.62)	62.80 (15.58)
Triglycerides	113.05 (53.14)	110.94 (45.21)	113.11 (59.66)	107.85 (45.77)	110.98 (52.40)	110.46 (43.78)
Lipoprotein subclasses, mean (SD)						
LDL particle number, nmol/L	1378.4 (300.12)	1406.9 (251.54)	1410.10 (341.14)	1349.50 (283.64)	1352.9 (281.12)	1328.2 (243.28)
LDL size, nm	21.17 (0.64)	21.19 (0.63)	21.22 (0.64)	21.29 (0.61)	21.21 (0.59)	21.25 (0.64)
Large HDL, mg/dL	28.13 (13.82)	29.00 (15.30)	29.53 (14.55)	30.30 (15.62)	28.78 (14.36)	29.47 (15.99)
Large VLDL, mg/dL	13.78 (27.92)	14.06 (21.89)	15.37 (33.99)	14.49 (23.06)	16.38 (26.81)	16.09 (22.58)

LDL, low-density lipoprotein; HDL, high-density lipoprotein; VLDL, very low-density lipoprotein.

<sup>a</sup>To convert total cholesterol, LDL cholesterol, and HDL cholesterol to SI units, multiply by 0.0259; to convert triglycerides to SI units, multiply by 0.0113.

characteristics between the 25 women who withdrew and those who completed the trial.

### Compliance

Genistein levels were significantly different between the soy group and the placebo group after 6 weeks (4,312 vs 711 nmol/L,  $P < 0.0001$ ) and 12 weeks (3,009 vs 1,031 nmol/L,  $P = 0.006$ ), demonstrating that compliance was good. A similar pattern was seen for diadzein at 6 weeks (11,199 vs 1,015 nmol/L,  $P < 0.0001$ ) and 12 weeks (11,749 vs 2,347 nmol/L,  $P = 0.006$ ). Self-reported compliance was also good, with 98% of participants in the soy group reporting using at least 80% of their packets throughout the study. In the placebo group, 96% of participants reported at least 80% compliance at 6 weeks and 93% at 12 weeks.

### Lipoproteins and lipoprotein subclasses

The lipoprotein and lipoprotein subclass outcomes are shown in Table 2. In the soy group, the total cholesterol, LDL cholesterol, and LDL particle number decreased significantly as compared with placebo at 6 weeks. Although this decrease continued at 12 weeks in the soy group, the difference from the placebo group was attenuated for total cholesterol ( $P = 0.21$ ) and LDL particle number (0.07). Multivariate analyses controlling for age, race, change in weight, change in dietary fat intake, and change in kilocalorie expenditure revealed that treatment (soy vs placebo) remained a significant independent predictor of change in total cholesterol ( $P = 0.01$ ), LDL cholesterol ( $P = 0.02$ ), and LDL particle number ( $P = 0.002$ ) after 6 weeks of dietary soy supplementation.

Exploratory subgroup analysis using multiple linear regression controlling for possible covariates revealed that the soy supplement intervention was significantly more effective in lowering LDL particle number in those with higher baseline levels of LDL cholesterol ( $\geq 4.14$  nmol/L,  $P = 0.007$  vs  $< 4.14$  nmol/L,  $P = 0.18$ ), those who were not obese at baseline (BMI  $< 30$ ,  $P = 0.004$  vs  $\geq 30$ ,  $P = 0.80$ ), and younger age ( $< 56$ ,  $P = 0.008$  vs  $\geq 56$ ,  $P = 0.49$ ). It was less effective in African American women (African American,  $P = 0.08$  vs white,  $P = 0.04$ ); however, African American women also were significantly more likely to be obese. Only a small percentage (5%) of these postmenopausal women were equol producers, which precluded any meaningful subgroup comparisons based on equol-producing status.

### DISCUSSION

This is the first clinical trial in which the effect of dietary soy with isoflavones on lipoprotein subclasses was examined in postmenopausal women. The significant decrement in LDL particle number in the soy group compared with the placebo group is a particularly meaningful finding given that four recent studies provide persuasive evidence that LDL particle number is a stronger predictor of incident coronary heart disease events or disease progression than LDL cholesterol levels alone<sup>33-36</sup> or apolipoprotein B.<sup>33,36</sup>

A fall in LDL cholesterol is not necessarily accompanied by a decrease in LDL particle number. For example, there might be an increase in the cholesterol content of LDL without a change in LDL particle number. This might lead to smaller,

denser LDL particles, which appear to be more atherogenic than larger LDL particles.<sup>37</sup> We observed, however, that both the LDL cholesterol and LDL particle number did in fact decrease significantly in the treated group. Furthermore, there was no decrease in average LDL size, indicating that the treatment with soy protein did not cause an increase in small, dense LDL particles.

Studies in animal models have shown similar effects on lipoproteins and have shown a reduction in atherosclerosis in coronary arteries.<sup>38-40</sup> At least one study in nonhuman primates showed that the response to isoflavones was influenced by gender and may affect lipoprotein subclasses. In monkeys fed an atherogenic diet followed by a soy protein phytoestrogen-rich diet in a 6-month crossover trial, both males and females experienced lowering of LDL and very-low-density lipoprotein levels as compared with control values. However, female monkeys also showed an increase in HDL and a decrease in small, dense LDL particles and apolipoprotein B.<sup>38</sup>

There are several possible mechanisms for the lipid-lowering effects of isoflavone-containing soy protein. Isoflavones may cause an increase in the excretion of bile acids and thus enhance the removal of LDL cholesterol. It also has been proposed that isoflavones in soy protein may act as a selective estrogen receptor modulator and exert an effect on lipid metabolism through their biological similarities to estrogens.<sup>41,42</sup> Several studies in animals suggest that isoflavones may reduce lipid levels by increasing the activity of the LDL receptors.<sup>43,44</sup> There also is evidence that isoflavones may inhibit oxidation of LDL.<sup>44,45</sup>

It remains unclear whether the favorable changes in lipids and lipoproteins seen with soy protein are attributable to isoflavones or to soy protein itself. Some investigators have suggested that synergy between soy protein and isoflavones is necessary to reduce levels of cholesterol because soy isoflavone extracts provided without the protein had no cholesterol-lowering effect.<sup>46,47</sup>

To understand differences in results from this study and others and, in particular, the apparent attenuation of effect over time, several issues warrant consideration. Although adherence is the obvious concern, self-reported adherence to the soy supplement was good and was confirmed by a significant difference in urinary metabolites of isoflavones. In addition, there were no significant changes in the dietary intake of grams of protein within either the soy or placebo groups over the 12 weeks of the study.

A recent meta-analysis revealed a negative dose-response relation between the duration of intervention and the reduction of serum cholesterol.<sup>10</sup> In the studies reviewed, the most significant lowering effects of soy protein-containing isoflavones on total cholesterol and non-HDL cholesterol occurred within the initial short period of isoflavone exposure, and the lipid-lowering effect decreased as the duration of the intervention increased. The reason for this pattern is unclear. It has been proposed that it could be related to a physiologic adaptation mechanism to more prolonged supplementation or to decreased adherence during long periods of intervention.<sup>10</sup>

## CONCLUSIONS

In conclusion, serum lipids, lipoproteins, and some lipoprotein subclasses are significantly altered as a consequence of menopause.<sup>2-6</sup> The result is a more atherogenic lipid profile. Most women with serious aberrations in lipid levels will receive statin therapy, but those with borderline to moderate elevations in LDL cholesterol that occur with menopause are unlikely to be offered any preventive therapy. Furthermore, their menopause-associated aberrant lipoprotein subclass distributions (ie, elevations in LDL particle numbers) are unlikely to be recognized or treated. Using soy foods to replace foods high in animal protein that contain fat and cholesterol may help improve atherogenic lipid profiles and confer benefits to cardiovascular health in postmenopausal women. Soy protein alone will not lower blood cholesterol with the same effectiveness as cholesterol-lowering medications; however, the modest effects of soy protein on LDL cholesterol and LDL particle number may be beneficial for heart health in postmenopausal women who do not qualify for definitive pharmacotherapy.

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