See corresponding editorial on page 339.

Direct comparison of a dietary portfolio of cholesterol-lowering foods with a statin in hypercholesterolemic participants[1–3]

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ABSTRACT

Background: 3-Hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitors reduce serum cholesterol and are increasingly advocated in primary prevention to achieve reductions in LDL cholesterol. Newer dietary approaches combining cholesterol-lowering foods may offer another option, but these approaches have not been compared directly with statins in the same persons.

Objective: The objective was to compare, in the same subjects, the cholesterol-lowering potential of a dietary portfolio with that of a statin.

Design: Thirty-four hyperlipidemic participants underwent all three 1-mo treatments in random order as outpatients: a very-low-saturated-fat diet (control diet), the same diet plus 20 mg lovastatin (statin diet), and a diet high in plant sterols (1.0 g/1000 kcal), soy-protein foods (including soy milks and soy burgers, 21.4 g/1000 kcal), almonds (14 g/1000 kcal), and viscous fibers from oats, barley, psyllium, and the vegetables okra and eggplant (10 g/1000 kcal) (portfolio diets). Fasting blood samples were obtained at 0, 2, and 4 wk.

Results: LDL-cholesterol concentrations decreased by 8.5 ± 1.9%, 33.3 ± 1.9%, and 29.6 ± 1.3% after 4 wk of the control, statin, and portfolio diets, respectively. Although the absolute difference between the statin and the portfolio treatments was significant at 4 wk ($P = 0.013$), 9 participants (26%) achieved their lowest LDL-cholesterol concentrations with the portfolio diet. Moreover, the statin ($n = 27$) and the portfolio ($n = 24$) diets did not differ significantly ($P = 0.288$) in their ability to reduce LDL cholesterol below the 3.4-mmol/L primary prevention cutoff.

Conclusions: Dietary combinations may not differ in potency from first-generation statins in achieving current lipid goals for primary prevention. They may, therefore, bridge the treatment gap between current therapeutic diets and newer statins. *Am J Clin Nutr* 2005;81:380–7.

KEY WORDS National Cholesterol Education Program diet, blood lipids, almonds, soy protein, viscous dietary fiber, plant sterols, low saturated fat, treatment goals

INTRODUCTION

Recent studies suggest that newer dietary strategies may be as effective in reducing LDL-cholesterol concentrations as are first-generation statins (1, 2), but these 2 approaches to cholesterol reduction have not been compared directly in the same persons.

Drugs and diet have both been shown to be effective in reducing cardiovascular disease risk and mortality (3–9). Nevertheless, the apparent ineffectiveness of conventional dietary strategies to reduce serum cholesterol by comparison with statins has reduced enthusiasm for diet as a therapeutic option (10). In an attempt to increase the effectiveness of diet in reducing serum cholesterol, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (11) and the American Heart Association (12) recently recommend the use of functional foods or foods high in components that reduce cholesterol as options in the dietary strategy. These functional ingredients include viscous fibers, soy protein, plant sterols, and nuts. Furthermore, foods containing these components are all permitted by the US Food and Drug Administration to carry a health claim that they reduce the risk of cardiovascular disease (13–17). Individually, these foods have been shown to lower serum cholesterol by 4–7%. In combination, cholesterol reductions approaching those observed with the use of lovastatin, a first-generation statin, have been reported (1, 2).

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TABLE 1
Age, race, body weight, BMI, blood pressure, and blood lipids of the participants at baseline[1]

	Men ($n = 20$)	Women ($n = 14$)	P^2
Number of subjects			
European	16	13	–
Indian subcontinent	2	0	–
Chinese	1	0	–
Black	0	1	–
Hispanic	1	0	–
Age (y)	55.4 ± 8.6[3]	62.7 ± 6.9	0.013
Body weight (kg)	82.4 ± 10.9	67.8 ± 10.5	0.001
BMI (kg/m^2)	27.3 ± 3.2	27.3 ± 3.7	0.990
Blood pressure (mm Hg)			
Systolic	120.0 ± 12.4	121.6 ± 11.5	0.703
Diastolic	77.3 ± 6.8	76.0 ± 7.3	0.574
Cholesterol (mmol/L)			
Total	6.58 ± 1.02	6.75 ± 0.83	0.610
LDL	4.38 ± 0.82	4.49 ± 0.77	0.683
HDL	1.12 ± 0.16	1.32 ± 0.39	0.091
Triacylglycerols (mmol/L)	2.40 ± 1.11	2.07 ± 0.94	0.384

[1] To convert cholesterol and triacylglycerols to mg/dL, multiply by 38.67 and 88.57, respectively.
[2] Two-sample *t* test.
[3] $\bar{x}$ ± SD (all such values).

Despite the widespread use of statins and their effectiveness in reducing cardiovascular disease(18), diet is still the preferred treatment option in primary prevention (11). For this reason it seemed important to determine the extent to which diet could substitute for statins in achieving target LDL-cholesterol concentrations. This study, therefore, directly compared the effect of a statin with that of a combination of cholesterol-lowering foods (portfolio diet) consumed by the same participants. This approach permitted a direct comparison between interventions, which allowed relatively small differences to be detected and the proportion who achieved treatment goals on either intervention to be determined. Data from the first phase were published as a parallel study (2). The participants then continued by completing the 2 remaining treatments, which allowed direct comparisons to be made between all 3 treatments in the present study.

SUBJECTS AND METHODS

Participants

Thirty-four healthy hyperlipidemic participants ($n = 20$ men and 14 postmenopausal women) completed all 3 phases of the study. The mean (±SE) age of the subjects was 58.4 ± 8.6 y (range: 36–71 y) and the body mass index (BMI; in kg/m^2) was 27.3 ± 3.3 (range: 20.5–35.5). The participants' baseline characteristics are shown in **Table 1**. Fifty-five participants were recruited from hyperlipidemic patients attending the Risk Factor Modification Center, St Michael's Hospital, Toronto, and from newspaper advertisements. Four participants who were randomly assigned to treatment did not start the study. Forty-six participants completed the first phase, 43 the second phase, and 34 the third phase. Five participants were not able to begin the third phase of the study because of precautions undertaken to minimize exposure to the severe acute respiratory syndrome virus (**Figure 1**). All participants had previously elevated LDL-cholesterol concentrations (>4.1 mmol/L) (11). None of the participants had a history of cardiovascular disease, untreated hypertension (blood pressure > 140/90 mm Hg), diabetes, or renal or liver disease and none were taking medications known to influence serum lipid concentrations, apart from 3 women who were taking stable doses of thyroxine—one of whom was also receiving estrogen replacement therapy. Of the 34 participants who completed all treatments, 16 had been placed on statins and had discontinued them ≥2 wk before each treatment period. Five participants were taking antihypertensive medications at a constant dose before and during the study, and 7 participants took aspirin or other nonsteroidal antiinflammatory drugs during the study. The Ethics Committees of the University of Toronto and St Michael's Hospital approved the study. Written informed consent was obtained from the participants.

Study protocol

The study followed a randomized crossover design, and 34 participants completed all three 1-mo treatments, which were separated by 2–6-wk washout periods between treatments. Participants followed their own low-saturated-fat therapeutic diets for 1 mo before the start of the study and during the 2–6-wk washout periods between treatments. The subjects were initially stratified on the basis of sex and pretreatment LDL-cholesterol concentrations and were randomly assigned to start a very-low-saturated-fat dairy and whole-wheat cereal diet (control diet), this same diet plus a statin (statin diet), or a diet containing viscous fibers, plant sterols, soy foods, and almonds (portfolio diet). All foods were provided, except for fresh fruit and vegetables. Fasting body weights were checked weekly, and blood samples were obtained after 12-h overnight fasts at 2-wk intervals. On each clinic visit, blood pressure was measured twice in the nondominant arm with a mercury sphygmomanometer by the same observer. Seven-day diet histories were obtained for the week before the 1-mo treatment periods. Completed menu checklists were returned at weekly intervals during the 4-wk diet period and were checked by the dietitians, who also recorded the previous week's exercise to ensure that it was constant over the study period.

The participants recorded their overall feeling of satiety with the diets at weekly intervals by using a 9-point bipolar semantic scale, where −4 was excessively hungry, 0 was neutral and 4 was discomfort due to excess food intake. Fecal frequency was also recorded for the 7 d of week 4.

The statistician, whose location was geographically separate from the clinic, randomly assigned the participants by using a pseudorandom number-generating facility within the SAS statistical software package (19). The statistician held the code for the placebo or lovastatin tablets provided in the control and statin treatment groups, respectively. This aspect of the study, therefore, was double-blinded. The dietitians were not blinded to the diet because they were responsible for packing the patients' diets and for checking their diet records. The laboratory staff responsible for the analyses was blinded to treatment and received samples labeled with name codes and date.

Diets

Before the 4-wk study began, the participants ate their routine therapeutic low-fat diets with mean macronutrient profiles, which were close to current NCEP guidelines (≤7% of energy from saturated fat and <200 mg dietary cholesterol/d) (11) (**Table 2**).

Weight-maintaining diets were provided during the 4-wk study periods, based on estimated caloric requirements, with the

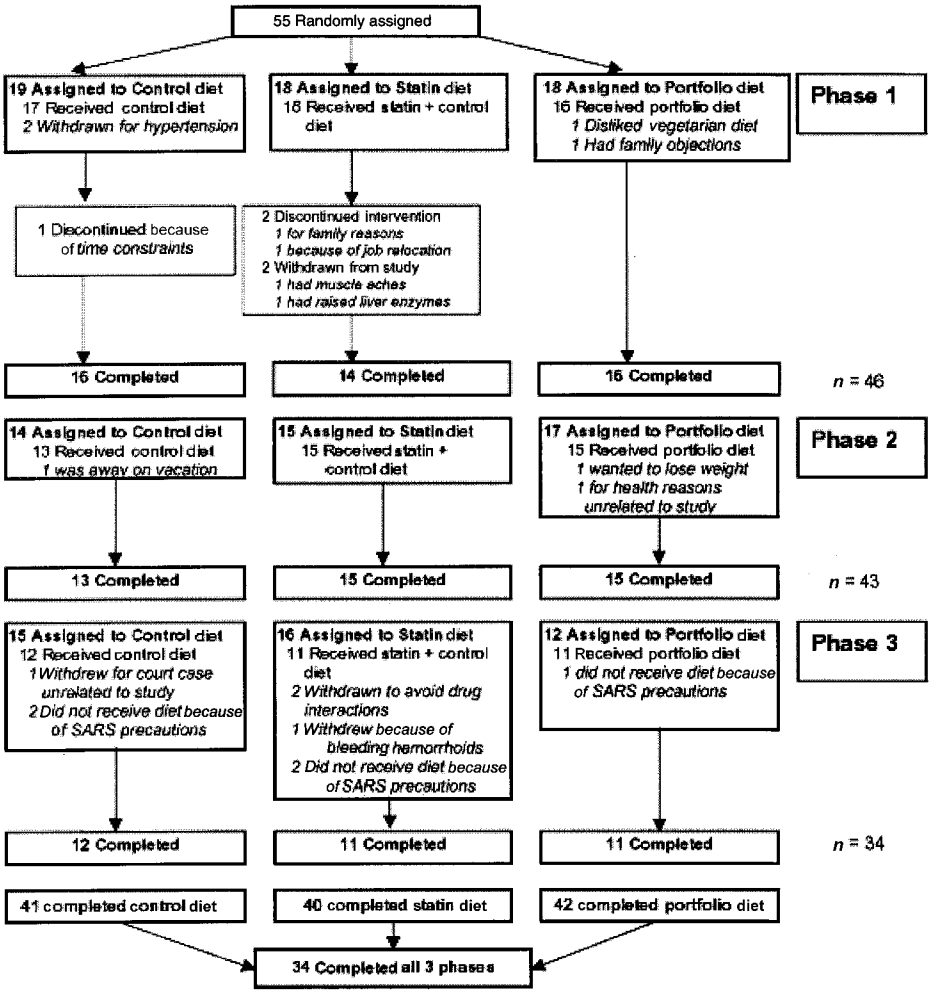

FIGURE 1. Flow diagram showing the progress of patients throughout the trial.

use of foods available in supermarkets and health food stores. All diets were vegetarian (**Table 3**). There were 4 main components of the dietary portfolio. A margarine enriched in plant sterol esters provided 1.0 g plant sterols/1000 kcal diet. Viscous fibers (≈10 g/1000 kcal diet) came from oats (4.24 g), barley (1.36 g), and psyllium (4.15 g). Okra and eggplant were also included as vegetable sources of viscous fiber (0.39 and 0.24 g) with 100 and 200 g of these vegetables to be eaten on alternate days. Psyllium contributed 40% of the total viscous fiber. Soy protein (21.4 g/1000 kcal) was given as soy milk and soy meat analogues, including soy burgers, soy dogs, and soy deli slices together with 14 g whole almonds/1000 kcal diet. This dietary portfolio was the same as that used in previous studies (1, 2).

Skim milk, fat-free cheese, yogurt, egg substitute, and liquid egg white were used in the control diet to achieve low intakes of saturated fat. A high fiber intake was provided via whole-wheat breakfast cereals [2.0 g total dietary fiber (TDF)/1000 kcal], bread (2.5 g TDF/1000 kcal), and wheat bran that was added to muffins containing a high amount of dairy protein (7.25 g TDF/1000 kcal diet). Sunflower oil (9 g/1000 kcal) and safflower oil (5 g/1000 kcal) high in monounsaturated fatty acids were also incorporated into the control diet (eg, muffins) to balance the fatty acid profile of the portfolio diet. The macronutrient profiles of the diets recorded as consumed in week 4 are given in **Table 4**.

Self-taring electronic scales (Salter Housewares, Kent, United Kingdom) were provided to all participants. The subjects were asked to weigh all food items consumed in the week before and during the study period. During the study period, all foods to be consumed by the participants were provided initially by courier and then at weekly clinic visits. The exceptions were fruit and low-calorie nonstarch-containing vegetables, which the participants were instructed to obtain from their local stores and were reimbursed on presentation of receipts. The participants were provided with a 7-d rotating menu plan on which they checked off each item as eaten and confirmed the weight of the foods. The same menu plan was used for all participants, but the menu could be modified to suit individual preferences provided that the goals for viscous fiber, soy protein, plant sterol, and almond consumption were met. Noncaloric beverages were not restricted. Commercial dishes were provided ready for microwave or oven cooking, and packs of instant soups were provided to be reconstituted with boiling water. Compliance was assessed from the completed weekly checklists and from the return of uneaten food items.

Statin

Twenty-milligram lovastatin tablets (Genpharm Inc, Etobicoke, Canada) were crushed and delivered in Vegiecap capsules

TABLE 2
Nutritional profiles of self-selected prestudy diets recorded by participants before randomization to the control, statin, and portfolio dietary treatments[1]

	Control group (n = 34)	Statin group (n = 31)	Portfolio group (n = 32)
Energy (kcal/d)	1824	1796	1812
Total protein			
(g/d)	82	84	86
(% of energy)	18.6	19.1	19.3
Vegetable protein			
(g/d)	34	32	33
(% of energy)	7.4	7.2	7.4
Available carbohydrate			
(g/d)	245	235	233
(% of energy)	53.8	52.2	52.1
Total dietary fiber			
(g/d)	29	29	28
(g/1000 kcal)	16.3	16.4	16.4
Total fat			
(g/d)	52	53	56
(% of energy)	25.3	26.6	26.9
SFA			
(g/d)	15	15	16
(% of energy)	7.2	7.6	7.5
MUFA			
(g/d)	21	22	22
(% of energy)	10.2	10.9	10.6
PUFA			
(g/d)	11	11	13
(% of energy)	5.6	5.6	6.0
Dietary cholesterol			
(mg/d)	189	182	188
(mg/1000 kcal)	99.7	102.4	105.2
Alcohol			
(g/d)	7	6	5
(% of energy)	2.3	2.1	1.7

[1] No significant differences were seen between treatments by ANOVA with Tukey's adjustment. SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.

TABLE 3
Representative 1-d menus for the control, statin, and portfolio diet phases

Control and statin diets	Portfolio diet
Breakfast	Breakfast
Bran flakes cereal	Hot oat-bran cereal
Skim milk	Soy beverage
Blueberries	Blueberries
Fat-free vanilla yogurt	Sugar and psyllium
Double-fruit jam	Oat-bran bread
	Test margarine
	Double-fruit jam
Snack[1]	Snack[1]
Bran muffin	Almonds
Control light margarine	Soy beverage
Fresh fruit	Fresh fruit
Lunch	Lunch
Soup	Soup
Vegetable couscous	Lentil with curry
Sandwich	Sandwich
Fat-free grilled cheese	Soy hot dogs
Whole-wheat bread	Oat-bran bread
Control light margarine	Test margarine
Garden salad	Lettuce
Mixed greens and lettuce	Tomato
Tomato	Cucumber
Cucumber	
Oil and vinegar dressing	
Snack[1]	Snack[1]
Bran muffin	Almonds
Control light margarine	Soy beverage
Fresh fruit	Psyllium
	Fresh fruit
Dinner	Dinner
Entrée: egg omelette	Entrée: tofu bake with ratatouille
Egg white	Firm tofu
Egg substitute	Eggplant
Fat-free cheese	Onions
Green peppers	Sweet peppers
Onions	
Safflower oil	
Side dish	Side dish
Cheese and spinach cannelloni	Pearled barley
Vegetables (eg, broccoli and cauliflower)	Vegetables (eg, broccoli and cauliflower)
Snack[1]	Snack[1]
Orange	Apple
Skim milk	Psyllium
	Soy beverage

[1] Optional.

(Capsugel, Morris Plains, NJ). Identical placebo capsules containing lactose and blue food coloring were also prepared (Pharmacy.ca, Toronto). Both lovastatin and placebo capsules were dispensed by the hospital pharmacy in identical containers marked with the participant's name, according to the randomization determined by the statistician. Participants were asked to take one capsule (20 mg lovastatin or placebo) daily in the evening for the 28 d of the study and to return the containers for capsule count at the end of the month.

Analyses

Serum was analyzed according to the Lipid Research Clinics protocol (20) for total cholesterol, triacylglycerol, and HDL cholesterol after dextran sulfate magnesium chloride precipitation (21). LDL-cholesterol concentrations were calculated (22). Serum apolipoprotein (apo) A-I and apo B were measured by nephelometry (intraassay CVs of 2.2% and 1.9%, respectively) (23). The diets were analyzed by using a program based on US Department of Agriculture (1).

Statistical analysis

The results were expressed as means ± SEs. The data were analyzed with a two-factor (diet and time) repeated-measures analysis of variance (ANOVA) by using the 3 treatments and weeks 0, 2, and 4 and with the diet-by-time interaction. After the establishment of a significant F test, the significance of the pairwise differences between treatments at each time point was assessed by least-squares means (19), with Tukey-Kramer adjustment for multiplicity of comparisons. The responses were normally distributed for all 3 treatments, except for triacylglycerol with the statin treatment and portfolio treatments and body

TABLE 4
Nutritional profiles of the control, statin, and portfolio diets provided to the participants and recorded as eaten at week 4[1]

	Control diet (n = 34)	Statin diet (n = 34)	Portfolio (test) diet (n = 34)
Energy (kcal/d)	2345	2333	2366
Total protein			
(g/d)	129	129	129
(% of energy)	22.1	22.3	21.9
Vegetable protein			
(g/d)	26[a]	26[a]	127[b]
(% of energy)	4.3[a]	4.5[a]	21.6[b]
Available carbohydrate			
(g/d)	309[a]	304[ab]	289[b]
(% of energy)	52.6[a]	52.1[a]	48.7[b]
Total dietary fiber			
(g/d)	55[a]	54[a]	77[b]
(g/1000 kcal)	23.1[a]	23.2[a]	32.8[b]
Total fat			
(g/d)	65[a]	65[a]	77[b]
(% of energy)	24.9[a]	25.1[a]	29.2[b]
SFA			
(g/d)	12[a]	12[a]	16.6[b]
(% of energy)	4.6[a]	4.7[a]	6.3[b]
MUFA			
(g/d)	27[a]	27[a]	32[b]
(% of energy)	10.3[a]	10.2[a]	12.1[b]
PUFA			
(g/d)	23[a]	24[a]	26[b]
(% of energy)	8.8[a]	9.1[a]	10.0[b]
Dietary cholesterol			
(mg/d)	28[a]	33[a]	55[b]
(mg/1000 kcal)	12.2[a]	14.4[a]	24.0[b]
Alcohol			
(g/d)	0.4	0.9	0.2
(% of energy)	0.1	0.3	0.1

[1] SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid. Values in the same row with different superscript letters are significantly different, $P < 0.05$ (paired comparison by least-squares-means procedure with Tukey's adjustment after establishment of a significant F test by ANOVA).

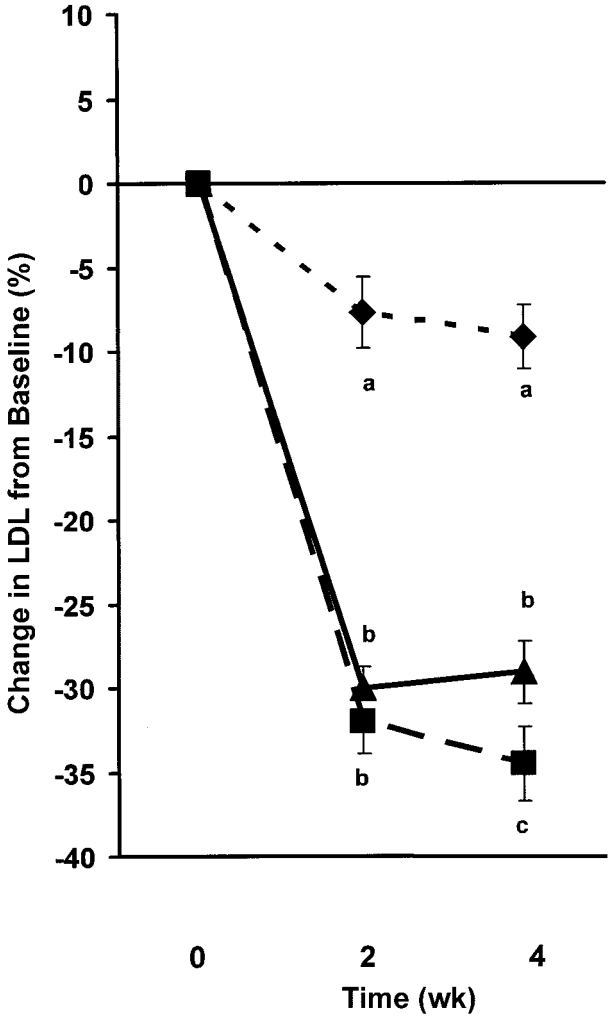

FIGURE 2. Mean (±SE) percentage change from baseline in LDL-cholesterol concentrations with the portfolio (▲; n = 34), control (◆; n = 34), and statin (■; n = 34) diets. Data for the 3 time points were analyzed with a two-factor repeated-measures ANOVA, with interaction based on actual data and not on the change from baseline. The diet effect and the diet-by-time interaction were significant ($P < 0.001$). Values at the same time point with different lowercase letters are significantly different, $P < 0.020$ (paired comparison by least-squares-means procedures with Tukey's adjustment).

weight on statin treatment. Fisher's exact test for 2 × 2 contingency tables was used to assess whether the statin or portfolio diet was significantly different in achieving treatment goals in terms of LDL-cholesterol reduction. The cutoffs used for LDL cholesterol were <3.4 and <2.6 mmol/L, which have been considered appropriate for primary and secondary prevention, respectively (11). An additional analysis was also carried out, which included all participants who had completed only 1 or 2 of the 3 phases (3 and 9 participants, respectively).

RESULTS

Compliance was good, as assessed from completed metabolic diet checklists and the return of uneaten food items; 93% of all calories provided were recorded as consumed with all 3 treatments, and 98% of the capsules provided were taken. All participants believed that they were eating as much food as they were capable of without experiencing discomfort (ie, they had a satiety rating <3.0) at week 4 (control group: 2.0 ± 0.2; statin group: 1.8 ± 0.2; portfolio group: 2.6 ± 0.2). Fecal frequency was greater with the portfolio diet ($P < 0.001$) than with the other treatments (control diet: 1.48 bowel movements/d; statin diet: 1.43 bowel movements/d; portfolio diet: 1.88 bowel movements/d), although the actual increase was <1 bowel movement in 2 d. The participants' body weights were not significantly different between treatments at the end of week 4 (control group: 75.9 ± 2.2 kg; statin group: 76.2 ± 2.2 kg; portfolio group: 76.4 ± 2.3 kg).

Blood lipids

No significant differences in baseline blood measurements were seen between the 3 treatment groups. The percentage changes from baseline in LDL cholesterol were −8.5 ± 1.9%, −33.3 ± 1.9%, and −29.6.±1.3% with the control, statin, and portfolio diets, respectively (**Figure 2**). ANOVA indicated a highly significant F test for the effect of diet on LDL cholesterol ($P < 0.001$) and a diet-by-time interaction ($P < 0.001$). With the statin and portfolio treatments, the absolute LDL-cholesterol concentrations were both significantly lower than those with the control treatment ($P < 0.001$),

TABLE 5
Effect of the control, statin, and portfolio diet treatments on blood lipids, C-reactive protein, and blood pressure in the 34 subjects[1]

	0 wk			2 wk			4 wk			
	Control diet	Statin diet	Portfolio diet	Control diet	Statin diet	Portfolio diet	Control diet	Statin diet	Portfolio diet	*P* for interaction[2]
Body weight (kg)	76.1	76.4	76.4	76.0	76.5	76.1	75.9	76.4	76.2	0.702
Cholesterol (mmol/L)										
Total[3]	6.79	6.84	6.76	6.30[a]	5.08[b]	5.16[b]	6.23[a]	4.97[b]	5.25[b]	0.001
LDL	4.57	4.49	4.51	4.19[a]	3.03[b]	3.14[b]	4.13[a]	2.91[c]	3.17[b]	0.001
HDL[3]	1.24	1.24	1.23	1.14	1.18	1.19	1.11	1.17	1.15	0.221
Triacylglycerols (mmol/L)	2.17	2.45	2.25	2.15[a]	1.91[a,b]	1.84[b]	2.18	1.96	2.04	0.007
Apolipoproteins (g/L)										
Apo A-I	1.58	1.61	1.57	1.45	1.49	1.47	1.45	1.47	1.46	0.883
Apo B[3]	1.45	1.46	1.43	1.35[a]	1.05[b]	1.05[b]	1.34[a]	1.02[c]	1.09[b]	0.001
Ratios										
Total:HDL cholesterol[3]	5.64	5.74	5.76	5.78[a]	4.46[b]	4.60[b]	5.76[a]	4.41[c]	4.74[b]	0.001
LDL:HDL cholesterol[3]	3.79	3.77	3.84	3.83[a]	2.67[b]	2.80[b]	3.80[a]	2.59[c]	2.85[b]	0.001
Apo B:apo A-I[3]	0.93	0.92	0.93	0.95[a]	0.71[b]	0.74[b]	0.94[a]	0.70[c]	0.76[b]	0.001
Blood pressure (mm Hg)										
Systolic	119	121	121	118	118	118	116	117	116	0.741
Diastolic	75	77	77	73[a]	75[a,b]	76[b]	73	73	72	0.053
10-y CHD risk (%)[4]	10.8	11.6	11.4	11.1[a]	8.0[b]	8.4[b]	10.7[a]	7.7[b]	8.4[b]	0.001

[1] CHD, coronary heart disease. To convert cholesterol and triacylglycerol values to mg/dL, multiply by 38.67 and 88.57, respectively. To convert apolipoprotein A-I and B values to mg/dL, multiply by 100. Values for a given time point with different superscript letters are significantly different, $P < 0.05$ (paired comparison by least-squares-means procedure with Tukey's adjustment after establishment of a significant *F* test by two-factor repeated-measures ANOVA).
[2] Significance of the time-by-treatment interaction in the general linear model.
[3] The main effect of diet was significant ($P < 0.05$).
[4] According to the Framingham study cardiovascular disease risk equation (24).

whereas the difference between the statin and the portfolio treatments were also significant ($P = 0.013$). However, 9 participants (26%) showed a better response to the portfolio diet than to the statin diet. In general, there was a similar pattern of significance in the other lipid risk factors, as seen for LDL cholesterol (**Table 5**). Thus, ANOVA indicated a significant *F* test for the effect of diet on total cholesterol, HDL cholesterol, apo B, and the ratios of total cholesterol to HDL cholesterol, LDL cholesterol to HDL cholesterol, and apo B to apo A-I. All of these measurements, with the exception of HDL cholesterol, showed significant diet-by-time interactions ($P < 0.001$). In addition, triacylglycerol showed a significant diet-by-time interaction ($P = 0.007$). These lipid measurements assessed by least-squares means also showed the lowest absolute concentrations at 4 wk on the statin and portfolio diets by comparison with the control diet. The statin treatment generally resulted in lower concentrations at 4 wk than did the portfolio diet. Exceptions that did not follow the LDL-cholesterol pattern included HDL cholesterol, for which the only significant difference was the higher concentration at 4 wk of the statin diet than at 4 wk of the control diet and the lack of any treatment difference in apo A-I at 4 wk. A significantly lower calculated overall risk of coronary heart disease was seen when the Framingham Study equation was used (24) at 4 wk of the statin and portfolio diets than at 4 wk of the control diet ($P < 0.001$); no significant difference between the statin and portfolio treatments was observed ($P = 0.199$). No significant differences were observed between the sexes.

Treatment goals

At 4 wk, the statin and portfolio treatments were not significantly different ($P = 0.288$) in their ability to reduce LDL-cholesterol concentrations below the 3.4 mmol/L (130 mg/dL) cutoff (statin diet: 79%, $n = 27$; portfolio diet: 71%, $n = 24$) (**Figure 3**); both diets were significantly more effective ($P < 0.001$) than was the control diet ($n = 8$). There was a trend for the statin diet to be numerically more effective in reaching the treatment goal of 2.6 mmol/L (100 mg/dL) than was the portfolio diet (statin diet: 26%, $n = 9$; portfolio diet: 9%, $n = 3$) ($P = 0.055$). None of the participants achieved this LDL-cholesterol concentration while consuming the control diet (Figure 3).

DISCUSSION

These data confirm the effectiveness of combining recently recommended dietary components (those recommended by the NCEP Adult Treatment Panel III (11) and the American Heart Association) (12) to maximize the cholesterol-lowering effect of diet (1, 2). The 29.1% reduction in LDL cholesterol achieved by diet was less than the 34.5% reduction achieved in the same participants with a 20-mg dose of lovastatin. However, the achievement of target treatment goals for mild-to-moderate hypercholesterolemia in uncomplicated primary prevention was not significantly different between the statin and portfolio groups.

Diet and lifestyle changes have always been recommended as the first line of treatment in conditions such as mild hyperlipidemia and early type 2 diabetes. However, as currently applied, the effect of diet in reducing serum cholesterol is at best modest (10, 11). By comparison, the current success with statins in reducing cardiovascular disease and all-cause mortality has greatly encouraged their general use as hypocholesterolemic agents, not only in secondary prevention but also in primary prevention.

Treatment goals in primary prevention include an LDL-cholesterol concentration <4.15 mmol/L (160 mg/dL) with no

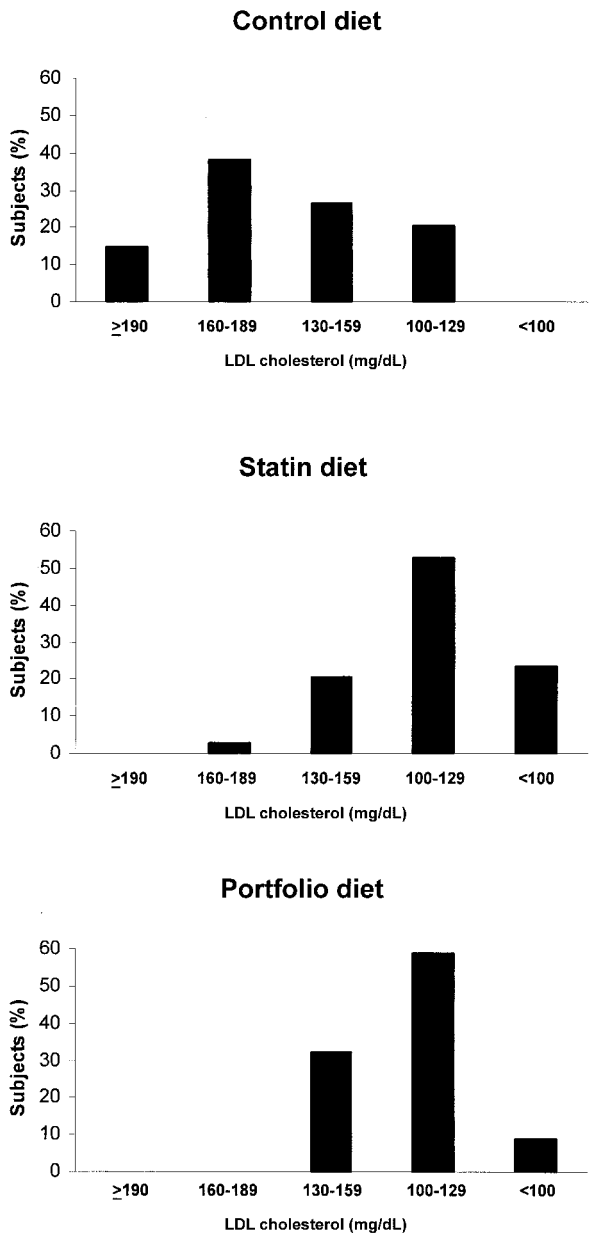

FIGURE 3. Percentages of the 34 subjects who achieved LDL-cholesterol treatment goals for primary prevention (very high concentrations: >190 mg/dL; high concentrations: 160–189 mg/dL; borderline high concentrations: 130–159 mg/dL; near or above optimal concentrations: 100–129 mg/dL; optimal concentrations: <100 mg/dL).

more than one risk factor and ≤3.4 mmol/L (120 mg/dL) with 2 or more risk factors. In the case of secondary prevention with established cardiovascular disease, an LDL-cholesterol concentration of 2.6 mmol/L (100 mg/dL) or less is advised (11). For primary prevention, drug therapy is recommended when diet has failed to reduce LDL-cholesterol concentrations to <3.4 mmol/L in persons with 2 or more risk factors or in persons who have a calculated 10-y CHD risk of 10–20% according to the Framingham cardiovascular disease risk prediction equation. Drugs are also advocated for high-risk persons or for those with established disease (secondary prevention) (11). Even before the latest NCEP guidelines, it was estimated that >25% of all middle-aged men in the west of Scotland should be prescribed cholesterol-lowering medications (25). The success of statins in reducing all-cause mortality in normocholesterolemic persons has further increased the proportion of the general population for whom a statin may be recommended (3–5). Nevertheless, there continue to be some patients for whom statins cannot be used because of side effects, intolerances, and personal preferences. The present demonstration that the same participants may achieve their treatment goals for primary prevention with diet or statin is therefore especially relevant today in providing an alternative to drug therapy for primary prevention.

The 4 dietary components used in the portfolio diet—viscous fiber, soy protein, plant sterols, and almonds—are all well recognized for their cholesterol-lowering properties (13–17, 26–38). In combination, they are each likely to contribute 4–7% to the overall cholesterol reduction observed (1, 2). Their mechanisms of action are complementary, which may enhance the effectiveness of this combination in lowering cholesterol. Viscous fibers increase bile acid loss, plant sterols reduce cholesterol absorption, soy proteins appear to reduce hepatic cholesterol synthesis and possibly increase the hepatic LDL receptor uptake of cholesterol, whereas almonds—which contain monounsaturated fats, plant sterols, vegetable proteins, fiber, and other phytochemicals—are likely to act through a variety of mechanisms (31–33, 39).

These physiologically active dietary components or the foods that contain them have attracted much recent attention internationally as so-called "functional foods" (40). Although in most jurisdictions health claims are only permitted for drugs and not for foods, legislation is being reexamined to permit health claims for foods. This move is aimed to allow recognition of foods with special properties, such as cholesterol-lowering, and thus fill the current void in treatment options between a generally good diet and drug therapy. In this respect the US Food and Drug Administration has led the way (13–17). The Japanese also have legislation (FOSHU), and Sweden, Holland, and Britain now have guidelines that will form the basis for the European Union regulations currently under discussion.

In conclusion, a diet that combines a number of cholesterol-lowering foods may provide an option for reducing mild-to-moderate elevations in serum LDL cholesterol in persons without preexisting cardiovascular disease. This option is relevant for those who are prepared to make significant dietary and lifestyle changes. By bridging the current therapeutic gap between contemporary low-saturated-fat diets and statin therapy, this dietary approach may be particularly useful for those at relatively low risk who have elevated cholesterol concentrations and are consuming low-saturated-fat diets and yet are not a high priority for statin treatment. It may also be helpful in combination with statins in reducing the need for high doses of drugs to meet target goals, especially in those with elevated liver and muscle enzyme concentrations. We believe that the identification of additional functional foods or food components over time has the potential to significantly enhance the efficacy of diet in controlling serum cholesterol and to provide a viable therapeutic option for the primary prevention of cardiovascular disease.

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