

Assessment of the longer-term effects of a dietary portfolio of cholesterol-lowering foods in hypercholesterolemia¹⁻³

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ABSTRACT

Background: Cholesterol-lowering foods may be more effective when consumed as combinations rather than as single foods.

Objectives: Our aims were to determine the effectiveness of consuming a combination of cholesterol-lowering foods (dietary portfolio) under real-world conditions and to compare these results with published data from the same participants who had undergone 4-wk metabolic studies to compare the same dietary portfolio with the effects of a statin.

Design: For 12 mo, 66 hyperlipidemic participants were prescribed diets high in plant sterols (1.0 g/1000 kcal), soy protein (22.5 g/1000 kcal), viscous fibers (10 g/1000 kcal), and almonds (23 g/1000 kcal). Fifty-five participants completed the 1-y study. The 1-y data were also compared with published results on 29 of the participants who had also undergone separate 1-mo metabolic trials of a diet and a statin.

Results: At 3 mo and 1 y, mean (\pm SE) LDL-cholesterol reductions appeared stable at $14.0 \pm 1.6\%$ ($P < 0.001$) and $12.8 \pm 2.0\%$ ($P < 0.001$), respectively ($n = 66$). These reductions were less than those observed after the 1-mo metabolic diet and statin trials. Nevertheless, 31.8% of the participants ($n = 21$ of 66) had LDL-cholesterol reductions of $>20\%$ at 1 y ($\bar{x} \pm$ SE: $-29.7 \pm 1.6\%$). The LDL-cholesterol reductions in this group were not significantly different from those seen after their respective metabolically controlled portfolio or statin treatments. A correlation was found between total dietary adherence and LDL-cholesterol change ($r = -0.42$, $P < 0.001$). Only 2 of the 26 participants with $<55\%$ compliance achieved LDL-cholesterol reductions $>20\%$ at 1 y.

Conclusions: More than 30% of motivated participants who ate the dietary portfolio of cholesterol-lowering foods under real-world conditions were able to lower LDL-cholesterol concentrations $>20\%$, which was not significantly different from their response to a first-generation statin taken under metabolically controlled conditions. *Am J Clin Nutr* 2006;83:582–91.

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

INTRODUCTION

New dietary strategies may have similar efficacy to first generation statins in reducing LDL-cholesterol concentrations (1–3), but the effectiveness of these approaches has not been tested

under real-world conditions. Both drugs and diet have been shown to be effective in reducing cardiovascular disease risk and mortality (4–10). However, the ease of application, the consistency and magnitude in LDL-cholesterol reduction achieved, and the clinical benefits associated with statins in large randomized controlled trials have made diet less of a focus even in primary prevention (11). To increase the relevance of dietary advice for the primary prevention of cardiovascular disease, the National Cholesterol Education Program Adult Treatment Panel III (ATP III) (12) and the American Heart Association (13, 14) have recommended the use of functional foods or foods high in components that reduce cholesterol as additional options to enhance the effectiveness of cholesterol-lowering diets. These functional ingredients include viscous fibers, soy protein, plant sterols, and nuts. The US Food and Drug Administration now allows foods with these components to carry a health claim indicating that they reduce the risk of cardiovascular disease (15–19). In a series of metabolically controlled studies, we assessed the efficacy of these cholesterol-lowering components when combined in the same diet (1–3). Our aim was to determine whether predicted reductions in LDL cholesterol of 30% could be achieved by diet. The data indicated that 28–35% reductions in LDL cholesterol

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² Supported by the Canada Research Chair Endowment of the Federal Government of Canada, the Canadian Natural Sciences and Engineering Research Council of Canada, Loblaw Brands Limited, the Almond Board of California, and Unilever Canada and Unilever Research & Development, Vlaarding, Netherlands.

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Received October 3, 2005.

Accepted for publication December 5, 2005.

TABLE 1
Baseline characteristics of first and second recruitment cohorts¹

	Cohort 1 (n = 35)	Cohort 2 (n = 31)	<i>p</i> ²
Age (y)	59.8 ± 1.5	58.6 ± 1.8	0.616
Weight (kg)	77.2 ± 2.2	72.6 ± 2.2	0.148
BMI (kg/m ²)	28.0 ± 0.6	26.4 ± 0.5	0.044
Total cholesterol (mmol/L)	6.67 ± 0.13	6.85 ± 0.15	0.358
LDL cholesterol (mmol/L)	4.35 ± 0.11	4.63 ± 0.15	0.125
HDL cholesterol (mmol/L)	1.22 ± 0.05	1.25 ± 0.07	0.797
Triacylglycerols (mmol/L)	2.42 ± 0.22	2.14 ± 0.16	0.328
Systolic blood pressure (mm Hg)	123 ± 2	121 ± 3	0.618
Diastolic blood pressure (mm Hg)	75 ± 1	74 ± 1	0.569

¹ All values are $\bar{x} \pm SE$. To convert cholesterol and triacylglycerols to mg/dL, multiply by 38.67 and 88.57, respectively.

² Difference between the cohorts was assessed by two-sample *t* test.

were possible (1–3). However, the question of whether this approach had any application in the real world remained. This issue is particularly important because, on the basis of emerging clinical trial evidence, guidelines for cholesterol control in clinical practice have encouraged the achievement of progressively lower cholesterol concentrations (20).

We therefore studied a group of 66 hyperlipidemic persons under real-world conditions over a 1-y period who were instructed on a self-selected dietary portfolio of cholesterol-lowering foods. Twenty-nine of these persons had completed ≥ 2 phases of a previous metabolic study that compared the effect of the dietary portfolio with those of a statin (20 mg lovastatin) (2, 21). We included the published data (2, 21) from the 4-wk metabolic studies on these 29 participants for comparison with their LDL-cholesterol reductions on the 1-y ad libitum study, in which the participants had to obtain their own food. Use of these data also allowed for a comparison between the effects of the ad libitum diet and the effects of a statin.

SUBJECTS AND METHODS

Participants

Sixty-six hyperlipidemic participants, 31 men and 35 postmenopausal women, were recruited to start the 1-y study. The participants had a mean ($\pm SE$) age of 59.3 ± 1.1 y (range: 32–86y), body mass index (in kg/m²) of 27.3 ± 0.4 (range: 19.1–36.8), and an LDL-cholesterol concentration of 4.48 ± 0.09 mmol/L (range: 3.25–6.75 mmol/L). The participants were recruited through 2 series of newspaper advertisements. Twenty-nine of the 66 participants had previously completed the statin and portfolio phases of a metabolic study; both phases had a 1-mo duration. Data on that study have been published elsewhere (2, 21). The participants' baseline characteristics are shown in **Table 1**. The first cohort of participants (*n* = 55) were recruited for 1-mo metabolic trials of portfolio, statin, and control diets; 29 participants completed at least a statin and metabolic portfolio phase and were among the 35 persons of the cohort of the study who proceeded to the long term (1-y) portfolio study (**Figure 1**). The participants in the second cohort (*n* = 62) were recruited directly for the long-term portfolio study; this recruitment contributed 31 persons, and thus a total of 66 persons were included in the 1-y portfolio study (**Figure 1**). All participants had high

LDL-cholesterol concentrations (>4.1 mmol/L) (12). The participants had no history of cardiovascular disease, diabetes, or renal or liver disease. At recruitment, 4 participants had untreated hypertension [blood pressure ≥ 140 (systolic)/90 (diastolic) mm Hg], 2 of whom showed blood pressure reductions below 140 (systolic)/90 (diastolic) mm Hg during the study without medication. Except for 8 women and 1 man who were taking stable doses of thyroxine and had normal thyroid stimulating hormone concentrations and 1 woman who was also taking a stable dose of estrogen replacement therapy, no participants were taking medications known to influence serum lipids. Twenty-three participants had been prescribed cholesterol-lowering medications as part of their usual care, but discontinued their use ≥ 2 wk before the start of the treatment period. Eight participants were taking antihypertensive medications at a constant dose before and during the study, 4 participants changed medications during the study, and 1 started taking antihypertensive medication at week 12. The Ethics Committees of the University of Toronto, St. Michael's Hospital, the Drug Directorate of Health Canada, and the Natural Health Products Directorate of Health Canada approved the study. Written informed consent was obtained from the participants.

Study protocol

The intervention was a single phase 1-y open label study of a self-selected (ad libitum) dietary portfolio of cholesterol-lowering foods. All participants were instructed to follow a low-saturated-fat ($<7\%$ of energy intake), low-cholesterol (<200 mg/d) diet for 2 mo before commencing the 1-y study. During the 1-y study, the participants were seen at weeks 0, 2, 4, 8, 12, 24, 32, 42, and 52. Between the 4th and 5th months, the participants were also recalled at random to obtain a blood sample with only 2 d notice (to prevent dietary preparation). For one-half of the participants, the sample was obtained in the post-Christmas period because we reasoned that this sample would provide the worst-case scenario (in terms of lipid-lowering effects) that may occur after the diet was prescribed. Body weights were checked and blood samples were obtained at each visit after the participants had fasted overnight for 12 h. Blood pressure was measured twice at each visit in the participants' nondominant arm by the same observer with the use of a mercury sphygmomanometer. Seven-day diet records were obtained for the week before the clinic visit and checked by the dietitian. The records were discussed with the dietitian and suggestions were made to enhance compliance. The previous week's exercise was also recorded, and the dietitian encouraged the participant to hold this constant over the prestudy and study periods. Compliance was assessed from the 7-d diet records. Previously published LDL-cholesterol data from the metabolic study in which 29 of the present study participants completed the metabolic portfolio and statin phases (2, 21) are also presented here for comparative purposes.

Diets

Before the study, the participants ate their routine therapeutic low-fat diets with mean macronutrient profiles that were close to the current ATP III guidelines ($\leq 7\%$ energy from saturated fat and <200 mg dietary cholesterol/d; 12) (**Table 2**). The dietary advice for the 1-y study was based on the consumption goals for the same 4 dietary components that had been emphasized in previous metabolic dietary portfolio studies (1–3). Foods were



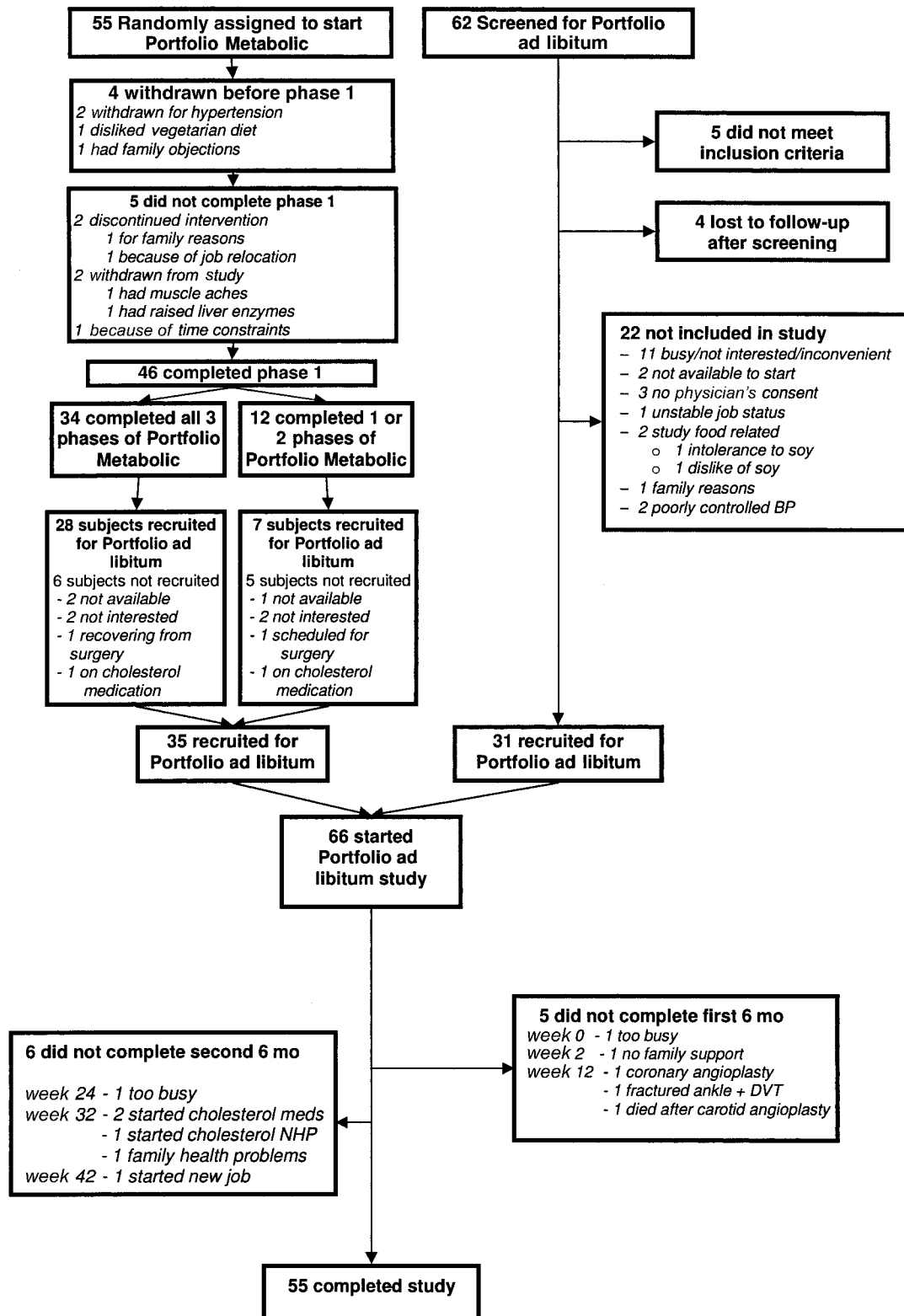


FIGURE 1. Flow diagram showing the progress of the participants through the trial. BP, blood pressure; NHP, Natural Health Products; DVT, deep vein thrombosis.

bought by participants from supermarkets and health food stores with the exception of bread, which was obtained at cost from the baker (Natural Temptations, Burlington, Canada), and the margarine, which was unobtainable in Canada and was provided to

all but 4 participants. In addition to their ongoing low-fat diet, the participants were instructed to consume the following 4 primary components of the dietary portfolio: 1.0 g plant sterols/1000 kcal from a plant sterol ester-enriched margarine; \approx 10 g viscous

TABLE 2

Nutritional profiles of the ad libitum dietary portfolio at weeks 0, 12, 24, and 52 of the 55 participants who completed the 1-y study¹

	Preportfolio (week 0) (n = 54)	Portfolio		
		Week 12 (n = 53)	Week 24 (n = 55)	Week 52 (n = 51)
Energy (kcal/d)	1579 ± 66	1763 ± 73	1744 ± 69	1675 ± 64
Total protein (% of energy)	18.9 ± 0.5	19.5 ± 0.4	19.4 ± 0.5	20.0 ± 0.4
Vegetable protein (% of energy)	7.7 ± 0.3	15.4 ± 0.5	14.9 ± 0.7	14.4 ± 0.7
Animal protein (% of energy) ²	11.2 ± 0.6	4.1 ± 0.3	4.5 ± 0.4	5.6 ± 0.5
Available carbohydrates (% of energy)	54.6 ± 1.0	48.3 ± 0.9	48.3 ± 0.8	48.9 ± 0.8
Total dietary fiber (g/1000 kcal)	17.8 ± 0.9	26.0 ± 0.8	27.7 ± 1.1	26.1 ± 1.1
Total fat (% of energy)	25.2 ± 0.9	31.2 ± 0.8	31.2 ± 0.8	29.8 ± 0.7
SFA (% of energy)	6.8 ± 0.4	5.8 ± 0.2	6.0 ± 0.2	5.9 ± 0.2
MUFA (% of energy)	10.1 ± 0.5	13.9 ± 0.4	13.8 ± 0.5	12.8 ± 0.4
PUFA (% of energy)	5.6 ± 0.3	10.0 ± 0.4	9.5 ± 0.3	9.2 ± 0.3
Dietary cholesterol (mg/1000 kcal)	89.5 ± 7.2	43.4 ± 5.2	43.3 ± 4.2	51.7 ± 6.5
Alcohol (% of energy)	1.3 ± 0.3	0.8 ± 0.2	0.9 ± 0.2	1.3 ± 0.4

¹ All values are $\bar{x} \pm \text{SEM}$. SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid. All values reported as a percentage of energy, except for percentage energy derived from protein and alcohol and total energy at 52 wk, were significantly different from their respective baseline values, $P < 0.05$ (ANOVA with Tukey adjustment).

² A significant increase in the percentage animal protein consumed was seen between weeks 12 and 52, $P = 0.007$ (repeated-measures ANOVA with spatial power covariance) (28).

fibers/1000 kcal from oats, barley, psyllium, okra, and eggplant; 22.5 g soy protein/1000 kcal from soy milk and soy meat analogues; and 23 g whole almonds/1000 kcal. All these 4 diet components have been advocated because of their ability to lower serum cholesterol (15–19). The participants were also instructed to consume additional sources of plant protein and fiber in the form of dried legumes and to eat the recommended 5–10 daily servings of fruit and vegetables (Table 3). Advice on eating a vegetarian diet without the use of dairy foods, eggs, or meat was given to the participants. If egg products were used, they were to consist of egg substitute and liquid egg whites. If meat or dairy foods were consumed, we emphasized restricting the amount consumed and selecting low-saturated-fat options to maintain a low-saturated-fat and low cholesterol dietary intake (Table 3). The importance of plant food based diets, which are high in fiber, vegetable proteins, and unsaturated fats, was stressed because the advantages of these diets in LDL-cholesterol management have been shown (22–24). This dietary portfolio has been previously described in detail (1–3). Self-taring electronic scales (Salter Housewares, Kent, England) were provided to all participants. They were asked to weigh and record all food items consumed in the week before the clinic visits.

Compliance with the self-selected dietary portfolio was assessed from the completed 7-d food records. These diet records were reviewed by the dietitian at each visit. Consumption of the 4 primary components of the diet, ie, soy protein foods, viscous fibers, almonds, and plant sterol margarine, were estimated from the food records and expressed as a percentage of the amount recommended for that person's energy requirement. If a person felt unable to consume the full amount of one component, an attempt was made to ensure that increased amounts of the other 3 components were consumed. Other aspects of the diet, including meat, dairy, fruit, and vegetable consumption, were also assessed and, where needed, advice was given (Table 3), but these dietary components did not contribute to the reported compliance score.

In the previously published metabolic dietary portfolio study, in which 29 of the present participants participated, foods were provided to achieve the same goals as those described for the present 1-y self-selected dietary portfolio (2, 21). For the statin phase of that study, a very-low-fat-dairy and high whole-grain cereal metabolic diet was used together with 20 mg lovastatin taken in the evening. The diet on the statin treatment had a similar macronutrient profile to the dietary portfolio, but lacked the specific cholesterol-lowering components (2, 21) (Table 2).

Analyses

Serum was analyzed for total cholesterol, triacylglycerol, and HDL cholesterol according to the Lipid Research Clinics protocol (25), after dextran sulfate-magnesium chloride precipitation (26). LDL cholesterol was calculated in mmol/L by the method of Friedewald et al [LDL cholesterol = total cholesterol – (triacylglycerols/2.2 + HDL cholesterol)] (27). Diets were analyzed for macronutrients, fatty acids, cholesterol, and fiber with the use of a computer program based on US Department of Agriculture data (1).

Statistical analysis

The results are expressed as means \pm SEs. Unless otherwise stated, an intent-to-treat with last-observation-carried-forward analysis was performed for those participants who did not complete the study. All statistical tests were performed at the $P < 0.05$ significance level. The effect of change over time from baseline was assessed with the use of a generalized linear mixed model, with spatial power covariance to adjust for unequal sampling periods (weeks 2, 4, 8, 12, 18, 24, 32, 42, and 52). The repeated-measures analysis had percentage change from week 0 as the response variable and week as the covariate predictor, with participant ID as the sole class variable (SUBJECT option in REPEATED statement). An analysis was also carried out with the use of only the 55 participants who completed the 1-y study.



TABLE 3

Foods recommended and not recommended as part of the ad libitum dietary portfolio

Food group (recommended quantity)	No. of servings	Examples of servings	Types of foods
Viscous fiber (15–20 g/d; 10 g/1000 kcal) ¹	3/1000 kcal (3 g/serving)	40 g dry oat bran 75 g oat bran specialty bread 38 g dry barley 3.5 g psyllium	Oat bran, oat meal, rolled oats, oat bran breads, barley, psyllium containing cereals, okra, eggplant
Soy protein (22.5 g/1000 kcal) ¹	(1 g/serving) 3.5/1000 kcal (6.25 g/serving)	75 g okra (frozen) 180 g eggplant (raw) 260 g “lite” soy beverage or 250 g fortified soy beverage 40 g extra firm low-fat tofu 62 g soy deli slices 85 g soy burgers 48 g soy hot dogs	Soy beverage, tofu, soy meat analogues, soy cheese slices
Other vegetable proteins (6–8 g/1000 kcal)	0.5/1000 kcal (8–16 g/serving)	100 g cooked beans, lentils, or chick peas 1 cup of instant lentil soup or instant vegetarian chili	Black, kidney, or white beans; yellow, red, green lentils; split peas, black-eyed peas
Plant sterols (1 g/1000 kcal) ¹	2.5/1000 kcal (0.4 g/serving)	5 g plant sterol margarine	Flora Pro-activ, Take Control ²
Nuts: almonds (23 g/1000 kcal) ¹	0.8/1000 kcal (28 g/serving)	28 g almonds	Almonds
Fruit and vegetables (2.5–5 servings/1000 kcal)	2.5–5/1000 kcal	100–120 g fruit 80 g cooked vegetables 85 g leafy vegetables	No restrictions
High monounsaturated fatty acid oils and margarines (11 g/1000 kcal)	2/1000 kcal (5 g/serving)	5 g margarine or oil	Olive, canola oil; plant sterol lite margarine
Sweets	2/1000 kcal (10 g/serving)	10 g strawberry jam	Sugar, double fruit jam
Fat-free or low-fat dairy foods	0 or ≤2/wk	250 g milk, 175 g yogurt, 42 g cheese	Skim milk, low-fat yogurt, low-fat or fat-free cheese, or cottage cheese
Egg whites and egg substitute	0 or ≤3 whole egg equivalent per wk	50 g egg white or egg substitute	Egg white, egg substitute, egg replacements
Poultry, fish, and red meats	0 or ≤3/wk	85 g cooked poultry, 95 g cooked fish, or 85 g cooked meat	White poultry meat, no skin; any fish; lean or extra lean red meats

¹ Primary components of the dietary portfolio.² Flora Pro-activ (Unilever UK, Purfleet, United Kingdom); Take Control (Unilever NA, Englewood Cliffs, NJ).

For multiple pair-wise comparisons between the self-selected, metabolic portfolio, and statin treatments, the significance of the differences in percentage reduction from baseline was assessed by least-squares means (28) with Tukey-Kramer adjustment. An analysis of variance (ANOVA) *F* test was performed to assess the effect of potential confounders, including sex and recruitment cohort, on LDL-cholesterol change. Because no potential confounders were found, these variables were excluded from further model specifications. In the least-squares means assessment, the model had percentage change from baseline to week 4 as the response variable with treatment (diet; 3 levels) and with participant ID as the random effect, which indicated the crossover aspect of the experimental design. The participants were also divided into groups 1, 2, and 3, which were defined on the basis of their LDL-cholesterol reductions from baseline to 52 wk (ie, group 1, ≥20%; group 2, 10–20%; and group 3, <10%). These groupings were selected to represent the following: 1) the <10% LDL-cholesterol reductions that may be seen after fiber supplementation or the use of low-saturated-fat and low-cholesterol diets (1–3, 9, 24, 29, 30); 2) the 10–20% LDL-cholesterol reductions that may be observed at the high end of the range for highly effective dietary cholesterol reductions and the minimum reduction considered therapeutically significant in the prestatin and early statin periods (8, 31–33); and 3) the >20% LDL-cholesterol reduction that is typical of the effect seen in most of the large statin trials (20, 34).

For a comparison of mean LDL-cholesterol changes between participant groups 1, 2, and 3 at week 4 on the self-selected portfolio, metabolic portfolio, and statin treatments, Tukey's test was used after establishment of a significant *F* value by ANOVA (28). The possibility of 2- and 3-way interactions between the cholesterol groups (based on the LDL-cholesterol response at 52 wk), the treatment (ad libitum portfolio, metabolic portfolio, and statin), and time at weeks 2 and 4 was tested by ANOVA (Proc GLM) (28). None of the interactions were significant.

Linear associations between mean LDL-cholesterol reduction and mean compliance measures were tested by using Pearson's correlation. Compliance was assessed for the 4 portfolio components (soy protein, plant sterols, viscous fibers, and almonds), where the prescribed amount represented 100%. Total compliance was the sum of the 4 individual compliances given equal weighting.

RESULTS

Compliance was satisfactory for almonds ($\bar{x} \pm \text{SE}$: 78.8 ± 3.2%) and for the plant sterol-enriched margarine (67.1 ± 3.2%), whereas it was less adequate for viscous fiber (55.1 ± 2.9%) and for soy protein (51.0 ± 3.0%). At 1 y, only 2 participants were following a vegan (no animal product) diet and 5 were following a lacto-ovo-vegetarian diet. The remaining participants were following

TABLE 4Blood lipid measurements at baseline and after 1 y of the ad libitum dietary portfolio study in 66 participants¹

	Total C	LDL-C	HDL-C	Triacylglycerol	Total:HDL-C	LDL-C:HDL-C
Prestudy	6.75 ± 0.10	4.48 ± 0.09	1.24 ± 0.04	2.29 ± 0.14	5.76 ± 0.16	3.82 ± 0.12
1 y	6.05 ± 0.11	3.87 ± 0.10	1.28 ± 0.05	1.98 ± 0.11	5.03 ± 0.16	3.23 ± 0.12
Change	-0.70 ± 0.09	-0.61 ± 0.09	0.04 ± 0.02	-0.31 ± 0.11	-0.73 ± 0.10	-0.59 ± 0.08
P ²	< 0.0001	< 0.0001	0.0256	0.0051	< 0.0001	< 0.0001

¹ All values are $\bar{x} \pm \text{SE}$. Total C, total cholesterol; LDL-C, LDL cholesterol; HDL-C, HDL cholesterol. A last-observation-carried-forward analysis was performed for 11 participants for weeks 0 ($n = 1$), 2 ($n = 1$), 12 ($n = 3$), 24 ($n = 2$), 32 ($n = 3$), and 42 ($n = 1$).

² Significance of change was determined with Student's paired t test (2-tailed, PROC MEANS) (28).

an omnivorous diet. For those participants who completed the study, although total protein remained similar to prestudy values ($18.9 \pm 0.5\%$ of energy at prestudy compared with $20.0 \pm 0.4\%$ at 1 y), animal protein intake as a percentage of total calories was reduced from $11.2 \pm 0.6\%$ to $5.6 \pm 0.5\%$ ($P < 0.001$). Over the 1 y of the self-selected dietary portfolio, a small but statistically significant weight loss was observed (-0.7 ± 0.3 kg; $n = 66$; $P = 0.036$).

Blood lipids

On the ad libitum portfolio, near-maximum reductions in LDL cholesterol and the ratio of total to HDL cholesterol were seen at 12 wk, and these were sustained to 1 y. Thus, mean ($\pm \text{SE}$) LDL cholesterol was reduced at 12 wk by $14.0 \pm 1.6\%$ ($P < 0.001$) and at 1 y by $12.8 \pm 2.0\%$ ($P < 0.001$). LDL cholesterol significantly increased in the post-Christmas sample at week 18. The absolute changes in blood lipids over the 1 y are presented in **Table 4**. The reductions for the 55 participants who completed the study were similar to those for the group as a whole at 12 wk (LDL cholesterol: $16.1 \pm 1.4\%$, $P < 0.001$; total:HDL cholesterol: $14.4 \pm 1.5\%$, $P < 0.001$) and at 1 y (LDL cholesterol: $14.6 \pm 2.1\%$, $P < 0.001$; total:HDL-cholesterol: $12.7 \pm 1.7\%$, $P < 0.001$) (**Figure 2**). No significant difference in LDL-cholesterol reduction was seen between the sexes or between the 2 recruitment cohorts. Significant time trends in total cholesterol and HDL cholesterol were seen for changes from baseline, but these trends were not reflected in the LDL cholesterol, total:HDL cholesterol, LDL:HDL cholesterol, or triacylglycerol responses.

The participants on the ad libitum portfolio study were also divided into 3 groups based on their 1-y LDL-cholesterol response: those with LDL-cholesterol reductions from baseline $>20\%$ (group 1), those with LDL-cholesterol reductions 10–20% (group 2), and those with LDL-cholesterol reductions $<10\%$ (group 3). At 1 y, 31.8% of the participants showed LDL-cholesterol reductions $>20\%$ [group 1; $n = 21$ of 66; \bar{x} ($\pm \text{SE}$) LDL-cholesterol reduction: $29.7 \pm 1.6\%$]. The respective percentage of participants in groups 2 and 3 were 27.3% ($n = 18$ of 66; LDL-cholesterol reduction: $15.6 \pm 0.8\%$) and 40.9% ($n = 27$ of 66; $2.2 \pm 2.0\%$). Similar results were obtained with the analysis of the 55 participants who completed the study: group 1 participants (LDL-cholesterol reduction: $30.3 \pm 1.6\%$) accounted for 34.6% of the total number of participants ($n = 19$ of 55).

Compliance and change in LDL cholesterol

The mean LDL-cholesterol changes for the 2–52-wk period were used to calculate the correlation with the respective means of the total and individual compliance measures. Mean total

compliance over 1-y and LDL-cholesterol change were significantly correlated ($r = -0.42$, $P < 0.001$; $n = 65$). Only 2 of the 26 participants who had a compliance $<55\%$ achieved an LDL-cholesterol reduction at 1-y that was $>20\%$. Associations between compliance with individual dietary components and the change in LDL-cholesterol were also seen for consumption of soy ($r = -0.52$, $P < 0.001$), fiber ($r = -0.39$, $P = 0.001$), and almonds ($r = -0.33$, $P = 0.008$) (**Table 5**).

Comparison with metabolic portfolio and statin treatments

To determine whether the participants who showed a less adequate response on the self-selected portfolio diet (groups 2 and 3; ie, those with $<20\%$ reduction in LDL cholesterol) were biologically poor responders under all circumstances, the effect of the self-selected portfolio was compared with the published data on 29 of the present participants who had previously undertaken metabolic portfolio and statin diets (2, 21). No significant differences between the mean 1-y LDL-cholesterol reductions on the self-selected portfolio and the LDL-cholesterol reductions on the metabolic portfolio and statin treatments were seen for the group 1 participants (**Figure 3**). However, for the participants in groups 2 and 3, the LDL-cholesterol reductions at 1 y on the self-selected portfolio diet were significantly less ($P \leq 0.007$) than their responses on the metabolic portfolio and statin treatments (**Figure 3**). In contrast, no significant differences in LDL-cholesterol reduction were seen between groups 1, 2, and 3 for either the metabolic portfolio or statin treatments. These data indicate that the differences in LDL-cholesterol responses between groups 1, 2, and 3 were seen only on the ad libitum study and provide no support for the concept that participants in groups 2 and 3 were biologically poor responders, but rather that compliance was likely to be the issue.

DISCUSSION

Application of a diet that combined several cholesterol-lowering foods under free-living real-world conditions resulted in a mean LDL-cholesterol reduction of $\approx 13\%$, which was sustained over a 1-y period. However, approximately one-third of the participants had LDL-cholesterol reductions of $\geq 20\%$. Such reductions approach the levels seen with the first generation statins, which have been associated with a 25–35% sparing in coronary heart disease mortality (5–6).

The diet also tended to raise HDL-cholesterol concentrations and was associated with total:HDL cholesterol reductions of



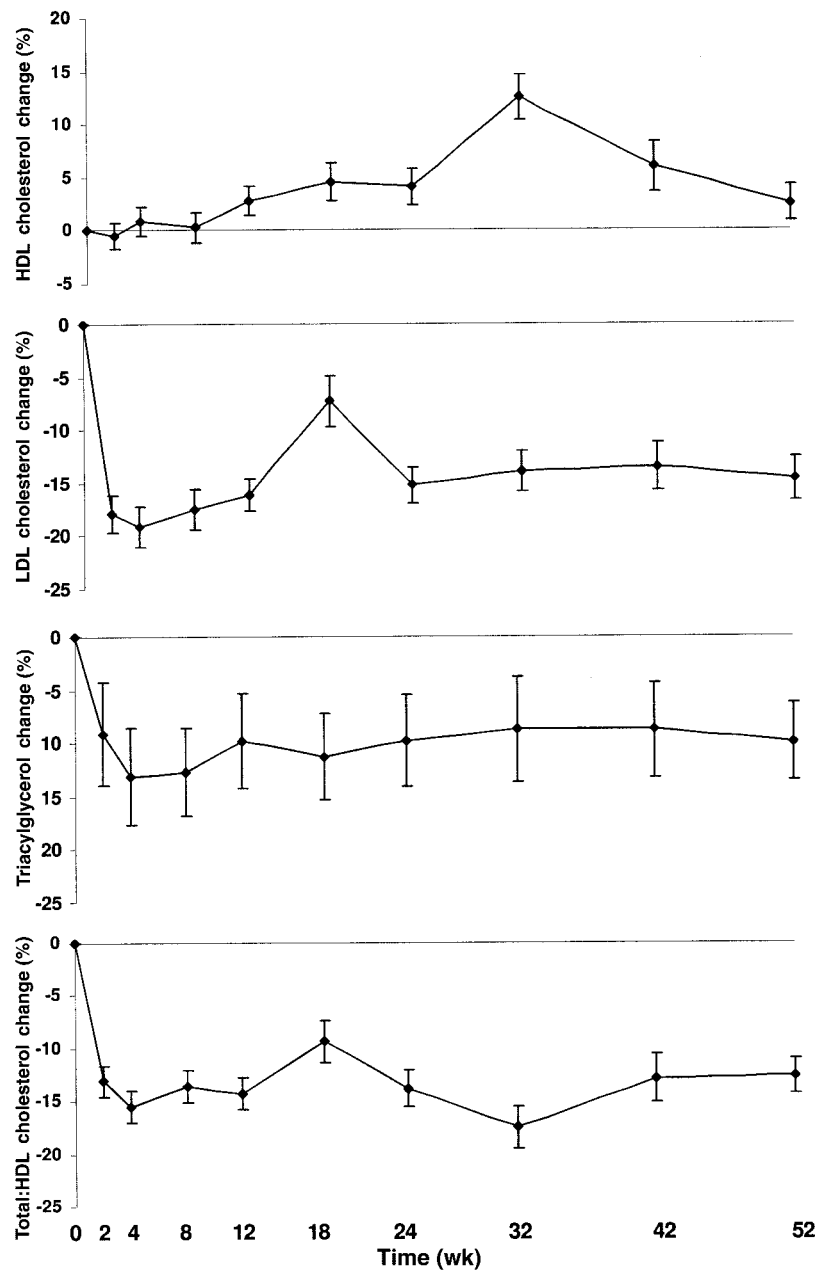


FIGURE 2. Mean (\pm SE) percentage change from baseline in serum lipids in the 55 participants who completed the 52-wk study. Changes from baseline were assessed by paired *t* test (two-tailed) with Bonferroni adjustment for 9 comparisons. Reductions at all time points were significant for LDL cholesterol and the ratio of total to HDL cholesterol ($P = 0.036$ to <0.001). For HDL cholesterol, only the increase at week 32 was significant ($P < 0.001$); for triacylglycerols, only the reduction at week 8 was significant ($P = 0.028$).

12.7% and with a small but significant reduction in serum triacylglycerol concentrations. These lipid changes would also be predicted to have a favorable effect on coronary heart disease events (12, 35–38).

Larger LDL-cholesterol reductions were anticipated in persons who, before starting the study, were consuming diets more representative of the general population in terms of saturated fatty acid and cholesterol intakes. Diets that conform to the current ATP III criteria ($<7\%$ saturated fat/d and <200 mg cholesterol/d) reduce LDL cholesterol by $\leq 18\%$ compared with typical North American diets with intakes of 14% saturated fat and 147 mg cholesterol/1000 kcal (31). Before commencing the present

TABLE 5

Correlation between mean change in LDL cholesterol and mean dietary adherence from weeks 2 to 52¹

	<i>r</i>	<i>P</i>	<i>n</i>
Total compliance	-0.42	0.0004	65
Fiber	-0.39	0.0012	65
Almonds	-0.33	0.0080	65
Plant sterols	-0.20	0.1232	61
Soy	-0.52	< 0.0001	65

¹ Linear associations were determined between mean LDL-cholesterol reduction and mean dietary adherence with the use of Pearson's correlation (PROC CORR) (28).



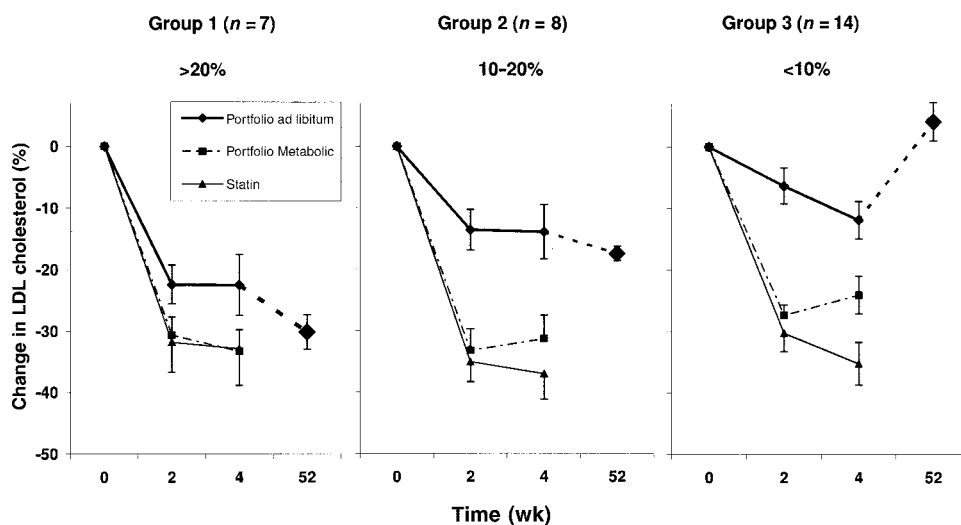


FIGURE 3. Mean (\pm SE) percentage change from baseline in LDL cholesterol in the 29 participants who underwent the 1-y ad libitum dietary portfolio and the 1-mo metabolic dietary portfolio and statin treatment. The participants are divided into 3 groups on the basis of their 52-wk LDL-cholesterol reductions in response to the ad libitum dietary portfolio ($>20\%$, $10\text{--}20\%$, and $<10\%$). No significant group \times treatment \times time interaction was seen over the 4-wk treatment period (ANOVA) (28). No significant differences in response to either the metabolic dietary portfolio or the statin drug were seen between the 3 groups at week 4 (ANOVA with Tukey's test). Only the LDL-cholesterol reductions at 52 wk in groups 2 and 3 were significantly different from the 4-wk metabolic values, $P < 0.05$ (least-squares means with Tukey's adjustment) (28).

study, our participants were already eating diets that conformed to the current recommendations for saturated fat and cholesterol intakes (6.9% saturated fat and 144 mg cholesterol/d).

The ad libitum LDL-cholesterol reduction of 13% was close to the value predicted from metabolic data (39) and was within the 10–15% considered to be clinically meaningful by early statin and prestatin drug criteria (32, 33). It was also greater than the minimum 8–9% LDL-cholesterol reduction required to see a reduction in all-cause mortality (40).

Viscous fiber, soy protein, plant sterols, and almonds are well-recognized for their cholesterol-lowering properties (15–19, 29, 41–53). The potential bioactive components of almonds are likely several (47) and may relate to their plant protein, monounsaturated fat, and plant sterol contents (42–49). Few long-term studies have assessed the effect of portfolio components. In the few studies undertaken, LDL-cholesterol reductions for single foods have ranged from 6% to 15% (54–57). No long-term studies have reported on combinations of these functional foods. One recent 1-mo study assessed the effect of a vegetarian diet containing the components used in the present study but at lower levels and showed LDL-cholesterol reductions of $\approx 10\%$, although the reduction in total:HDL-cholesterol did not reach significance (24).

Furthermore, few studies have assessed the effect of functional foods and food components taken with a diet that is very low in saturated fat. A year long study of 2 g sterol/d supplemented in margarine consumed with a diet relatively high (14%) in saturated fat resulted in a 15% reduction in LDL-cholesterol (56), and similar changes were reported in a meta-analysis of the effects of both plant sterols and stanols (hydrogenated sterols) (42, 57). The first major meta-analysis of the effect of soy protein also suggested a 13% LDL-cholesterol reduction with a mean consumption of 47g soy protein/d (35); another analysis suggested a more modest effect (58). However, at very-low-saturated-fat levels, the effects of soy protein may be attenuated (59) and the effects

of plant sterols may also be attenuated (60). When dietary saturated fat levels are low, we believe 5% LDL-cholesterol reductions from each of the 4 portfolio components might be more realistic (2).


We observed an increase in LDL cholesterol in the random post-Christmas blood samples. Serum lipids are known to rise during winter months (61). The post-Christmas sample, taken at 4.5 mo with ≤ 2 d notice, was specifically placed to assess the worst-case scenario.

Genes may change the response to diet. Carriers of the *APOE*E4* allele may respond more favorably than noncarriers to soy protein (62) and viscous fiber (30, 63), although not to plant sterols (64). Abnormalities in the *ABC G5-8* gene may change the plant sterol effect on cholesterol absorption and plasma concentrations (65). However, genetic differences do not appear to explain the large differences in response between the 3 groups of persons on the ad libitum study; their responses to the metabolic diet and to the statin were uniform.

The obvious answer to the dietary variability is poor dietary compliance. Our self-reported data provide support for this as an explanation, although our numbers are too small to come to more than a qualified conclusion. No strong association existed between compliance and change in LDL cholesterol because of 2 persons who recorded extremes of good dietary compliance with a relative lack of effect of diet on LDL cholesterol and who acted as highly influential points in the correlation. Nevertheless, compliance with single foods such as almonds and margarine (compliance: 79% and 64%, respectively) may be easier to achieve than compliance with more complex groups of foods such as sources of viscous fiber and soy protein (compliance: 55% and 50%, respectively), despite their significant relation to LDL-cholesterol reduction.

Intakes of the portfolio components that were less than those prescribed in the current study were also shown to produce worthwhile serum lipid reductions (24). We believe that the combination

approach to dietary treatment may greatly enhance its effectiveness, as was shown for combination drug therapy and is now accepted in the dietary management of hypertension (66–69).

In conclusion, we showed that a significant proportion of motivated persons can achieve a sustained and clinically meaningful reduction in LDL cholesterol of >20% by dietary means. As a greater variety of soy-, viscous fiber-, plant sterol-, and almond-containing foods become available, such diets will become easier to follow. They will then provide an option for those who, due to personal preference or, more rarely, due to side effects, may wish to use diet rather than medications as the primary prevention to control serum cholesterol concentrations. We believe that the quest for options such as these will become increasingly important as the optimal concentrations of LDL cholesterol are progressively reduced (20). 

We thank Kathy Galbraith of Natural Temptations Bakery, Burlington, Canada, for her assistance on this project and the study participants for their enthusiasm and attention to detail.

DJAJ, CWCK, and DAF were the study supervisors. DJAJ, CWCK, and DAF contributed to the study concept and design and were responsible for the funding of the study. DJAJ, CWCK, DAF, TK, AM, JMWW, RdS, AE, EV, CH, and PWC contributed to the acquisition of the data. DJAJ, CWCK, TK, RGJ, LAL, PWC, and WS contributed to the analysis and interpretation of the data. DJAJ and CWCK were responsible for the drafting of the manuscript. DJAJ, CWCK, DAF, TN, TK, AM, JMWW, RdS, AE, EV, EAT, LAL, CH, RGJ, PWC, and WS contributed to the critical revision of the manuscript for important intellectual content. CWCK, AM, DAF, TN, JMWW, RdS, AE, EAT, KGL, CH, RGJ, LAL, PWC, and WS were responsible for the administrative, technical, or material support for the study. EV contributed statistical expertise. DJAJ has served on the Scientific Advisory Board of Unilever and Solae. DJAJ and CWCK have been on the speakers panel for the Almond Board of California. CWCK, DAF, and EV receive partial salary funding from research grants provided by Unilever, Loblaws, and the Almond Board of California. EAT is employed by Unilever Food and Health Research Institute, Unilever R&D Vlaardingen, Netherlands. KGL is employed by the Almond Board of California, Modesto, California.

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