Increasing Vegetable and Fruit Intake: Randomized Intervention and Monitoring in an At-Risk Population

Stephanie A. Smith-Warner, Patricia J. Elmer, Theresa M. Tharp, Lisa Fosdick, Bryan Randall, Myron Gross, James Wood, and John D. Potter[1]

Division of Epidemiology, School of Public Health, University of Minnesota, Minneapolis, Minnesota 55455 [S. A. S-W., P. J. E., T. M. T., M. G., J. D. P.]; Now, Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts 02115 [S. A. S-W.]; Now, Center for Health Research, Kaiser Permanente, Portland, Oregon 97227 [P. J. E.]; Division of Biostatistics, School of Public Health, University of Minnesota, Minneapolis, Minnesota 55455 [L. F., B. R.]; Now, Boston Scientific Scimed, Inc., Maple Grove, Minnesota 55311 [B. R.]; and Digestive Healthcare P.A., Minneapolis, Minnesota 55404 [J. W.]; and Fred Hutchinson Cancer Research Center, Seattle, Washington 98109-1024 [J. D. P.]

Abstract

High vegetable and fruit (V&F) consumption has been associated with a lower risk of several cancers. However, little is known about the ability of individuals to increase their intakes markedly.

In this 1-year randomized, controlled diet intervention study of men and women with a recent history of adenomas, the intervention group ($n = 100$) was asked to increase V&F intake to at least eight servings per day; the control group ($n = 101$) continued eating their usual diet. End-point measures included V&F intake assessed by 3-day diet records, plasma carotenoids, serum lipids, urinary sodium and potassium, and body weight.

The intervention group increased their daily V&F intake an average of 5.5 servings over 1 year; the control group had an average decrease of 0.5 servings per day ($P < 0.001$). Plasma total carotenoids, α-carotene, β-carotene, β-cryptoxanthin, and lutein/zeaxanthin were each statistically significantly elevated over baseline (11–54%) in the intervention group compared with the control group over the duration of follow-up ($P < 0.001$). Urinary potassium excretion was elevated 14% over baseline in the intervention group compared with no change in the control group ($P < 0.001$). Modest decreases in the intervention but not the control group were observed for total and low-density lipoprotein cholesterol. Plasma lycopene, triglycerides, high-density lipoprotein cholesterol, body weight, and urinary sodium were not affected by the intervention.

V&F intake was significantly increased in this motivated population at higher risk of colon cancer and maintained for at least 12 months, as assessed using diet records and an ensemble of biomarkers.

Introduction

Increased V&F[2] intake has been consistently associated with a lower risk of a number of cancers, particularly those of epithelial origin, including colon cancer (1, 2) as well as heart disease (3, 4). Both vegetables and fruit contain a wide array of compounds that may inhibit cancer, thus conferring a potential chemoprotective effect (5). In addition, high V&F consumption has been associated with overall diet quality and lower consumption of meats, fats, and simple sugars (6–10), each of which has been associated with an increased risk of colorectal cancer (2, 11). Together, these properties constitute a strong rationale for making public health recommendations to increase V&F intake (2) and for conducting intervention trials designed to increase V&F consumption. Within the context of intervention trials, it is important to determine to what extent V&F intake can be increased, particularly in individuals at high risk of cancer. These trials can help elucidate which educational approaches are effective in increasing V&F intake, the benefits and barriers to increasing V&F consumption, and the consequences (both positive and negative) of making these dietary changes. Additionally, it is important to determine whether biomarkers of V&F intake can be identified for use in monitoring both individual and population dietary changes. Finally, it is important to establish how increasing V&F intake affects various metabolic processes. As a way to examine some of these questions, we conducted the Minnesota CPRU diet intervention trial to increase V&F consumption in a population with adenomatous polyps who were thus at high risk of colorectal cancer and potentially motivated to change their diet.

Subjects and Methods

The Minnesota CPRU was established in 1990 and was funded by the National Cancer Institute. The primary goals involved increasing understanding of the etiology and prevention of colorectal neoplasia. Integral to the structure of the CPRU was the partnership between the University of Minnesota and DH, a large community-based gastroenterology practice with 10 clinics throughout the greater Twin Cities metropolitan area. We conducted a randomized, controlled 12-month clinical trial with two treatment arms: intervention and control (Fig. 1). The aims of the study were: (1) to implement a 1-year structured dietary intervention to increase V&F intake to at least eight servings per day; and (2) to evaluate changes in dietary intake

Received 9/8/99; revised 12/15/99; accepted 12/23/99.
The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

[1] To whom requests for reprints should be addressed, at Fred Hutchinson Cancer Research Center, 1100 Fairview Avenue North, MP 702, Seattle, WA 98109-1024.

[2] The abbreviations used are: V&F, vegetable and fruit; CPRU, Cancer Prevention Research Unit; DH, Digestive Healthcare, P.A.; NDS, Nutrition Data System; HDL, high-density lipoprotein.

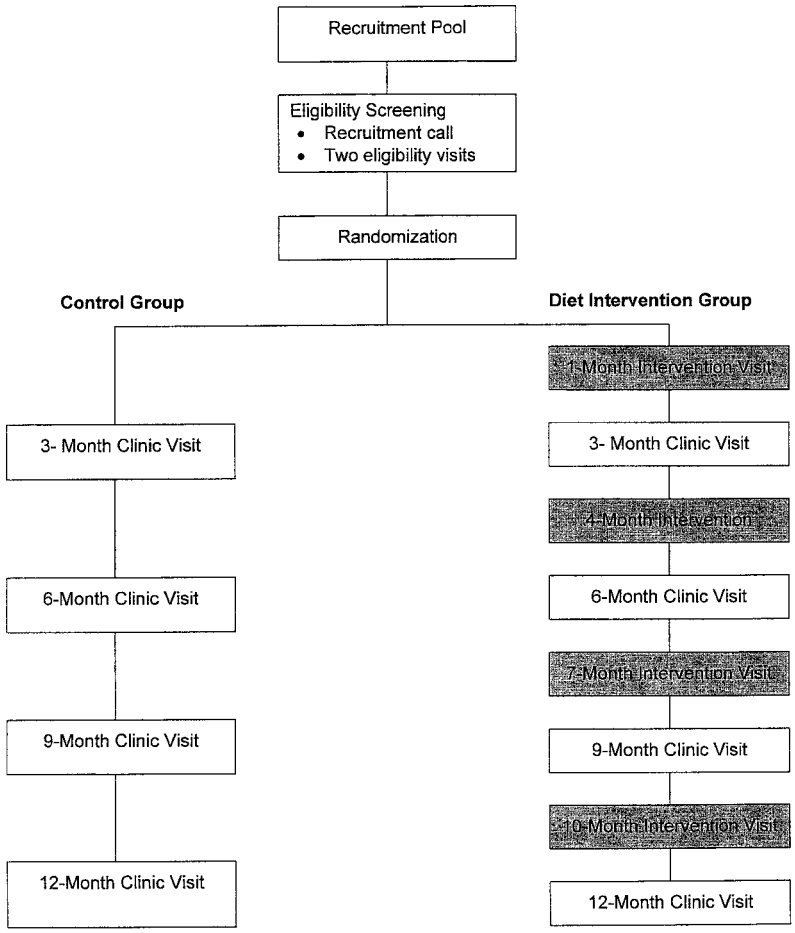

Fig. 1. Minnesota CPRU V&F Intervention Study design.

and physiological parameters, including plasma carotenoids, serum lipids, and urinary electrolyte excretion as measures of adherence and effect. The project was approved by the University of Minnesota Internal Review Board Human Subjects Committee.

Study Population

DH served as the clinical center and the source of participants for this study. The recruitment protocol was implemented using the staff and resources of DH and the University of Minnesota Divisions of Epidemiology and Biostatistics. Recruitment began August 1991 and continued through September 1993. Patients were identified through a CPRU case-control study and the DH patient database. All eligibility and clinic visits were conducted at the DH facility.

Eligibility and Exclusion Criteria

DH patients aged 30–74 years with a diagnosis of colorectal adenomatous polyps within the preceding 5 years were potentially eligible for the study. Eligibility was determined using information obtained through medical chart review, including medical history, results of colonoscopy examination, and pathology review; self-administered questionnaires; and telephone and face-to-face interviews. All diagnoses of adenomatous polyps were verified by the CPRU study pathologist. Major exclusions included: body weight >150% of desirable weight-for-height; medical conditions, including gastrointestinal disorders, diabetes mellitus, cardiovascular disease, cancer, or any serious health condition that would limit participation; special diet restrictions, including diabetic, vegetarian, and renal-disease diets; food sensitivities that would interfere with a tolerance of increased V&F consumption; plans to relocate or travel extensively; involvement in any other study requiring dietary changes; intention to become pregnant; consumption of >35 alcoholic beverages/week; urinary protein levels of ≥30 mg/dl; urinary glucose levels of ≥0.25 g/dl; and refusal to participate or sign the consent form.

Study Design

Study candidates attended two clinic screening visits following an initial telephone interview. Those who remained eligible and interested at the final eligibility visit were randomly assigned to one of two study groups stratified by sex: intervention or control. Participants in the intervention group ($n = 100$) were asked to increase V&F intake to at least eight servings per day. The control group ($n = 101$) continued eating their usual diet. Informed, written consent was obtained from all participants before randomization. Both groups attended 3-, 6-, 9-, and 12-month postrandomization clinic visits. Additionally, the intervention group was seen for four individual diet intervention appointments.

Dietary Intervention

The intervention goal was to increase V&F consumption to at least eight servings per day before the 3-month clinic visit, with a secondary emphasis on increasing the intake of β-carotene-rich V&F. After randomization, participants met with a study nutritionist to formulate a plan for gradually increasing the number of V&F servings in their diets. The initial goal involved an increase of at least two servings per day. Participants then monitored their V&F intake for the next 2 weeks using a Daily V&F Record. This self-monitoring instrument served as a teaching tool—it included lists of commonly eaten V&F and the definition of a serving for each item. It also was used by study nutritionists to assess progress toward, or maintenance of, dietary change at intervention visits. Positive reinforcement and feedback from the study team were provided during intervention sessions to enhance long-term motivation.

Behavior modification strategies were derived from social learning theory (12, 13). Nutrition counseling focused on goal setting, verbal commitments to behavioral intentions, and use of self-monitoring tools. These sessions emphasized the development of skills essential to participant adherence, including the ability to identify V&F in various forms and dishes, associated serving sizes, and planning and tracking daily intake. Participants worked with intervention staff to identify personal barriers to adherence and to develop plans to overcome these barriers. Educational materials included tip sheets, a V&F cookbook, quarterly newsletters, and a list of high β-carotene V&F. Visit reminder cards, telephone follow-up for rescheduling missed visits, refrigerator magnets, newsletters, "carrot" birthday cards, and V&F calendars were used as memory prompts and to enhance participant identification with the project. In addition, the intervention attempted to enhance spousal and family support.

End-Point Evaluation

All measures were collected at the baseline and at the 3-, 6-, 9-, and 12-month postrandomization clinic visits for intervention and control participants.

Dietary Intake—Diet Records. Dietary intake was determined from diet records completed for the 3 consecutive days before the clinic visits. Participants described consumption of all foods, beverages, and nutrient supplements and included brand names, serving sizes, methods of preparation, and names of restaurants. A study nutritionist reviewed the diet records for completeness. Serving sizes were verified using standard food models (NASCO, Ft. Atkinson, WI) and measures. Mean daily nutrient intakes were derived using the Minnesota NDS software (version 2.3, Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN).

Plant foods were categorized as V&F on the basis of their preparation, macro- or micro-nutrient content, or proportion of the food that was vegetable or fruit using the CPRU V&F classification scheme (14). The fat, salt, or sugar content of plant foods was not used as a criterion for excluding foods as V&F. Intake was evaluated using the following categories: vegetables without juice (referred to as vegetables), fruits without juice (fruit), V&F juice (juice), and vegetables, fruit, and juice (total V&F). To estimate V&F consumption, the NDS codes for vegetables ($n = 149$), fruits ($n = 85$), and juice ($n = 23$) were identified.

Because present dietary guidelines give recommendations for V&F intake in servings and because the intervention was based on servings, the results of this study are presented as servings rather than grams. A serving was defined as one-fourth cup for dried fruits; one-half cup for raw, cooked, canned, and pickled V&F, high fat fruits, and mature beans; three-fourths for vegetable and fruit juice, and 1 cup for raw, leafy greens (14). These definitions were based on the Dietary Guidelines for Americans (15). Because the quantity of each food in NDS is stored as a gram weight, servings were defined using the gram weight corresponding to the volumetric serving size for each V&F. Daily total consumption was calculated by summing the servings of individual V&F consumed on each day.

Physiological End Points. Fasting blood samples (25 ml) were protected from light and were stored at −70°C. Samples were analyzed in batches by the University of Minnesota, Division of Epidemiology, Biochemical Epidemiology and Lipid Research Core Laboratory and the Molecular Cancer and Biomarkers Research Core. Plasma carotenoids were determined using high-performance liquid chromatography using the method of Bieri *et al.* (16), with calibration as described by Craft *et al.* (17). One minor modification of the assay was the inclusion of *N*,*N*-diisopropylethylamine (0.015%) in the high-performance liquid chromatography solvent to improve analyte recovery. Carotenoids analyzed included α-carotene, β-carotene, β-cryptoxanthin, lycopene, and zeaxanthin-plus-lutein (referred to as lutein). Calibration for all assays was done using crystalline standards (Hoffman-LaRoche, Basel, Switzerland; Sigma Chemical Co., St. Louis, MO). Quality control procedures included routine analysis of plasma pools containing high and low concentrations of each analyte. In addition, the laboratory routinely analyzes National Institutes of Standards and Technology reference sera and is a participant in the National Institutes of Standards and Technology Fat-Soluble Vitamin Quality Assurance Group. Because plasma lycopene is uncorrelated with V&F intake (18), the variable, total carotenoids was calculated as the sum of α-carotene, β-carotene, β-cryptoxanthin, and zeaxanthin-plus-lutein.

Serum lipids and lipoproteins were measured by standard methods with a Beckman Synchron CX5 analyzer (19–21). Total HDL cholesterol was precipitated by the dextran-sulfate method. Total cholesterol, HDL cholesterol, and triglycerides were measured enzymatically. Low-density lipoprotein cholesterol was estimated by the Friedewald equation (22). Calibration standards for total and HDL cholesterol and triglycerides were obtained from Beckman, Inc. Control samples from Solomon-Park included high and low concentrations of total and HDL cholesterol and triglycerides. Both control and calibration samples were run daily. External reference materials were obtained from the Centers for Disease Control and Prevention, and analysis was done on a quarterly basis.

Overnight urine samples were collected for the 2 nights before each clinic visit. The dates and times for each collection period and completeness of collections were verified. Sodium and potassium concentrations were determined by an ion-selective electrode-based methodology. Analysis was done with a Beckman Synchron CX5 analyzer. Calibration of the instrument was done daily with standard solutions from Beckman, Inc. Control samples were obtained from Ciba-Corning and analyzed as every ninth sample. External reference materials were obtained from the College of American Pathologists, and analysis was done quarterly.

Body weight was measured using a calibrated, beam-balance scale. Participants were asked to remove their shoes and heavy outer garments before being weighed.

All participants completed health questionnaires to assess medical history, physical activity, life-style factors, and diet satisfaction. A study nurse also surveyed for symptoms poten-

tially related to an increased V&F intake including: digestive symptoms (*i.e.*, heartburn, nausea, abdominal bloating, belching, gas, abdominal pain), large bowel symptoms (*i.e.*, constipation, loose stools, diarrhea, blood in stools), general well being (*i.e.*, appetite, fatigue, drowsiness, sleeping patterns, nervousness), and other symptoms (*i.e.*, headache, dizziness, low libido, weakness).

Statistical Analysis

Statistical analyses were performed by the Statistical and Data Management Core of the CPRU in the Division of Biostatistics, University of Minnesota. Summary statistics were computed for each dietary and physiological variable at each time point. Each plasma carotenoid variable was log-transformed to improve normality. Log-transformed data did not change statistical significance; therefore, raw scale data are reported here. All randomized participants were included in the analyses regardless of compliance with the intervention (intention-to-treat analysis). The stratification variable used for all analyses was the same as used in the design of the study, namely sex of participants. Treatment groups were assessed for comparability of baseline characteristics by stratified ANOVA for continuous variables and χ^2 tests for categorical variables. For continuous variables, average mean change from baseline is reported for each treatment group. For each diet and physiological variable, all follow-up measurements for each participant were averaged, and the baseline measurement was subtracted. Significance probabilities are from models comparing the changes between the groups, including indicators for sex and the baseline level of the variable considered. Analyses were conducted using the Statistical Analysis System, version 6.08 (SAS Institute Inc., Cary, NC). No adjustments were made for multiple comparisons.

Results

Participant Characteristics

To attain the recruitment goal of 200 participants, a candidate pool of 1032 colorectal adenomatous polyp patients was identified. Of these potential study participants, 894 were contacted for screening. After a telephone interview, 280 (27%) of the candidates remained eligible and agreed to attend the first eligibility visit. The most common exclusions were lack of interest (340 participants), time and travel constraints (129 participants), and medical reasons (78 participants). A total of 251 individuals attended the first eligibility visit, 203 attended the second eligibility visit, and 201 (19.5% of the initial total candidate pool) were randomized into the study. During the eligibility visits, lack of interest, time and travel constraints, and medical reasons also were the primary reasons for not participating in the trial.

There were no differences between the intervention and control groups for any baseline characteristics. Most participants were white, their mean age was 59 years, and 71% were male (Table 1). Seventeen percent of the participants were smokers, and 83% consumed alcohol. Sixty-two percent of the men and 43% of the women were employed. The mean annual household income was $53,700 for men and $42,900 for women. Eighty-seven percent of the men and 72% of the women in the study were married. The average time since adenomatous polyp diagnosis was ~10 months.

Attendance and Adherence to Study Protocol

For all randomized participants, attendance averaged 93% of all clinic visits. Ninety-two percent of the randomized participants completed the study: 88% of the intervention group and 96% of the control group. The largest loss of participants in the intervention group (seven participants) occurred between randomization and the 3-month follow-up visit. Two of these participants were found to be ineligible after randomization and were not followed subsequently. However, they are included in the intent-to-treat analyses presented here. In the control group, the largest dropout occurred between the 3- and 6-month follow-up visits (four participants). Overall, compared to those who completed the study, more of the dropouts were smokers and were employed, and fewer were college graduates, although these differences were not statistically significant.

Table 1 Baseline characteristics of the intervention and control groups

	Intervention (n = 100) Mean or %	Control (n = 101) Mean or %	P
Demographics			
Age (yr)	58.6	60.0	0.21
Male (%)	71.0	71.3	0.96
Household income ($1000)	51.3	49.8	0.57
Education (yr)	14.6	14.5	0.70
Married (%)	79.0	87.1	0.12
Employed (%)	61.0	52.5	0.21
White (%)	99.0	99.0	0.99
Lifestyle and physiologic variables			
Tobacco			
% smokers	17.0	17.8	0.88
No. of cigarettes/day among smokers	19.6	16.0	0.26
Body mass index (kg/m^2)			
Men	28.3	28.4	0.90
Women	25.8	26.2	0.75
Alcohol			
% consumers	81.4	85.4	0.55
No. of drinks/wk among drinkers	4.7	3.9	0.26
Nutrient supplements			
% users	42.0	36.6	0.44
% users of β-carotene supplements	5.0	3.0	0.46

Intervention Results

V&F Intake. At baseline, vegetable, fruit, juice, and total V&F intakes did not differ between the intervention and control groups. Total daily V&F intake for all participants averaged 7 servings consisting of 4.0 servings of vegetables, 2.4 servings of fruit, and 0.6 servings of juice (Table 2; Fig. 2). Approximately 30% of the participants in each group consumed at least eight servings per day (the study intervention goal). Over the 12-month follow-up period, V&F intake declined to 0.5 servings/day in the control group. For the Intervention group, a 65% increase in V&F intake to 11.8 servings/day (5.5 servings of vegetables, 4.7 servings of fruit, and 1.6 servings of juice) was observed by the 3-month visit. The increase in consumption was maintained over the duration of the study. Based on average intakes over the follow-up period, 86% of the intervention participants met or exceeded the daily goal of at least eight servings; only 17% of the control group consumed eight or more servings per day. The difference between the intervention and control groups for the change in mean V&F intake during the study (4.7 *versus* −0.5 servings/day, respectively) was statistically significant ($P < 0.001$).

V&F consumption was examined for men and women separately and for two age groups (<60 and ≥60 years). The change in mean V&F intake was significantly higher in the intervention *versus* control groups over follow-up in both men

Table 2 V&F intake at baseline and average over follow-up for the intervention and control groups

Servings/day	Intervention		Control		P^c
	Baseline[a] mean (SD)	Average over follow-up[b] mean (SD)	Baseline[a] mean (SD)	Average over follow-up[b] mean (SD)	
Vegetables	4.3 (2.4)	5.5 (1.6)	3.7 (1.8)	3.5 (1.1)	<0.001
Fruits	2.4 (2.1)	4.9 (2.8)	2.4 (1.8)	2.1 (1.5)	<0.001
Juice	0.5 (0.6)	1.6 (0.9)	0.6 (0.7)	0.6 (0.6)	<0.001
Total V&F	7.3 (3.3)	11.9 (3.3)	6.7 (2.8)	6.2 (2.2)	<0.001

[a] Mean of 3-day diet records.
[b] Mean of 12 days of diet records collected at 3-, 6-, 9-, and 12-month follow-up visits.
[c] *P* calculated for intervention *versus* control group for the change in servings per day (average over follow-up minus baseline) for each variable with sex and baseline levels of the variable in the model.

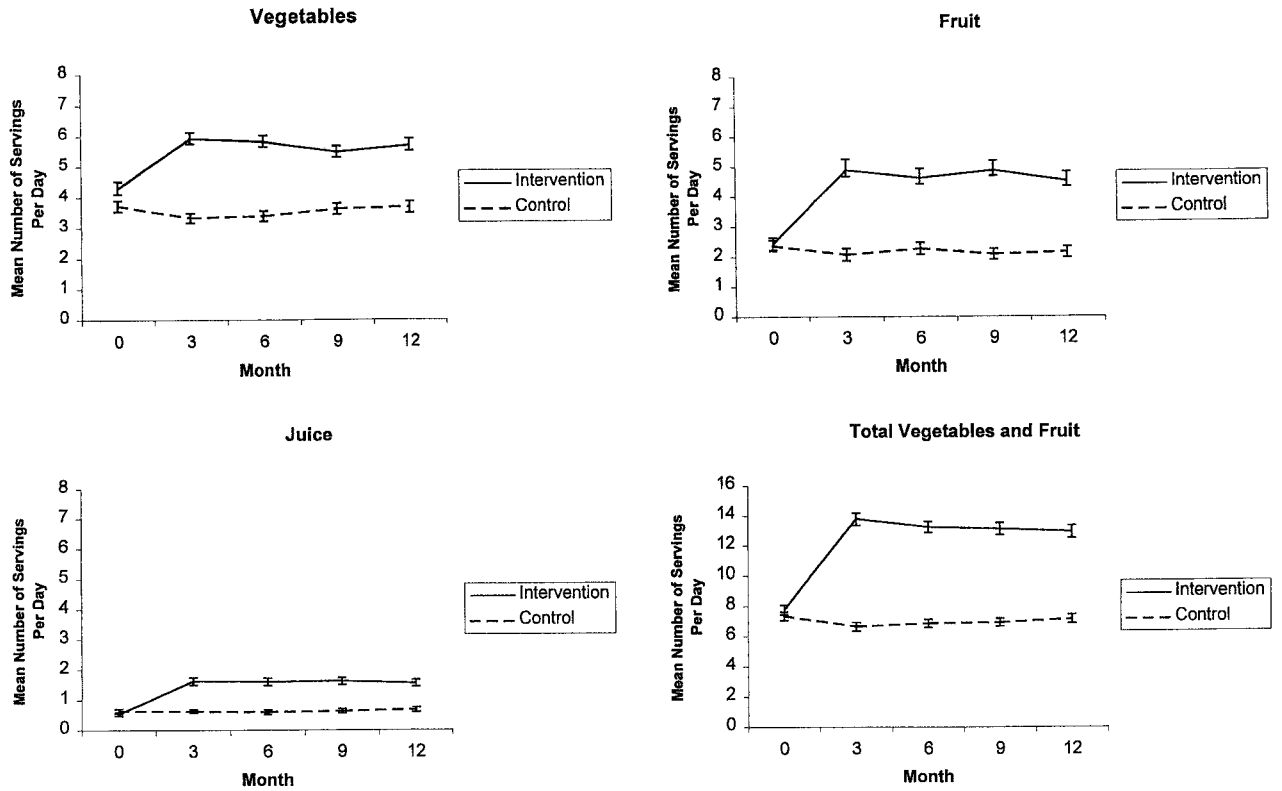

Fig. 2. Mean (± SE) vegetable, fruit, and juice intake over 12 months in the intervention and control groups.

($P < 0.001$) and women ($P < 0.001$). Only the change in juice consumption differed between men and women: men increased juice consumption by 1.2 servings/day, women by 0.6 servings/day during follow-up ($P = 0.03$; men *versus* women). There were no differences in total intake for any of the V&F groups between the two age groups.

The most common strategies that participants used to increase V&F consumption were: adding V&F to dinner, adding V&F to lunch, eating fruit at breakfast, and drinking more juice. Participants reported that personal motivation, the one-on-one meetings with the study nutritionist, which provided personalized feedback, and the Daily V&F Record were the most helpful in increasing V&F consumption during the first half of the intervention. During the second half of the intervention, personal motivation and the Daily V&F Record continued to be reported as the most helpful strategies.

Major Contributors to V&F Intake. At baseline, five vegetables (potatoes, carrots, tomatoes, lettuce, broccoli), four fruits (apples, oranges, bananas, grapefruit), and orange juice accounted for ~60% of the V&F consumed by all participants. Of these, only tomato intake differed between the study groups (intervention: 2.4 servings/week; control: 1.4 servings/week; $P = 0.02$). During follow-up, these same foods continued to make up the majority of the V&F consumed in both the intervention and control groups. Intakes of these 10 V&Fs remained relatively unchanged in the control group over the follow-up period, but increased in the intervention group. Carrot consumption, which was highlighted as part of the intervention message, more than tripled to 5.4 servings/week. For broccoli, which was also emphasized in the intervention, intake increased by 50% to 1.6 servings/week. Lettuce intake increased by 50% to five servings per week. Intake doubled for apples, oranges,

Table 3 V&F intake by botanical and nutrient subgroups at baseline and average over follow-up for the intervention and control groups

Servings/day	Intervention		Control		P^c
	Baseline[a] mean (SD)	Average over follow-up[b] mean (SD)	Baseline[a] mean (SD)	Average over follow-up[b] mean (SD)	
Botanical subgroups (14)					
Compositae (*e.g.* lettuce)	0.47 (0.55)	0.71 (0.68)	0.60 (0.73)	0.43 (0.32)	<0.001
Cruciferae (*e.g.* broccoli)	0.38 (0.50)	0.53 (0.43)	0.33 (0.40)	0.32 (0.32)	<0.001
Ericaceae (*e.g.* blueberries)	0.11 (0.29)	0.14 (0.23)	0.15 (0.35)	0.12 (0.20)	0.27
Leguminosae (*e.g.* beans)	0.29 (0.43)	0.44 (0.37)	0.20 (0.30)	0.22 (0.19)	<0.001
Liliaceae (*e.g.* onions)	0.22 (0.26)	0.29 (0.30)	0.22 (0.29)	0.18 (0.13)	<0.001
Rosaceae (*e.g.* apples)	1.11 (1.46)	2.40 (1.97)	1.05 (1.24)	0.97 (0.78)	<0.001
Rutaceae (*e.g.* oranges)	0.66 (0.92)	1.61 (0.88)	0.74 (0.89)	0.86 (0.80)	<0.001
Solanaceae (*e.g.* potatoes)	1.69 (1.18)	1.83 (0.71)	1.50 (1.16)	1.36 (0.70)	<0.001
Umbelliferae (*e.g.* carrots)	0.36 (0.45)	0.97 (0.73)	0.32 (0.46)	0.34 (0.25)	<0.001
Nutrient subgroups					
High β-carotene	0.54 (0.66)	1.32 (0.81)	0.58 (0.71)	0.47 (0.36)	<0.001
High lutein	0.86 (0.84)	1.43 (0.81)	0.98 (0.90)	0.77 (0.43)	<0.001
High lycopene	0.60 (0.70)	0.92 (0.76)	0.43 (0.52)	0.39 (0.37)	<0.001
High vitamin C	0.38 (0.58)	0.90 (0.76)	0.47 (0.74)	0.56 (0.56)	<0.001
Green leafy vegetables	0.48 (0.56)	0.75 (0.68)	0.62 (0.74)	0.47 (0.33)	<0.001

[a] Mean of 3-day diet records.
[b] Mean of 12 days of diet records collected at 3-, 6-, 9-, and 12-month follow-up visits.
[c] P calculated for intervention *versus* control group for the change in servings per day (average over follow-up minus baseline) for each variable with sex and baseline levels of the variable in the model.

and bananas to 11.3, 8.7, and 5.7 servings/week, respectively. Grapefruit intake increased by 60% to 1.6 servings/week. Orange juice consumption more than doubled to 5.3 servings/week. The change in intake of these 10 foods accounted for two-thirds of the total V&F increase in the intervention group.

V&F Intake by Botanical Groups and Nutrient Content. Because of the interest in specific phytochemicals that may be related to cancer prevention, we also classified V&F by their botanical families and by selected antioxidant nutrients (Table 3). Intakes of these subgroups showed little or no change in the control group. Significant increases in consumption were seen in the intervention group for Umbelliferae (increased by 170% from baseline level), Rutaceae (144%), Rosaceae (116%), Leguminosae (52%), and Compositae (51%). Small increases were also observed for Cruciferae, Liliaceae, and Solanaceae. Green leafy vegetable consumption increased significantly by 56%. When V&Fs were classified by their nutrient content, intake in the intervention group increased 144% for the high β-carotene group and 137% for the high vitamin C group.

Nutrient Intake. During the trial, the intervention group demonstrated marked increases in intakes of nutrients present in V&F as well as changes in the macronutrient composition of the diet (Table 4). Vitamin C consumption increased by 37% above baseline intakes, folacin by 24%, and fiber by 27% (all $P \leq 0.001$). Total energy intake did not change in the intervention group, although the proportion of energy contributed by carbohydrates increased from 49% to 54%, and total fat decreased from 34% to 31%. Both saturated and monounsaturated fatty acid intakes showed statistically significant decreases, whereas polyunsaturated fatty acid consumption remained unchanged. The increased V&F diet did not result in lowered mineral intakes. Consistent with the increased V&F consumption, potassium intake increased 21% above baseline levels in the intervention group; sodium intake showed no change. For the control group, nutrient intakes changed little.

All dietary carotenoids increased significantly in the intervention group compared to the control group (Table 4). For the intervention group, increases in intake varied by specific carotenoid and ranged widely: α-carotene (185%), β-carotene (121%), β-cryptoxanthin (171%), lutein (67%), and lycopene (47%).

Biological Measures of Adherence and Change. Several biological measures were used to monitor compliance and measure physiological change. Plasma carotenoid levels increased in the intervention group; the changes were observed by 3 months and were maintained throughout the study (Fig. 3; Table 5). Total carotenoids (without lycopene) increased by 22% in the intervention group, but remained unchanged in the control group ($P < 0.001$). For the individual carotenoids, increases above baseline levels were 54% for α-carotene, 25% for β-carotene, 23% for β-cryptoxanthin, and 11% for lutein for the intervention group. Changes in these carotenoids over the trial were all statistically significantly different between the intervention and control groups ($P < 0.001$). Lycopene was unchanged in the intervention group but declined in the control group.

During the trial, the intervention group experienced modest changes in serum lipid components (Table 5). Total cholesterol decreased 3 mg/dl in the intervention group and increased 2 mg/dl in the control group ($P = 0.05$). Low-density lipoprotein cholesterol levels fell 2.5% in the intervention group from 150 mg/dl at baseline to 146 mg/dl over follow-up and increased by 3 mg/dl in the control group ($P = 0.02$). HDL cholesterol levels declined by <2 mg/dl in both groups ($P = 0.34$). In addition, triglycerides increased slightly in both groups ($P = 0.24$).

Body weight remained essentially constant throughout the study, and no differences were observed between the intervention and control groups. Urinary potassium levels increased by 14% in the intervention group only ($P < 0.001$); urinary sodium excretion did not differ between the groups. Plasma glucose levels remained unchanged.

With the increased V&F intake, the intervention group experienced a statistically significant increase in bowel-

Table 4 Mean daily nutrient intake at baseline and average over follow-up for the intervention and control groups

Nutrients/day[a]	Intervention		Control		P^d
	Baseline[b] mean (SD)	Average over follow-up[c] mean (SD)	Baseline[b] mean (SD)	Average over follow-up[c] mean (SD)	
Energy (kcals)	2222.3 (650.4)	2202.4 (461.2)	2302.7 (641.8)	2188.2 (585.4)	0.33
Protein (% kcals)	16.0 (3.5)	15.5 (2.6)	15.4 (3.0)	15.8 (2.4)	0.12
Carbohydrates (% kcals)	49.0 (8.3)	54.2 (6.7)	47.7 (9.2)	48.7 (7.1)	<0.001
Total fat (% kcals)	33.6 (6.7)	30.6 (5.7)	35.5 (7.5)	34.5 (5.5)	<0.001
Saturated fatty acids (% kcals)	11.3 (3.0)	10.1 (2.4)	12.0 (3.3)	11.8 (2.6)	<0.001
Monounsaturated fatty acids (% kcals)	12.6 (2.9)	11.3 (2.3)	13.4 (3.3)	13.0 (2.5)	<0.001
Polyunsaturated fatty acids (% kcals)	7.0 (2.2)	6.6 (1.6)	7.4 (2.5)	7.0 (1.4)	0.137
Alcohol (% kcals)	3.2 (5.0)	2.3 (3.6)	3.2 (5.5)	2.7 (4.7)	0.265
Cholesterol (mg)	305.8 (159.8)	264.0 (110.9)	308.0 (191.2)	286.3 (121.7)	0.09
Fiber (g)	20.1 (6.5)	25.5 (6.7)	19.2 (6.4)	19.1 (5.7)	<0.001
Vitamin A (μg retinol equivalents)	1754.0 (1661.2)	2645.7 (1485.2)	1612.1 (1411.2)	1811.6 (1176.4)	<0.001
α-carotene (μg)	670.1 (975.8)	1912.6 (1567.4)	632.7 (850.1)	707.8 (601.5)	<0.001
β-carotene (μg)	3446.0 (3093.0)	7618.0 (3872.5)	3207.6 (2804.9)	3143.0 (1846.8)	<0.001
β-cryptoxanthin (μg)	41.8 (64.9)	113.1 (88.9)	52.9 (92.0)	62.6 (72.2)	<0.001
Lycopene (μg)	3028.6 (3513.1)	4461.4 (4234.6)	2427.8 (2801.4)	2082.1 (1527.1)	<0.001
Lutein (μg)	1663.8 (1241.5)	2785.0 (1307.1)	1922.7 (2048.2)	1667.8 (1022.8)	<0.001
Vitamin D (mg)	8.1 (5.9)	6.6 (12.7)	7.9 (6.7)	11.6 (24.6)	0.038
Vitamin C (mg)	237.5 (293.6)	324.9 (230.3)	218.3 (252.6)	235.0 (279.9)	0.001
Folacin (μg)	403.8 (213.3)	501.8 (198.0)	383.0 (284.4)	399.3 (214.1)	<0.001
Calcium (mg)	903.7 (408.1)	918.6 (330.9)	961.7 (563.9)	916.4 (360.0)	0.455
Sodium (mg)	3729.1 (1243.0)	3647.5 (1057.7)	3767.0 (1338.7)	3589.4 (963.9)	0.504
Potassium (mg)	3379.3 (1005.9)	4097.9 (847.9)	3270.5 (963.8)	3089.5 (761.5)	<0.001
Iron (mg)	23.3 (33.1)	23.3 (15.0)	20.1 (11.9)	19.9 (9.2)	0.104

[a] From diet records with food and supplements, NDS-coded.
[b] Mean of 3-day diet records.
[c] Mean of 12 days of diet records collected at 3-, 6-, 9-, and 12-month follow-up visits.
[d] P calculated for intervention *versus* control group for the change (average over follow-up minus baseline) in each variable with sex and baseline levels of the variable in the model.

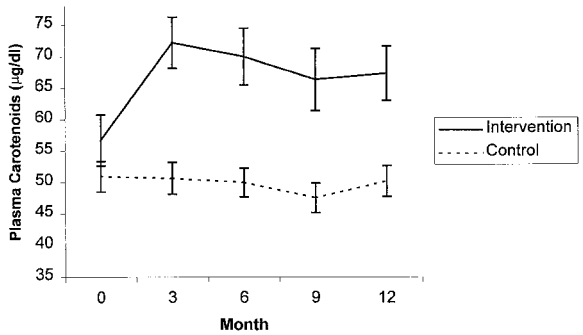

Fig. 3. Mean (± SE) total plasma carotenoids over 12 months in the intervention and control groups.

movement frequency (from 9.2 to 10.0/week) compared to a slight decline (9.0 to 8.6/week) among the control group (P = 0.003). After initiation of the increased V&F intake, more participants in the intervention group (n = 24) reported problems with flatulence compared to the control group (n = 11; P = 0.01); however, this difference did not persist beyond the 3-month visit. Further, none of the participants who reported this symptom discontinued the high V&F diet as a result. At the 6-month visit, the control group reported more indigestion (n = 17 *versus* 9 for control *versus* intervention; P = 0.001) and fatigue (n = 9 *versus* 2 for control *versus* intervention; P = 0.004) compared to the intervention group. No statistically significant differences in reported side effects, by treatment group, were found for the 9- or 12-month visits.

Discussion

V&F intake in the United States (23–25) is below the recommended minimum of five servings per day (15, 26). For example, the 1989–1991 Continuing Surveys of Food Intake by Individuals, a national population-based survey, found that average daily V&F consumption in the United States is 4.3 servings, and only one-third of the United States population consumes five or more servings of V&F per day (23). There is interest in the preventive potential of V&F (2–4) and the development of methods to increase V&F consumption, whether in the general population, clinical settings, or high-risk groups. Further, the capacity to monitor changes in intake is crucial in a dietary intervention where blinding is not possible and where the desire to please (in both the research and clinical settings) may result in overestimates of adherence.

In this diet-intervention study, we found that V&F intake almost doubled from 7 servings/day at baseline to an average of 12 servings/day in the intervention group over the 12-month follow-up period. Increases were observed for vegetable, fruit, and juice intakes, with the greatest change occurring in fruit consumption. Consumption of V&Fs high in β-carotene and vitamin C also increased substantially. The participants achieved these changes via increased serving sizes of foods already being consumed and increased frequency of consumption; generally, they did not increase the intake of V&Fs that were new to them. The increase in consumption was maintained over the follow-up period.

Several clinical trials have intervened specifically on V&F consumption (27–39). Like our study, five of these studies had intervention goals to increase V&F consumption to at least eight servings per day (27–29, 35, 39). Two of the studies were

Table 5 Biologic measures of adherence and of change between baseline and follow-up: intervention and control groups

Biologic measures	Intervention		Control		P^a
	Baseline mean (SD)	Average over follow-up mean (SD)	Baseline mean (SD)	Average over follow-up mean (SD)	
Plasma carotenoids (μg/dl)					
Total carotenoids[b]	56.7 (40.5)	69.2 (39.0)	50.9 (24.5)	49.3 (22.2)	<0.001
α-Carotene	6.9 (8.5)	10.6 (8.9)	5.8 (4.2)	5.8 (4.4)	<0.001
β-Carotene	22.0 (24.1)	27.5 (24.1)	19.0 (14.7)	17.4 (12.7)	<0.001
β-Cryptoxanthin	7.8 (4.9)	9.6 (5.0)	7.6 (5.1)	7.9 (4.1)	<0.001
Lutein	19.3 (7.6)	21.5 (8.1)	18.6 (6.6)	18.0 (6.3)	<0.001
Lycopene	40.8 (15.2)	41.0 (14.4)	39.4 (17.6)	36.7 (11.6)	0.014
Serum lipids (mg/dl)					
Total cholesterol	217.2 (39.8)	214.3 (36.0)	218.6 (35.1)	220.5 (31.3)	0.05
Low-density lipoprotein cholesterol	149.7 (35.4)	146.2 (33.1)	150.2 (32.0)	152.7 (29.1)	0.02
HDL cholesterol	42.4 (13.8)	40.6 (12.9)	43.2 (14.6)	41.7 (13.7)	0.34
Triglycerides	129.6 (68.0)	144.2 (99.7)	125.6 (64.1)	131.3 (63.9)	0.24
Blood pressure (mm Hg)					
Systolic	127.7 (17.0)	126.1 (15.7)	127.8 (17.2)	127.2 (17.9)	0.37
Diastolic	76.0 (8.3)	75.3 (7.1)	76.9 (9.3)	75.8 (8.6)	0.90
Other					
Body mass index (kg/m^2)	27.7 (3.8)	27.5 (3.7)	27.8 (3.8)	27.9 (3.9)	0.19
Body weight (pounds)	183.5 (33.9)	184.1 (33.2)	183.1 (32.3)	183.9 (32.6)	0.57
Plasma glucose (mg/dl)	99.0 (14.2)	100.9 (17.7)	101.1 (12.0)	101.9 (14.3)	0.55
Urinary potassium (meq/8 h)	16.6 (7.0)	18.9 (7.4)	16.1 (7.2)	16.1 (6.0)	<0.001
Urinary sodium (meq/8 h)	55.8 (22.1)	54.7 (18.1)	55.9 (24.3)	54.7 (18.4)	0.74
Bowel movements (No./wk)	9.2 (4.2)	10.0 (4.5)	9.0 (3.4)	8.6 (2.9)	0.003

[a] *P* calculated for intervention *versus* control group for the change (average over follow-up minus baseline) for each variable with sex and baseline levels of the variable in the model.
[b] Total carotenoids include the sum of α-carotene, β-carotene, β-cryptoxanthin, and lutein (see "Subjects and Methods").

conducted in high-risk populations (27, 29), as was our study; the remaining three studies were conducted in healthy volunteers (28, 35, 39).

Of these five studies, only the randomized, controlled intervention study of 93 women with early-stage breast cancer (27) enrolled participants for as long a period of time as our study (1 year). That study focused on a somewhat broader target of dietary change (V&F, fat, and fiber) than our study. The intervention goals were to consume five servings of vegetables, 16 ounces of fresh vegetable juice, three servings of fruit, 30 g of fiber, and 15% of energy from fat. Similar to our study, the increase in V&F consumption was achieved by 6 months and maintained over the follow-up period. Findings from their study showed that mean vegetable and mean fruit consumption at 12 months of follow-up in the intervention group increased to 6.7 and 4.0 servings/day, respectively, whereas consumption in the control group did not change. At 12 months, 23% of the intervention group and none of the control group consumed over eight servings of vegetables per day.

In a 3-month, uncontrolled study of 19 former cancer patients (29), the intervention was focused on increasing the intake of specific types of V&F (one serving each of dark green vegetables, yellow-orange vegetables, tomato products and other vegetables, three servings of vitamin C-rich fruits, and one serving of other fruits). Total V&F intake increased from 4.2 servings to 9.5 servings/day. Statistically significant increases in intake were noted for each of the targeted food groups, with the greatest change in the vitamin C-rich fruit and total fruit, a finding consistent with our study.

In two (28, 35) of the three studies conducted in healthy volunteers (28, 35, 39), the interventions were conducted for 6–8 weeks. Our previous experience in a randomized, controlled 6-week pilot study to increase V&F consumption showed an increase in daily V&F intake from 3.6 servings at baseline to 5.8 servings (35). Zino *et al.* (28) conducted an 8-week randomized controlled trial in 90 volunteers with no history of chronic disease who consumed no more than three V&F servings per day at baseline. That study used an intervention message similar to our study and emphasized increasing total V&F consumption; the specific V&Fs to be consumed were not emphasized. Mean V&F consumption at week 4 was 2.1 servings/day in the control group and 7.1 servings/day in the intervention group. Recently, Maskarinec *et al.* (39) reported on a 6-month trial in 29 healthy women, which had an intervention goal of consuming at least nine servings of V&F a day. Mean daily V&F consumption at 6 months increased by 4.1 servings to 7.4 servings in the intervention group compared to a 0.9 serving increase in the control group ($P = 0.0001$). Both fruits and vegetables increased by approximately two servings per day in the intervention group. Other V&F intervention trials, which have had more modest intervention goals, generally, but not always (36), have shown a <0.75 serving increase in daily V&F intake in high-risk populations (30), in callers to the Cancer Information Service (34), at work sites (31, 38), and among children (32, 33, 37).

Because dietary interventions cannot be blinded, the use of objective biological markers that are responsive to changes in the quantity and variety of foods consumed is necessary to establish adherence to the intervention. Feeding studies have demonstrated that useful biomarkers of V&F intake include plasma or serum carotenoids (40–46), plasma ascorbate (47), and urinary potassium (48). Serum carotenoids have been shown to be responsive to the feeding of carotenoid-rich foods within 1–3 days (49). We previously reported from the Minnesota CPRU feeding study that plasma carotenoids were responsive to the feeding of high-vegetable diets (40). In that study, changes in individual carotenoids varied depending on the vegetables fed. Plasma α-carotene, β-carotene, and lutein

were useful biomarkers of carrots and spinach, two carotenoid-rich vegetables; lutein was particularly increased in the diet where broccoli and cauliflower were fed (40). In addition to feeding studies, observational studies have shown positive correlations between V&F consumption and plasma or serum carotenoids (18, 50–55).

In agreement with previous V&F intervention trial findings (27–29, 39, 56), we observed significant increases in total and individual plasma carotenoids (except lycopene) ranging from 11% for lutein to 54% for α-carotene in the intervention group. Consistent with the self-reported dietary behaviors, the carotenoid levels increased by 3 months and were sustained over 12 months, indicating that major increases in V&F intake can be attained and that these dietary behaviors can be maintained over time at relatively stable levels. Additionally, the carotenoid levels achieved by the intervention group were similar to levels reported by Campbell *et al.* (18) in a free-living Minnesota population specifically selected because of their high V&F intakes.

As hypothesized, urinary potassium levels increased in the intervention group compared to the control group, confirming its utility as part of an ensemble of biomarkers of V&F intake. Urinary sodium levels did not change in either the intervention or control groups.

National surveys have suggested that individuals with high V&F intakes have lower fat intakes (6). This was seen in the present study. Average fat intake over the 12-month follow-up period was 30.6% in the intervention group compared to 34.5% in the control group. Similar results have been observed in other V&F intervention studies that did not specifically target fat consumption (28, 29, 36, 39).

In our study, the difference in serum total cholesterol over follow-up between the intervention and control groups was 5 mg/dl (a 2.3% difference). This change could be due to the decrease in dietary fat in the intervention group as well as the potential lipid-lowering properties of some kinds of dietary fiber (57). Although this reduction is small, the National Cholesterol Education Program has reported that, on average, every 1% reduction in serum cholesterol results in a 2% reduction in coronary heart disease rates (58). In contrast to our study, cholesterol levels were similar between the intervention and control groups in the intervention study by Zino *et al.* (28); however, follow-up was no more than 8 weeks in this study. Likewise, no difference in cholesterol levels between the intervention and control groups was observed in a 6-month V&F intervention study of 29 healthy women (39).

As observed in V&F intervention trials of shorter duration (35, 36, 39), we saw no change in weight over the 12-month intervention period.

The effects of a substantial increase in V&F consumption on gastrointestinal function have not been examined previously. Our study found a slight increase in reports of flatulence during the first 3 months of the study; however, these symptoms resolved and were not of sufficient magnitude to limit or discontinue dietary changes. In addition, intervention group participants, when compared with control participants, attributed beneficial effects to the dietary change, including improved bowel function and less fatigue.

In our diet-intervention study, baseline V&F intakes exceeded intakes observed in national surveys (23–25). The participants in our study may have been especially interested in their diets because they had been recently diagnosed with colorectal adenomatous polyps, providing motivation for making dietary changes. Other factors contributing to the high intake observed at baseline could be related to demographic characteristics of our population because V&F intakes have been shown to increase with age and education (24). In addition, the CPRU V&F classification scheme, our methodology for estimating V&F consumption from diet records, was designed to include V&F in mixed dishes in estimates of total V&F consumption, which can result in a substantial increase in intake estimates (23). Our V&F classification scheme also used a uniform criterion of one-half cup to define a serving of raw fruits rather than the combination of "one medium or one-half cup fruit," regardless of whether the fruit is generally consumed as a single piece (*i.e.*, one apple). Because many fruits yield more than one-half cup, intake estimates may appear higher when one-half cup, rather than one medium fruit, defines a serving. For example, in a study that compared V&F intakes estimated from 24-h recalls in fourth-grade students, fruit consumption was 0.7 servings higher when the CPRU V&F classification scheme was used to estimate intake compared to a scheme which defined a fruit serving based on the following options depending on the fruits consumed: one medium fruit, one-half medium fruit, a wedge, and one-half cup (59).

Our intervention was conducted in a select group of highly motivated individuals who considered participating in a study focused on cancer prevention a worthwhile experience. All participants had been diagnosed with colorectal adenomatous polyps within the last 5 years and may have been aware that they had a higher risk of developing colorectal cancer. Consequently, participants may have been particularly receptive to making dietary changes compared to the general population. However, the three randomized clinical trials conducted in healthy volunteers, which had intervention goals similar to our study and which used individualized approaches, also found an approximate doubling in V&F consumption (28, 35, 39). In addition, the five previously reported V&F intervention studies (27–29, 35, 39), which had goals of increasing V&F intake to at least eight servings a day, were conducted in populations with different age, gender, and geographic characteristics. These results suggest that intervention messages to increase V&F consumption can be successful in healthy adult volunteers, as well as in high-risk adult populations. Selection bias may still limit the generalizability of these intervention programs to the general population because a substantial proportion of eligible participants were not randomized into our study, as with other trials (27, 29, 39), or studied volunteers who responded to mass media advertisements (28).

Results of this study show that a group of individuals at high risk for the development of colon cancer can successfully increase V&F intake and maintain that increase over a 1-year period. Significant changes in biological variables that may mediate the preventive potential of V&F were observed. Some of these biological changes show strong utility for the monitoring of dietary change at individual or population level. The increase in V&F consumption was well accepted, participants were enthusiastic about the diet, and long-term negative effects were not reported or observed.

Acknowledgments

We thank Brian Laing for developing the intervention materials, Jeff Ambord and Kari Elfstrom for coding the dietary data, and the members of the Minnesota Cancer Prevention Research Unit Survey Core and Laboratory Core for assistance with data collection.

References

1. Steinmetz, K. A., and Potter, J. D. Vegetables, fruit, and cancer. I. Epidemiology. Cancer Causes Control, *2:* 325–357, 1991.

2. WCRF Panel (J. D. Potter Chair). Food, Nutrition, and the Prevention of Cancer. A Global Perspective. Washington: WCRF/AICR, 1997.

3. Ness, A. R., and Powles, J. W. Fruit and vegetables, and cardiovascular disease: a review. Int. J. Epidemiol., *26:* 1–13, 1997.

4. Law, M. R., and Morris, J. K. By how much does fruit and vegetable consumption reduce the risk of ischaemic heart disease? Eur. J. Clin. Nutr., *52:* 549–556, 1998.

5. Steinmetz, K. A., and Potter, J. D. Vegetables, fruit, and cancer II: Mechanisms. Cancer Causes Control, *2:* 427–442, 1991.

6. Subar, A. F., Ziegler, R. G., Patterson, B. H., Ursin, G., and Graubard, B. U. S. dietary patterns associated with fat intake: the 1987 National Health Interview Survey. Am. J. Public Health, *84:* 359–366, 1994.

7. Randall, D. E., Marshall, J. R., Brasure, J., and Graham, S. Patterns in food use and compliance with NCI dietary guidelines. Nutr. Cancer, *15:* 141–158, 1991.

8. Ursin, G., Ziegler, R. G., Subar, A. F., Graubard, B. I., Haile, R. W., and Hoover, R. Dietary patterns associated with a low-fat diet in the National Health Examination Follow-up Study: identification of potential confounders for epidemiologic analyses. Am. J. Epidemiol., *137:* 916–927, 1993.

9. Osler, M., and Heitman, N. B. L. Food patterns associated with intakes of fat, carbohydrate, and dietary fibre in a cohort of Danish adults followed for six years. Eur. J. Clin. Nutr., *51:* 354–361, 1997.

10. Elmståhl, S., Holmqvist, O., Gullberg, B., Johansson, U., and Berglund, G. Dietary patterns in high and low consumers of meat in a Swedish cohort study. Appetite, *32:* 191–206, 1999.

11. Potter, J. D. Colorectal cancer: molecules and populations. J. Natl. Cancer Inst., *91:* 916–932, 1999.

12. Bandura, A. Social Learning Theory. Englewood Cliffs, NJ: Prentice Hall, 1977.

13. Bandura, A. Social Foundations of Thought & Action. Englewood Cliffs, NJ: Prentice Hall, 1986.

14. Smith, S. A., Campbell, D. R., Elmer, P. J., Martini, M. C., Slavin, J. L., and Potter, J. D. The University of Minnesota Cancer Prevention Research Unit vegetable and fruit classification scheme (United States). Cancer Causes Control, *6:* 292–302, 1995.

15. United States Department of Agriculture, and United States Department of Health, and Human Services. Nutrition, and Your Health. Dietary Guidelines for Americans. Home and Garden Bulletin. Washington: United States Government Printing Office, 1990.

16. Bieri, J. G., Brown, E. D., and Smith, J. C. Determination of individual carotenoids in human plasma by high performance chromatography. J. Liq. Chromatogr., *8:* 473–484, 1985.

17. Craft, N. E., Brown, E. D., and Smith, J. C. Effects of storage and handling conditions on concentrations of individual carotenoids, retinol and tocopherol in plasma. Clin. Chem., *34:* 44–48, 1988.

18. Campbell, D. R., Gross, M. D., Martini, M. C., Grandits, G. A., Slavin, J. L., and Potter, J. D. Plasma carotenoids as biomarkers of vegetable and fruit intake. Cancer Epidemiol. Biomark. Prev., *3:* 493–500, 1994.

19. Trinder, P. Simple turbometric method for the determination of serum cholesterol. Ann. Clin. Biochem., *6:* 165–166, 1969.

20. Allain, C. C., Poon, L. S., Chan, C. S. G., Richmond, W., and Fu, P. C. Enzymatic determination of total serum cholesterol. Clin. Chem., *20:* 470–475, 1974.

21. Roeschlau, P., Bernt, E., and Gruber, W. Enzymatic determination of total cholesterol in serum. Z Klin. Chem. Klin. Biochem., *12:* 403–407, 1974.

22. Friedewald, W. T., Levy, R. I., and Frederickson, D. S. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without the use of the preparative centrifuge. Clin. Chem., *18:* 499–502, 1972.

23. Krebs-Smith, S. M., Cook, A., Subar, A. F., Cleveland, L., and Friday, J. US adults' fruit and vegetable intakes, 1989 to 1991: a revised baseline for the Healthy People 2000 objective. Am. J. Public Health, *85:* 1623–1629, 1995.

24. Subar, A. F., Heimendinger, J., Patterson, B. H., Krebs-Smith, S. M., Pivonka, E., and Kessler, R. Fruit and vegetable intake in the United States: the baseline survey of the Five A Day for Better Health Program. Am. J. Health Promot., *9:* 352–360, 1995.

25. Serdula, M. K., Coates, R. J., Byers, T., Simoes, E., Mokdad, A. H., and Subar, A. F. Fruit and vegetable intake among adults in 16 states: results of a brief telephone survey. Am. J. Public Health, *85:* 236–239, 1995.

26. United States Department of Agriculture, and United States Department of Health, and Human Services. Nutrition, and Your Health. Dietary Guidelines for Americans. Home and Garden Bulletin. Washington: United States Government Printing Office, 1995.

27. Pierce, J. P., Faerber, S., Wright, F. A., Newman, V., Flatt, S. W., Kealey, S., Rock, C. L., Hryniuk, W., and Greenberg, E. R. Feasibility of a randomized trial of a high-vegetable diet to prevent breast cancer recurrence. Nutr. Cancer, *28:* 282–288, 1997.

28. Zino, S., Skeaff, M., Williams, S., and Mann, J. Randomised controlled trial of effect of fruit and vegetable consumption on plasma concentrations of lipids and antioxidants. Brit. Med. J., *314:* 1787–1791, 1997.

29. Le Marchand, L., Hankin, J. H., Carter, F. S., Essling, C., Luffey, D., Franke, A. A., Wilkens, L. R., Cooney, R. V., and Kolonel, L. N. A pilot study on the use of plasma carotenoids and ascorbic acid as markers of compliance to a high fruit and vegetable dietary intervention. Cancer Epidemiol. Biomark. Prev., *3:* 245–51, 1994.

30. Havas, S., Anliker, J., Damron, D., Langenberg, P., Ballesteros, M., and Feldman, R. Final results of the Maryland WIC 5-A-Day promotion program. Am. J. Public Health, *88:* 1161–1167, 1998.

31. Sorensen, G., Stoddard, A., Hunt, M. K., Hebert, J. R., Ockene, J. K., Avrunin, J. S., Himmelstein, J., and Hammond, S. K. The effects of a health promotion-health protection intervention on behavior change: the Well Works Study. Am. J. Public Health, *88:* 1685–1690, 1998.

32. Foerster, S. B., Gregson, J., Beall, D. L., Hudes, M., Magnuson, H., Livingston, S., Davis, M. A., Joy, A. B., and Garbolino, T. The California Children's 5 a Day—Power Play! campaign: evaluation of a large scale social marketing initiative. Fam. Community Health, *21:* 46–64, 1998.

33. Perry, C. L., Bishop, D. B., Taylor, G., Murray, D. M., Mays, R. W., Dudovitz, B. S., Smyth, M., and M. S. Changing fruit and vegetable consumption among children: The 5-a-Day Power Plus Program in St. Paul, Minnesota. Am. J. Public Health, *88:* 603–609, 1998.

34. Marcus, A. C., Heimendinger, J., Wolfe, P., Rimer, B. K., Morra, M., Cox, D., Lang, P. J., Stengle, W., Van Herle, M. P., Wagner, D., Fairclough, D., and Hamilton, L. Increasing fruit and vegetable consumption among callers to the CIS: results from a randomized trial. Prev. Med., *27:* S18–S28, 1998.

35. Elmer, P. J., Slavin, J. L., Steinmetz, K., Malone, M., Mo, J. P., and Potter, J. D. Can fruit and vegetable intakes be increased for cardiovascular disease prevention? Circulation, *87:* 682, 1993.

36. Cox, D. N., Anderson, A. S., Reynolds, J., McKellar, S., Lean, M. E. J., and Mela, D. J. Take Five, a nutrition education intervention to increase fruit and vegetable intakes: impact on consumer choice and nutrient intakes. Br. J. Nutr., *80:* 123–131, 1998.

37. Nicklas, T. A., Johnson, C. C., Myers, L., Farris, R. P., and Cunningham, A. Outcomes of a high school program to increase fruit and vegetable consumption—Gimme 5—a fresh nutrition concept for students. J. Sch. Health, *68:* 248–253, 1998.

38. Sorensen, G., Stoddard, A., Peterson, K., N, C., Hunt, M. K., Stein, E., Palombo, R., and Lederman, R. Increasing fruit and vegetable consumption through worksites and families in the Treatwell 5-a-Day study. Am. J. Public Health, *89:* 54–60, 1999.

39. Maskarinec, G., Chan, C. L. Y., Meng, L., Franke, A. A., and Cooney, R. V. Exploring the feasibility and effects of a high-fruit and -vegetable diet in healthy women. Cancer Epidemiol. Biomark. Prev., *8:* 919–924, 1999.

40. Martini, M. C., Campbell, D. R., Gross, M. D., Grandits, G. A., Potter, J. D., and Slavin, J. L. Plasma carotenoids as biomarkers of vegetable intake: The University of Minnesota Cancer Prevention Research Unit feeding studies. Cancer Epidemiol. Biomark. Prev., *4:* 491–496, 1995.

41. Bowen, P. E., Garg, V., Stacewicz-Sapuntzakis, M., Yelton, L., and Schreiner, R. S. Variability of serum carotenoids in response to controlled diets containing six servings of fruits and vegetables per day. Ann. NY Acad. Sci., *691:* 241–243, 1993.

42. Kim, H., Simpson, K. L., and Gerber, L. E. Serum carotenoids and retinol of human subjects consuming carrot juice. Nutr. Res, *8:* 1119–1127, 1988.

43. Yeum, K-J., Booth, S. L., Sadowski, J. A., Liu, C., Tang, G., Krinsky, N. I., and Russell, R. M. Human plasma carotenoid response to the ingestion of controlled diets high in fruits and vegetables. Am. J. Clin. Nutr., *64:* 594–602, 1996.

44. Micozzi, M. S., Brown, E. D., Edwards, B. K., Bieri, J. G., Taylor, P. R., Khachik, F., Beecher, G. R., and Smith, J. C. Plasma carotenoid response to chronic intake of selected foods and β-carotene supplements in men. Am. J. Clin. Nutr., *55:* 1120–1125, 1992.

45. Rock, C. L., Lovalvo, J. L., Emenhiser, C., Ruffin, M. T., Flatt, S. W., and Schwartz, S. J. Bioavailability of β-carotene is lower in raw than in processed carrots and spinach in women. J. Nutr., *128:* 913–916, 1998.

46. Paiva, S. A. R., Yeum, K-J., Cao, G., Prior, R. L., and Russell, R. M. Postprandial plasma carotenoid responses following consumption of strawberries, red wine, Vitamin C or spinach by elderly women. J. Nutr., *128:* 2391–2394, 1998.

47. Tsugane, S., Fahey, M. T., Kobayashi, M., Sasaki, S., Tsubono, Y., Akabane, M., and Gey, F. Four food-frequency categories of fruit intake as a predictor of plasma ascorbic acid level in middle-aged Japanese men. Ann. Epidemiol., *8:* 378–383, 1998.

48. Appel, L. J., Moore, T. J., Obarzanek, E., Vollmer, W. M., Svetkey, L. P., Sacks, F. M., Bray, G. A., Vogt, T. M., Cutler, J. A., Windhauser, M. M., Lin, P-H., and Karanja, N. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N. Engl. J. Med., *336:* 1117–1124, 1997.

49. Brown, E. D., Micozzi, M. S., Craft, N. E., Bieri, J. G., Beecher, G., Edwards, B. K., Rose, A., Taylor, P. R., and Smith, J. C. Plasma carotenoids in normal men after a single ingestion of vegetables or purified β-carotene. Am. J. Clin. Nutr., *49:* 1258–1265, 1989.

50. Drewnowski, A., Rock, C. L., Henderson, S. A., Shore, A. B., Fischler, C., Galan, P., Preziosi, P., and Hercberg, S. Serum β-carotene and vitamin C as biomarkers of vegetable and fruit intakes in a community-based sample of French adults. Am. J. Clin. Nutr., *65:* 1796–1802, 1997.

51. Michaud, D. S., Giovannucci, E. L., Ascherio, A., Rimm, E. B., Forman, M. R., Sampson, L., and Willett, W. C. Associations of plasma carotenoid concentrations and dietary intake of specific carotenoids in samples of two prospective cohort studies using a new carotenoid database. Cancer Epidemiol. Biomark. Prev., *7:* 283–290, 1998.

52. Polsinelli, M. L., Rock, C. L., Henderson, S. A., and Drewnowski, A. Plasma carotenoids as biomarkers of fruit and vegetable servings in women. J. Am. Diet Assoc., *98:* 194–196, 1998.

53. Tucker, K. L., Chen, H., Vogel, S., Wilson, P. W. F., Schaefer, E. J., and Lammi-Keefe, C. J. Carotenoid intakes, assessed by dietary questionnaire, are associated with plasma carotenoid concentrations in an elderly population. J. Nutr., *129:* 438–445, 1999.

54. Wang, Y., Ichiba, M., Oishi, H., Iyadomi, M., Shono, N., and Tomokuni, K. Relationship between plasma concentrations of β-carotene and α-tocopherol and life-style factors and levels of DNA adducts in lymphocytes. Nutr. Cancer, *27:* 69–73, 1997.

55. Kitamura, Y., Tanaka, K., Kiyohara, C., Hirohata, T., Tomita, Y., Ishibashi, M., and Kido, K. Relationship of alcohol use, physical activity and dietary habits with serum carotenoids, retinol and alpha-tocopherol among male Japanese smokers. Int. J. Epidemiol., *26:* 307–314, 1997.

56. Hiniger, I., Chopra, M., Thurnham, D. I., Laporte, F., Richard, M.-J., Favier, A., and Roussel, A-M. Effect of increased fruit and vegetable intake on the susceptibility of lipoprotein to oxidation in smokers. Eur. J. Clin. Nutr., *51:* 601–606, 1997.

57. Brown, L., Rosner, B., Willett, W. W., and Sacks, F. M. Cholesterol-lowering effects of dietary fiber: a meta-analysis. Am. J. Clin. Nutr., *69:* 30–42, 1999.

58. National Cholesterol Education Program. Second Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II), NIH Publ. No. 93-3095: NIH/National Heart, Lung, and Blood Institute, 1993.

59. Eldridge, A. L., Smith-Warner, S. A., Lytle, L. A., and Murray, D. M. Comparison of three methods for counting fruits and vegetables for fourth-grade students in the Minnesota 5 A Day Power Plus Program. J. Am. Diet Assoc., *98:* 777–782, 1998.

Increasing Vegetable and Fruit Intake: Randomized Intervention and Monitoring in an At-Risk Population

Stephanie A. Smith-Warner, Patricia J. Elmer, Theresa M. Tharp, et al.

Cancer Epidemiol Biomarkers Prev 2000;9:307-317.