Supplement Users Differ from Nonusers in Demographic, Lifestyle, Dietary and Health Characteristics[1,2,3]

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ABSTRACT This study delineates demographic, lifestyle, dietary and health factors associated with the use of supplements at varying levels. Data are from a population-based cohort of 2,152 middle- to older-age adults living in Beaver Dam, Wisconsin. Information was collected by in-person interviews between 1988–1990. Associations were adjusted for gender and age. Use of supplements was more prevalent among women, persons with more than 12 years of education, those with relatively low body mass indices, persons with active lifestyles, and persons who never smoked as compared to current smokers ($P \leq 0.05$). Supplement users had higher intakes of most of the micronutrients from food that were examined in this study, including the antioxidant vitamins C and E and certain carotenoids ($P \leq 0.05$). Intakes of dairy products and also foods that are important sources of vitamin C and carotenoids were higher among users of supplements, but relationships differed by gender and by the type and level of supplement intake. These findings suggest that several factors need to be considered potential confounders in observational studies that examine the etiologic role of supplements in the occurrence of chronic disease. J. Nutr. 128: 2355–2362, 1998.

KEY WORDS: • *ascorbic acid* • *carotene* • *humans* • *supplements* • *vitamin E*

A crucial step in the design, analysis and interpretation of observational studies in humans is to understand and adjust for factors that influence apparent relationships between diet and disease. Studies investigating associations between the use of supplements and disease or death have the potential to be influenced by several demographic and lifestyle factors. Previous studies have shown that supplement users sometimes differ from nonusers in characteristics such as the following: gender, race, socioeconomic status, age, use of tobacco, consumption of alcohol and level of exercise (Bender et al. 1992, Block et al. 1988, Koplan et al. 1986, Kurinij et al. 1986, Levy and Schucker 1987, Looker et al. 1988, Steward et al. 1985, Subar and Block 1990). Supplement users have also been shown to have higher nutrient intakes from diet than nonusers (Garry et al. 1982, Koplan et al. 1986, Kurinij et al. 1986, Looker et al. 1988) , although these associations were examined for specific types of supplements in only one study (Slesinski et al. 1996).

There is also evidence that supplement use may be associated with health factors (Bender et al. 1992, Block et al. 1988, Read et al. 1989, Shapiro et al. 1983, Subar and Block 1990). For example, supplement users were shown to have lower adiposity (Block et al. 1988, Kurinij et al. 1986, Subar and Block 1990). Bender et al. (1992) showed that supplement use was highest among persons who considered their health excellent or very good and lowest among those who considered their health good. Nevertheless, persons reporting no specific adverse health conditions were less likely to use a supplement than those with one or more adverse conditions.

The purpose of this study was to examine demographic, lifestyle, dietary and health factors associated with the use of multinutrient supplements and supplemental [ascorbic acid (vitamin C) or α-tocopherol (vitamin E)] in the Beaver Dam Eye Study. We examined multinutrient supplements and vitamins C and E because they are among the most common supplements taken in the United States (Subar and Block 1990). Vitamins C and E are of particular interest due to their hypothesized role as antioxidants in helping to prevent chronic diseases. Data in this paper are from a cohort of middle- to older-age adults and as such are particularly relevant to studies that examine nutritional factors associated with chronic diseases of aging. Findings from community-based

[1] Presented in part at the Society for Epidemiologic Research, June 1996, [Lyle, B. J., Mares-Perlman, J.A., Klein, B.E.K., Klein, R. & Greger, J. L. (1996) Nutrient Supplements are Associated with Dietary Intakes of Antioxidants and Certain Antioxidant-Containing Foods. Am. J. Epidemiol. 143: S35 (abs.)] and at Experimental Biology, April 1996 [Lyle, B. J., Mares-Perlman, J.A., Klein, B.E.K., Klein, R. & Greger, J. L. (1996) Demographic, Behavioral, and Medical Correlates of Multinutrient Vitamin C and Vitamin E Supplements. FASEB J. 10: A485 (abs.)].

[2] This research is supported by National Institutes of Health grant EYO 8012 to J.A.P., EYO 6594 to R. K. and B.E.K., and in part by an unrestricted grant to the Department of Ophthalmology and Visual Sciences from Research to Prevent Blindness.

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Manuscript received 12 November 1997. Initial review completed 6 April 1998. Revision accepted 10 August 1998.

cohorts help validate results from national telephone surveys, which generally do not obtain the same level of detail about dietary and supplement use behaviors. This paper is unique in examining correlates for various levels of supplemental intake, taking into account both frequency of use and amounts of nutrients in supplements. For vitamins C and E, we tested the hypothesis that a greater proportion of persons taking high doses from supplements, as compared to low-to-moderate doses, exhibit certain demographic, lifestyle and health characteristics.

MATERIALS AND METHODS

Population

The Beaver Dam Eye Study is an on-going study of middle-and older-aged adults in a primarily Caucasian community in southcentral Wisconsin. The entire population of persons 43–86 y of age residing in Beaver Dam, Wisconsin, was identified by private census and recruited to participate in the study. Of the 5,925 persons eligible, 4,926 (83.1%) participated. A 50% random sample of the noninstitutionalized subjects ($n = 2{,}429$) was invited to participate in the nutrition portion of the study. Of these, 24 persons moved or died, 6 could not be located, and 23 were physically or mentally unable to respond. Ninety percent ($n = 2{,}152$) of the remaining subjects participated in the nutrition portion of this study. The study was approved by the University of Wisconsin Human Subjects Review Board and informed consent was obtained from each person.

Data collection

Medical histories and information about demographic and lifestyle characteristics were ascertained using a standardized interview, which was administered between 1988–1990 in conjunction with physical examinations. Physical activity was assessed by asking subjects how many times per week they exercised enough to work up a sweat. Information on the use of specific nutrient supplements and diet was collected as part of a second in-person interview approximately one month following their examination.

Diet was assessed using a 100-item modified form of the food frequency questionnaire developed by Block et al. (1986 and 1989) and version 2.1 of the nutrient database associated with this questionnaire. This questionnaire was shown to rank persons in the Beaver Dam population's recent diets similarly to ranks based on food records (Mares-Perlman et al. 1993). Food intakes were converted into servings that correspond with the USDA's Food Guide Pyramid (U.S.D.A. 1992). As part of the diet questionnaire, participants were asked whether they took any vitamin or mineral supplement. Persons who reported taking any type of supplement were asked to state the brand name, how many pills they took per day or week and the nutrient content of each pill, with the latter confirmed by inspecting labels on the containers. When nutrient content information was not available from the subject, the composition was determined directly from the manufacturer or from the Physicians Desk Reference (Medical Economics Company 1980–1990).

Analyses

Subjects were classified as users of multinutrient supplements if they took a broad-spectrum multivitamin product ($n = 618$). Three persons were taking a multinutrient supplement so infrequently that intakes were not likely to be biologically meaningful (0.13, 0.23 and 0.26 times per week). These persons were classified as nonusers. Because 77% of users reported taking one multinutrient pill per day, it was not feasible to categorize multinutrient users by level.

Sources of supplemental vitamins C and E from multinutrient and single supplements were combined because total intakes are most relevant in studies examining nutrient intakes and etiology of disease. Nine persons who reported taking supplemental vitamin C were classified as nonusers because their average intakes were less than 6 mg/d (which was 10% of the 60 mg/d Recommended Dietary Allowance [RDA]) (National Research Council 1989). Among users of supplements containing vitamin C, 356 ingested ≤60 mg/d (median 60 mg/d), 179 ingested >60–300 mg/d (median 120 mg/d)and 207 ingested >300 mg/d (median 560 mg/d). These cutpoints were somewhat arbitrary, but effectively distributed the subjects among groups that correspond to low, medium and high levels relative to the RDA.

Three persons were classified as nonusers of vitamin E because their intakes from supplements were less than 0.8 mg α-tocopherol equivalents (TE)/d (which was 10% of the 8 mg α-TE/d RDA for adult women). Users were divided into two levels of use with 508 persons classified as low-to-moderate users at ≤20 mg α-TE/d (median 20 mg α-TE/d) and 184 moderate-to-high level users at >20 mg α-TE/d (median 268 mg α-TE/d). The 20 mg α-TE/d cutpoint was chosen because it was the amount most commonly reported (52% of users reported ingesting 20 mg α-TE/d).

Statistical methods

SAS version 6.09 (SAS Institute Inc., Cary, NC) was used to conduct chi square tests and regressions. Chi-square tests were conducted to determine associations between supplement use and demographic, lifestyle and health characteristics. Age- and gender-stratified analyses were inspected to rule out effect modification prior to adjustments for gender and age. The Cochran-Mantel-Haenszel method was used to adjust for gender and age. Proportions presented in this paper were gender- and age-standardized to the nutrition study cohort using the direct method of standardization.

Dietary intakes of foods and nutrients (expressed per 4.18 MJ) were transformed using the natural log scale to normalize skewed distributions and then entered into linear regression models using PROC GLM LSMEANS in SAS to adjust for age, gender and total energy intake. Regression coefficients were used to calculate log-transformed average dietary intakes for each level of supplement use. Back-transformation of these intakes resulted in geometric means.

RESULTS

Demographic factors

Women were more likely than men to take multinutrient supplements and to ingest vitamins C and E from supplements **(Table 1)**. Results for gender were the same when adjusted for age. Older men were more likely than younger men to take supplements, but among women, use of these supplements was similar regardless of age. Education beyond high school was associated with greater use of multinutrient supplements and with vitamins C and E from supplements.

Lifestyle factors

Supplement use was more prevalent among physically active persons (Table 1). Persons who consumed approximately seven or more servings of alcoholic beverages per week (≥91 g ethanol) were less likely to take supplements than those who drank less. However, this association was statistically significant only for users of multinutrient supplements ($P = 0.03$). Among men, the association with wine differed from alcohol consumption overall. Men who drank wine were more likely to take a multinutrient supplement than those who did not (32% vs. 24%, respectively, $P = 0.05$). Use of supplements was significantly lower among persons who smoked at the time of the survey as compared to those who reported having never smoked.

Health factors

Persons with relatively lower body mass indices were more likely to use supplements **(Table 2)**. Self-reported perceived health was not associated with the use of supplements. The

TABLE 1

Percentage of persons in the Beaver Dam Eye Study (1988–90) with the indicated demographic and lifestyle characteristics who used multinutrient, vitamin C, or vitamin E supplements[1]

	Multinutrient Supplement	Vitamin C from Supplements				Vitamin E from Supplements		
	User	Nonuser	≤60 mg/d	>60–300 mg/d	>300 mg/d	Nonuser	≤20 mg α-TE/d[2]	>20 mg α-TE/d[2]
				%				
Gender								
Women (*n* = 1190)	32	61	19	10	10	64	26	10
Men (*n* = 962)	25	71	14	6	10	73	20	7
P-value[3]	<0.001				0.001			<0.001
Age/y								
Women								
43–54 (*n* = 366)	33	62	20	10	8	65	27	8
55–64 (*n* = 311)	32	63	19	9	9	62	26	12
65–74 (*n* = 316)	33	56	19	12	12	62	28	9
75+ (*n* = 197)	28	64	17	10	9	67	23	10
P-value	0.37				0.34			0.89
Men								
43–54 (*n* = 327)	22	75	12	7	6	76	18	6
55–64 (*n* = 269)	22	73	11	4	12	74	19	7
65–74 (*n* = 259)	27	67	17	5	11	70	21	8
75+ (*n* = 107)	31	63	18	7	12	65	27	7
P-value	0.03				0.01			0.02
Household Income								
<$10,000 (*n* = 303)	28	65	19	8	9	69	25	7
$10–< $20,000 (*n* = 570)	29	64	16	9	10	68	25	6
$20–< $30,000 (*n* = 456)	30	65	18	8	10	66	25	9
$30–< $45,000 (*n* = 429)	26	70	13	8	9	70	19	11
$45,000+ (*n* = 307)	31	64	24	7	5	68	27	5
P-value	0.51				0.10			0.91
Education								
< 12 y (*n* = 595)	25	68	14	9	9	71	19	9
12 y (*n* = 934)	27	68	15	7	9	69	23	8
> 12 y (*n* = 621)	35	59	21	10	10	63	28	9
P-value	<0.001				0.05			0.02
Married								
Ever (*n* = 2078)	28	66	16	8	9	68	23	9
Never (*n* = 74)	40	54	19	11	17	57	36	7
P-value	0.08				0.05			0.46
Physical Activity[4]								
Sedentary (*n* = 1629)	26	67	16	8	9	70	22	8
Active (*n* = 523)	36	60	18	10	12	60	27	12
P-value	<0.001				0.006			<0.001
Total Alcohol, g ethanol/wk								
< 91 g (*n* = 1747)	30	65	18	8	10	67	24	9
≥ 91 g (*n* = 395)	23	71	11	11	7	74	20	6
P-value	0.03				0.30			0.09
Smoking								
Never (*n* = 961)	31	63	18	8	11	66	25	9
Past (*n* = 758)	27	67	15	7	10	69	23	8
Current (*n* = 432)	25	69	15	9	7	72	22	6
P-value (never, past)	0.17				0.36			0.30
P-value (never, current)	0.01				0.02			0.02
Packyears, smokers only								
Tertile 1[5] (*n* = 411)	28	66	16	6	12	68	23	9
Tertile 2 (*n* = 384)	26	68	14	8	11	70	20	9
Tertile 3 (*n* = 387)	25	68	14	10	8	71	24	5
P-value	0.13				0.10			0.04

[1] Except for the data on age and gender, proportions were standardized to the age and gender distribution of the entire cohort.
[2] α-tocopherol equivalents.
[3] *P*-values for gender and age were from Mantel-Haenszel chi-square tests for trend. All other *P*-values, except smoking, were from Cochran-Mantel-Haenszel tests for linear trend, adjusted for gender and age. *P*-values for smoking were from gender– and age–adjusted Cochran-Mantel-Haenszel chi-square tests conducted separately for never versus past and for never versus current.
[4] Subjects were classified as active if they exercised to a sweat three or more times/week.
[5] Tertile medians were: T1 = 5, T2 = 25, T3 = 52 packyears.

TABLE 2

Percentage of persons in the Beaver Dam Eye Study (1988–90) with the indicated health characteristics who used multinutrient, vitamin C, or vitamin E supplements[1]

	Multinutrient Supplement	Vitamin C from Supplements				Vitamin E from Supplements		
	User	Nonuser	≤60 mg/d	>60–300 mg/d	> 300 mg/d	Nonuser	≤20 mg α-TE/d[2]	>20 mg α-TE/d[2]
				%				
Body Mass Index, kg/m[2]								
Quintile 1[3] (*n* = 428)	36	55	22	8	15	60	30	10
Quintile 2 (*n* = 430)	30	65	18	9	8	66	26	7
Quintile 3 (*n* = 428)	27	70	13	5	12	70	21	9
Quintile 4 (*n* = 426)	27	67	16	10	7	70	21	9
Quintile 5 (*n* = 428)	23	72	13	9	7	74	19	7
P-value[4]	<0.001				<0.001			<0.001
Hypertension								
No (*n* = 1376)	31	64	18	9	9	66	25	9
Yes (*n* = 776)	25	69	15	6	10	71	21	8
P-value	0.002				0.09			0.04
Heart disease, Men								
43–54 y								
No (*n* = 317)	21	76	11	6	6	78	17	6
Yes (*n* = 10)	70	30	30	40	0	30	70	0
P-value	<0.001				0.02			0.021
55–64 y								
No (*n* = 245)	23	72	11	4	12	75	19	7
Yes (*n* = 24)	17	79	8	4	8	71	17	12
P-value	0.49				0.51			0.45
65–74 y								
No (*n* = 222)	28	66	18	5	12	69	22	9
Yes (*n* = 37)	22	73	16	3	8	76	16	8
P-value	0.40				0.35			0.55
75+ y								
No (*n* = 84)	32	60	18	8	14	64	29	7
Yes (*n* = 23)	26	74	17	4	4	70	22	9
P-value	0.60				0.12			0.80
Cancer, Women								
43–54 y								
No (*n* = 337)	34	61	20	10	9	64	27	8
Yes (*n* = 29)	24	76	14	10	0	72	21	7
P-value	0.27				0.09			0.45
55–64 y								
No (*n* = 273)	66	63	18	9	10	62	25	14
Yes (*n* = 38)	34	61	24	13	3	63	34	3
P-value	0.74				0.67			0.32
65–74 y								
No (*n* = 258)	71	56	19	13	12	62	29	9
Yes (*n* = 58)	29	59	21	9	12	66	26	9
P-value	0.48				0.61			0.63
75+ y								
No (*n* = 163)	28	65	17	10	8	69	23	7
Yes (*n* = 34)	32	62	18	9	12	14	24	24
P-value	0.58				0.62			0.01

[1] Proportions were standardized to the age and gender distribution of the entire cohort for body mass index and hypertension.
[2] α-tocopherol equivalents.
[3] Quintiles medians were: Q1 = 22, Q2 = 25, Q3 = 27, Q4 = 30, and Q5 = 35 kg/m[2].
[4] *P*-values using the Cochran-Mantel-Haenszel test for linear trend. For body mass index and hypertension, tests for trend were adjusted for gender and age.

age- and gender-standardized percentage of people using multivitamin supplements was 27, 29 and 29% among people who reported excellent, good and fair, or poor health, respectively ($P = 0.66$). In examining associations between supplement use and 12 specific disease conditions, we found there were some conditions that were related to more likely use of supplements, but other conditions that were related to less likely use of supplements. After adjusting for gender and age, we found persons with hypertension were less likely to take supplements than those without hypertension (Table 2). The use of high levels of vitamin E in supplements was less common in persons with a history of gout than in persons without (9 vs. 4%, respectively; $P = 0.03$). On the other hand, persons were more likely to take supplemental vitamin E at any level if they had

TABLE 3

Geometric mean nutrient intakes from diet for users and nonusers of supplements in the Beaver Dam Eye Study ($n = 2{,}152$)[1]

	Multinutrient Supplements			Vitamin-C from Supplements					Vitamin-E from Supplements			
	Nonusers	Users	% Difference	A Nonusers	B ≤60 mg/d	C >60–300 mg/d	D >300 mg/d	% Difference (D-A)/A × 100	A Nonuser	B ≤20 mg α-TE/d[2]	C >20 mg α-TE/d[2]	% Difference (C-A)/A × 100
						unit/d						
Energy (MJ)	6.61	6.61	0	6.62	6.64	6.41	6.67	+0.8	6.61	6.71	6.29[4]	−4.9[4]
% Fat energy	38	37[3]	−3.3[3]	38	37[3]	37[3]	37[3]	−3.7[3]	38	37[3]	36[3]	−5.1[3]
						unit/4.18 MJ						
Fiber (g)	6.9	7.4[3]	−7.6[3]	6.9	7.3[4]	7.1	7.9[3]	+13.8[3]	6.9	7.3[3]	7.9[3]	+14.9[3]
α-Carotene (μg)	153	168[3]	+9.6[3]	153	161	157	177[4]	+15.1[4]	152	160	189[3]	+24.3[3]
β-Carotene (μg)	673	748[3]	+11.2[3]	669	722[4]	711	807[3]	+20.6[3]	667	717[4]	864[3]	+29.5[3]
Folate (μg)	141	152[3]	+7.8[3]	141	149[3]	146	160[3]	+13.8[3]	141	148[3]	162[3]	+14.9[3]
Niacin (mg)	10	10	0	10	10	10	10	−1.5	10	10	10	−1.7
Riboflavin (mg)	0.9	1.0[3]	+9.4[3]	0.9	1.0	1.0	1.0	+6.4	0.9	1.0[3]	1.0[3]	+11.8[3]
Thiamin (mg)	0.65	0.68[3]	+4.2[3]	0.65	0.68[3]	0.65	0.69[3]	+5.5[3]	0.65	0.67[3]	0.70[3]	+7.4[3]
Vitamin-C (mg)	65	72[3]	+10.2[3]	65	69	66	80[3]	+23.6[3]	65	69[4]	80[3]	+23.7[3]
Vitamin-E (mg α-TE[2])	5.4	5.7[3]	+4.8[3]	5.4	5.5	5.5	5.9[3]	+8.6[3]	5.4	5.6	5.9[3]	+9.4[3]
Calcium (mg)	411	461[3]	+12.3[3]	411	459[3]	438	450[3]	+9.3[3]	409	454[3]	473[3]	+15.4[3]
Iron (mg)	6.5	6.7[3]	+2.8[3]	6.5	6.6	6.5	6.7	+3.1	6.5	6.6	6.7	+3.2
Zinc (mg)	4.8	5.1[3]	+5.0[3]	4.8	5.0[3]	5.0	5.0[4]	+3.6[4]	4.8	5.0[3]	5.1[3]	+5.9[3]

[1] Intakes were based on nutrients contributed from foods and excludes contributions from supplements of all types. Variables were adjusted for gender, age and energy using linear regression. Variables were log-transformed prior to regression and back-transformed following regression. As such, the intakes shown are geometric means, which estimate median intakes.
[2] α-tocopherol equivalents.
[3] $P \leq 0.01$ for geometric mean nutrient intakes by supplement users compared to nonusers.
[4] $P \leq 0.05$ for geometric mean nutrient intakes by supplement users compared to nonusers.

a history of ulcers of the gastrointestinal tract (39% compared to 31%, respectively; $P = 0.02$).

We did not observe any associations, after age and gender standardization, between the use of supplements and self-reported histories for several other chronic diseases in the overall group. In the overall group, the percentage of multivitamin users was not significantly different in people with or without heart disease (35% vs. 29%), with or without cancer (27% vs. 29%), with or without diabetes (22% vs. 29%) and with or without cataract (27% vs. 29%). However, associations were markedly apparent in certain gender and age strata. Men 43–54 years of age with a history of heart disease were more likely than those without to use a multinutrient supplement (70% vs. 21%, $p < 0.001$). Women 75 plus years of age with a history of cancer were 3.2 times more likely than those without such a history to take high levels of supplemental vitamin E ($P = 0.006$ for nonusers compared to users of >20 mg α-TE/d). Men aged 55 to 64 y with a history of cataract were more likely than those without to use a supplement containing vitamin E (18% vs. 6%, $P = 0.02$).

Dietary factors

Multinutrient supplement users had more nutrient-dense diets than nonusers, as indicated by modest but consistently higher average intakes (per 4.18 MJ) from diet of all but one of the 11 vitamins and minerals examined in this study. As shown in **Table 3**, multinutrient supplement users had higher intakes of thiamin, riboflavin, folate, α- and β-carotene, vitamins C and E, calcium, iron and zinc ($P \leq 0.01$ for all nutrients). Users also had slightly lower average fat intakes (37% energy from fat as compared to 38% for nonusers). The difference in fat intake appeared to be due to users' lower average intakes of both unsaturated fats (24.0% compared to 24.7% for nonusers) and saturated fats (12.5% compared to 13.0%).

Higher consumption of fruit (especially citrus fruits) and dairy products were the most prominent individual dietary factors associated with the use of multinutrient supplements **(Table 4)**. The association between the use of multinutrient supplements and fruit was due to higher intakes by men, but not by women. For example, men who used multinutrient supplements ingested 63% more citrus fruit than nonusers ($P < 0.01$), whereas women users ingested only 8.5% ($P > 0.05$) more citrus fruit.

Compared to nonusers, the highest level users of supplemental vitamin C consumed diets that were lower in percentage of energy as fat; higher in 9 out of 12 micronutrients; lower in sweet baked goods; and higher in fruits, vegetables and dairy products (Tables 3 and 4). In addition to consuming more vegetables overall, users of supplemental vitamin C ingested significantly more cruciferous and red or orange vegetables. Differences between nonusers and the highest level users of supplemental vitamin C were similar to, but of greater magnitude, than differences between nonusers and users of multinutrient supplements.

Associations between vitamin E from supplements and dietary factors were similar to those described for vitamin C, but consistently of greater magnitude (Tables 3 and 4). In addition to the foods associated with the other supplements, average intakes of leafy green vegetables were significantly higher among the highest level users of supplemental vitamin E and sweets and white potatoes were significantly lower. For

TABLE 4

Geometric mean intakes of selected foods for users and nonusers of supplements in the Beaver Dam Eye Study (n = 2,152)[1]

	Multinutrient Supplements			Vitamin-C from Supplements					Vitamin-E from Supplements			
	Nonusers	Users	% Difference	A Nonusers	B ≤60 mg/d	C >60–300 mg/d	D >300 mg/d	% Difference (D-A)/Ax100	A Nonuser	B ≤20 mg α-TE/d[2]	C >20 mg α-TE/d[2]	% Difference (C-A)/Ax100
	Servings[3] *per 4.18 MJ*											
Fruit, All	0.83	0.97[4]	+17.1[4]	0.83	0.92[5]	0.89	1.08[4]	+31.5[4]	0.82	0.93[4]	1.11[4]	+35.4[4]
Citrus fruit	0.24	0.30[4]	+27.3[4]	0.24	0.27	0.28	0.37[4]	+54.3[4]	0.24	0.28[5]	0.40[4]	+69.4[4]
Other fruit	0.43	0.49[4]	+13.9[4]	0.43	0.46	0.46	0.52[4]	+22.0[4]	0.42	0.47[5]	0.56[4]	+32.2[4]
Vegetables, All	1.21	1.23	+1.5	1.21	1.21	1.14	1.31[5]	+7.7[5]	1.21	1.19	1.35[4]	+11.6[4]
Leafy green	0.16	0.18	+12.8	0.16	0.17	0.16	0.19	+22.6	0.16	0.16	0.21[5]	+31.9[5]
Cruciferous	0.11	0.11	+3.3	0.11	0.10	0.11	0.13[4]	+27.4[4]	0.11	0.10	0.14[4]	+28.4[4]
Red & orange vegetables[6]	0.12	0.13	+7.6	0.12	0.12	0.12	0.14[5]	+15.2[5]	0.12	0.12	0.16[4]	+34.7[4]
Legumes	0.09	0.09	+0.6	0.09	0.10	0.09	0.10	+5.4	0.09	0.09	0.09	+1.6
White potatoes	0.30	0.27	−8.4	0.30	0.28	0.24[4]	0.29	−4.3	0.30	0.28	0.24[4]	−19.5[4]
Other vegetables	0.14	0.14	−2.2	0.14	0.14	0.13	0.14	−0.4	0.14	0.13	0.16	+11.3
Fats and Oils of Plant Origin[7]	0.75	0.76	+0.8	0.76	0.75	0.75	0.74	−3.4	0.75	0.76	0.76	+0.4
Salty Snacks	0.05	0.06	+5.6	0.05	0.05	0.06	0.06	+8.0	0.05	0.06	0.06	+2.6
	Servings[3] *per 4.18 MJ*											
Nuts and Seeds	0.02	0.02	+9.9	0.02	0.02	0.02	0.03	+25.9	0.02	0.02	0.02	+19.5
Sweets[8]	0.49	0.48	−2.7	0.50	0.51	0.44	0.42	−15.3	0.50	0.50	0.37[4]	−26.9[4]
Sweet baked goods	0.10	0.09	−11.4	0.11	0.10	0.09	0.08[5]	−25.1[5]	0.11	0.10	0.07[4]	−37.7[4]
Dairy Products	0.39	0.49[4]	+26.0[4]	0.39	0.45	0.49[5]	0.47[5]	+20.8[5]	0.38	0.48[4]	0.52[4]	+35.3[4]

[1] Variables were adjusted for gender, age and energy using linear regression. Variables were log-transformed prior to regression and back-transformed following regression. As such, the intakes shown are geometric means, which estimate median intakes.
[2] α-tocopherol equivalents.
[3] Servings correspond to amounts considered to be a serving for each food group in the USDA's Food Guide Pyramid (USDA 1992).
[4] $P \leq 0.01$ for geometric mean food intakes by supplement users compared to nonusers.
[5] $P \leq 0.05$ for geometric mean food intakes by supplement users compared to nonusers.
[6] Red and orange vegetables included carrots, tomatoes and tomato juice, winter squash, sweet potatoes, sweet red peppers and beets.
[7] Fats and oils of plant origin included margarine on breads and vegetables, margarine used in cooking, vegetable shortening used in cooking, oils used in cooking and salad dressings.
[8] Sweets included doughnuts, cookies, cakes and pastry; pies; chocolate and other candy; sugar added to cereal or coffee; dairy desserts and other nondairy desserts. Sweet baked goods included only doughnuts, cookies, cakes, pastry and pies.

supplemental vitamin E, associations with intakes of all fruit and of vitamin C were of greater magnitude for men than women.

DISCUSSION

Demographic and lifestyle factors

Associations between supplements and demographic and lifestyle factors observed in this study were consistent with general trends reported in other populations, with the two exceptions of age and physical activity (Block et al. 1988, Koplan et al. 1986, Levy and Schucker 1987, Looker et al. 1988, Steward et al. 1985, Subar and Block 1990). First, age has been more strongly associated with supplement use in some other population groups, possibly because the other groups were comprised of a wider range of ages (Koplan et al. 1986, Looker et al. 1988, Subar and Block 1990). Second, physical activity was more strongly related to supplement use in the Beaver Dam cohort than in National Health and Nutrition Examination Survey (NHANES) I or the Nurses' Health Study (Block et al. 1988, Willett et al. 1981). This difference may be due to differing criteria for classifying persons as being physically active. In this study, both frequency (≥3 times per week) and intensity (exercise to a sweat) were accounted for in classifying persons as physically active. Thus, a higher level of intense physical activity was required to be classified as physically active in the present study.

In this cohort, associations with the demographic and lifestyle factors were in the same direction for multinutrient supplements and vitamins C and E from supplements. This is not unexpected because vitamins C and E are commonly found in multinutrient supplements. Our hypothesis that the magnitude of associations would be consistently greater for the higher levels of supplemental vitamins C and E, as compared to the low and moderate levels, was observed for dietary, but not demographic and lifestyle factors.

Diet

In the Beaver Dam nutrition cohort, supplement users had diets that overall were more nutrient dense. This is consistent with data for users of any type of supplement from NHANES II data, for a cohort of healthy elderly persons in New Mexico, for women of childbearing age in NHANES I, and in a nationallyrepresentative population in the U.S. (Koplan et al. 1986, Kurinij et al. 1986, Garry et al. 1982, Slesinski et al. 1996). Two other studies did not show this association, although neither study examined nutrient density directly (Bowerman and Harrill 1983, Sempos et al. 1984). Results from this study showing that dietary associations are not specific to one or two nutrients suggest that it may be difficult to adjust for confounding of supplement use by diet when evaluating diet and disease associations. When several dietary components have the potential to reduce disease risk, adjustments for diet that account for only one or two nutrients (or foods) may be insufficient. More comprehensive measures of diet could be used to identify groups of people with diets high in many versus low in many nutrients (e.g., indexes of diet quality or some type of marker of a nutrient-dense diet). Associations between supplements and disease could then be tested separately in subgroups with relatively homogeneous diets to minimize the confounding effect of diet. Alternatively, these associations can be tested in populations of people with relatively homogeneous diets.

A new finding in this study was that the nutrient density effect may not be uniform across supplement types or levels of use. This means that associations between nutrients from the diet and use of any type of supplement could underestimate relations with specific types or levels of supplements. Therefore, when investigators evaluate the possibility that better diets explain associations between supplement use and health outcomes, it may be important to evaluate diet characteristics among people with different types and levels of supplement use.

We found that supplement use was associated with the consumption of certain foods that are important sources of antioxidant nutrients. Supplement users, compared to nonusers, generally had higher average intakes of foods that are important sources of vitamin C and carotenoids (i.e., fruits and certain vegetables). Looker et al. (1988) also showed that adults who were regular users of any type of supplement consumed more vegetables and fruits, especially those high in vitamin C. Although generally true in the Beaver Dam cohort, there were important differences in these associations.

In the Beaver Dam cohort, citrus fruit intake was significantly higher among men, but not women who were users of multinutrient supplements. Also, total vegetable intake was associated with the use of high levels of supplemental vitamins C and E, but not multinutrient supplements. And finally, compared to multinutrient supplement users, associations with specific vegetables were of greater magnitude for the users of vitamin C and of greatest magnitude for vitamin E. The latter two observations suggest that potentiallyimportant associations between foods and specific supplements could be missed if associations are examined for supplement use of any type rather than by specific types.

Health factors

There is little information available on the health status of supplement users (Bender et al. 1992, Read et al. 1989, Shapiro et al. 1983). Data from the 1986 National Health Interview Survey indicated that individuals with one or more self-reported physical conditions were more likely to use supplements than those with none (Bender et al. 1992). Despite the fact that perceived health was not associated with supplement use in this study, associations were observed between supplements and a number of specific chronic diseases. Some of the associations with disease were specific to one supplement type, and others were evident only in specific gender and age strata. A potentially important observation was that supplement use was more common only among middle-aged men with a history of heart disease, as compared to those without this health condition. Such findings suggest that relationships between supplement use and disease may be specific to population subgroups. Hence, it is important to examine gender and age strata when postulating associations between supplement use and disease and to examine supplement users by type of nutrient supplement rather than combining them into one group of supplement users.

According to the 1992 National Health Interview Survey, 46% of adults in the U.S. reported using a vitamin or mineral supplement at least once in the previous year and ~24% reported their use on a daily basis (Slesinski et al. 1995). Clearly, nutrient supplements are potentially important sources of nutrients that may play an etiologic role in chronic diseases. Data presented in this paper suggested that the use of multinutrient supplements and supplemental vitamins C and E may be associated with certain chronic diseases of aging, either in the total population or in gender and age strata. In addition, this study and other studies have shown that supplement users differ from nonusers in demographic, lifestyle and dietary factors that may affect observed associations between supplemental nutrient intakes and disease. Our findings suggest that gender, age, education, weight for height, physical activity, smoking, alcohol consumption and diet should be considered as potential confounders in observational studies that examine the etiologic role of supplements in the occurrence of chronic disease. Our results also raise concern that adjusting for specific foods and nutrients from foods may not completely adjust for differences in the overall nutrient density of diets among supplement users as compared to nonusers.

ACKNOWLEDGMENTS

The authors thank William E. Brady and Polly Newcomb, for their guidance.

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