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Vitamin Supplement Use and Fatal Non-Hodgkin's Lymphoma among US Men and Women

Shumin M. Zhang,[1,2] Eugenia E. Calle,[3] Jennifer M. Petrelli,[3] Eric J. Jacobs,[3] and Michael J. Thun[3]

The authors evaluated the association between use of individual supplements of vitamins A, C, and E only and multivitamins and fatal non-Hodgkin's lymphoma in a large prospective mortality study of US men and women. During 14 years of follow-up (1982–1996), 1,571 non-Hodgkin's lymphoma deaths among 508,351 men and 1,398 non-Hodgkin's lymphoma deaths among 676,306 women were documented. Long-term regular use of individual supplements of vitamins A, C, and E only and multivitamins was unrelated to fatal non-Hodgkin's lymphoma among either men or women. The multivariate relative risks for men who used supplements for 10 or more years were 1.03 (95% confidence interval (CI): 0.54, 2.00) for vitamin A supplements, 1.04 (95% CI: 0.78, 1.39) for vitamin C supplements, 1.06 (95% CI: 0.74, 1.51) for vitamin E supplements, and 1.14 (95% CI: 0.92, 1.40) for multivitamins. The multivariate relative risks for women who used supplements for 10 or more years were 1.40 (95% CI: 0.77, 2.54) for vitamin A supplements, 1.19 (95% CI: 0.89, 1.60) for vitamin C supplements, 1.27 (95% CI: 0.87, 1.84) for vitamin E supplements, and 1.21 (95% CI: 0.98, 1.50) for multivitamins. All associations became weaker when vitamin supplements were mutually adjusted. These findings do not support an important relation between long-term regular use of individual supplements of vitamins A, C, and E only and multivitamins and fatal non-Hodgkin's lymphoma. *Am J Epidemiol* 2001;153:1064–70.

ascorbic acid; lymphoma, non-Hodgkin; vitamin A; vitamin E; vitamins

Vitamin A supplementation has been shown to increase immune status in undernourished populations (1). Supplementation with vitamins C and E in healthy populations has been shown to enhance some parameters of cell-mediated immunity (2, 3). Because the risk of non-Hodgkin's lymphoma has been consistently related to suppressed immune status (4–7), we hypothesized that supplementation with vitamins A, C, and E would decrease the risk of non-Hodgkin's lymphoma.

Epidemiologic data relating use of individual supplements of vitamins A, C, and E only and multivitamins to incidence of non-Hodgkin's lymphoma are sparse. Overall, a lack of association with use of individual supplements of vitamins A, C, and E only has been suggested, but the findings for multivitamins are inconsistent (8–10). A population-based case-control study in Nebraska (8) reported a lower risk of non-Hodgkin's lymphoma with use of multivitamins for 9 or more years among men but not among women. In the Nurses' Health Study, a large prospective cohort of US women, those who regularly took multivitamins for 10 or more years unexpectedly had a significant 60 percent increased risk of developing non-Hodgkin's lymphoma compared with never users (10). However, multivitamin use was unrelated to risk of non-Hodgkin's lymphoma in the Health Professionals Follow-up Study, a large prospective cohort of US men (10). No available data have related use of any vitamin supplements to mortality from non-Hodgkin's lymphoma. Because of the positive association with vitamin supplement use suggested in the Nurses' Health Study, we examined the association between the use of individual supplements of vitamins A, C, and E only and multivitamins and mortality from non-Hodgkin's lymphoma in the Cancer Prevention Study II, a large prospective mortality study among US men and women.

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Abbreviation: CI, confidence interval.

[1] Department of Nutrition, Harvard School of Public Health, Boston, MA.
[2] Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA.
[3] Department of Epidemiology and Surveillance Research, American Cancer Society, Atlanta, GA.
Reprint requests to Dr. Shumin M. Zhang, Department of Nutrition, Harvard School of Public Health, 665 Huntington Avenue, Boston, MA 02115 (e-mail: Shumin.Zhang@channing.harvard.edu).

MATERIALS AND METHODS

Study cohort

The Cancer Prevention Study II was established in 1982 when approximately 1.2 million US men and women aged 30–104 years (median, 57 years) were enrolled by more than 77,000 volunteers in all 50 states, the District of Columbia, and Puerto Rico. Families were enrolled if at least one household member was age 45 years or more and all enrolled members were age 30 years or more. The partici-

pants completed a confidential mailed questionnaire in 1982 about their demographic characteristics, lifestyle, and medical history. During the first 6 years of follow-up, in September 1984, 1986, and 1988, the volunteers made personal inquiries about their enrollees' vital status. For deceased persons, death certificates were subsequently obtained from the state health departments and coded by a nosologist according to a simplified system based on the *International Classification of Diseases*, Ninth Revision (11). Computerized linkage with the National Death Index was used to extend follow-up through December 31, 1996, and to identify deaths among 21,704 (1.8 percent) participants who were lost to follow-up between 1982 and 1988 (12). Through December 31, 1996, 20.0 percent of the participants had died, 79.7 percent were still living, and 0.2 percent had follow-up truncated on September 1, 1988, because of insufficient data for the National Death Index linkage. Death certificates or multiple cause-of-death codes were obtained for 98.6 percent of all known deaths. We defined a death as being caused by non-Hodgkin's lymphoma if the death certificate indicated that non-Hodgkin's lymphoma (*International Classification of Diseases*, Ninth Revision, codes 202.0–202.9) (11) was the underlying cause of death.

During 14 years of follow-up, a total of 1,571 non-Hodgkin's lymphoma deaths among 508,351 men and 1,398 non-Hodgkin's lymphoma deaths among 676,306 women were documented. For the analyses presented here, participants were excluded from the 1982 baseline population if they had a previous diagnosis of cancer (other than nonmelanoma of skin cancer). For the analyses of each specific vitamin supplement and multivitamins, we also excluded participants who were irregular users of these supplements (fewer than six times per week in the month preceding enrollment in 1982). These exclusions left a total of 454,116 men and 575,802 women for analysis of vitamin A supplements, 413,701 men and 512,868 women for analysis of vitamin C supplements, 433,654 men and 542,169 women for analysis of vitamin E supplements, and 406,511 men and 493,365 women for analysis of multivitamins.

Assessment of use of individual supplements of vitamins A, C, and E only and multivitamins

The 1982 questionnaire included a section on medications and vitamin supplements. Participants were asked how many times in the previous month they had used individual supplements of vitamins A, C, and E only and multivitamins and how long they had used them (in years). Specifically, they were instructed to fill in two boxes ("times" and "years") for each vitamin. No information was collected on past use or dosage of individual supplements of vitamins A, C, and E only; on the brand or type of multivitamins; or on the use of supplements other than vitamins A, C, and E and multivitamins.

Statistical analysis

Person-years of observation for each participant were calculated from the date of enrollment in 1982 to the date of death or December 31, 1996, whichever came first. We categorized participants as nonusers or regular users of individual supplements of vitamins A, C, and E only and multivitamins (those who used supplements at least six times per week in the month preceding enrollment in 1982). Participants who reported using vitamin supplements fewer than six times per week were excluded from the analyses. Regular users were further subdivided into 0–4, 5–9, or 10 or more years of use.

Relative risks were calculated by dividing the mortality rates in exposure categories by the corresponding morality rate in the reference category (nonusers). Using the Cox proportional hazard regression method (13), we calculated relative risks and controlled for other potential risk factors for non-Hodgkin's lymphoma. All models were stratified by single year of age at enrollment. In multivariate analysis, we also simultaneously adjusted for race (White, Black, or other), religion (Protestant, Catholic, Jewish, Latter Day Saints, or no religion), education (not high school graduate, high school graduate, some college, or college graduate), geographic region (Northeast, Midwest, Northwest, North Central, Southeast, Southwest/California, South Central, and Nonregional), family history of non-Hodgkin's lymphoma (yes, no), height (<66, ≥66 to <68, ≥68 to <70, ≥70 to <72, ≥72 to <74, ≥74 to <76, or ≥76 inches (1 inch = 2.54 cm) for men; <62, ≥62 to <64, ≥64 to <66, ≥66 to <68, or ≥68 inches for women), body mass index (<21, ≥21 to <23, ≥23 to <25, ≥25 to <30, ≥30 to <35, or ≥35 kg/m^2), and smoking (never smoker, former smoker, pipe and cigar smoker, current smoker of 1–14, 15–24, 25–34, or 35 or more cigarettes per day for men; never, former, current smoker of 1–14, 15–24, 25–34, or 35 or more cigarettes per day for women). All of this information was collected from the 1982 baseline questionnaire. We adjusted for these factors because they were associated with non-Hodgkin's lymphoma in this population or other populations (14–20). In addition to these models, we ran models that simultaneously adjusted for use of all supplements, which categorized participants as nonusers and regular current users of 0–4, 5–9, and 10 or more years. For all relative risks, we calculated 95 percent confidence intervals. Tests for trend were conducted by using the median values for each category as a continuous variable. All p values were two-tailed.

RESULTS

In the 1982 baseline population, 1.3 percent of the men and 3.1 percent of the women were regular users of vitamin A supplements (six or more times per week) in the month preceding enrollment (tables 1 and 2). The corresponding percentages for vitamin C supplements were 11.0 for men and 13.2 for women, those for vitamin E supplements were 8.0 percent for men and 10.1 percent for women, and those for multivitamins were 17.2 percent for men and 19.8 percent for women (tables 1 and 2). Participants who used any one type of specific vitamin supplement also tended to use other supplements. Supplement users were slightly older among men, but not among women. Compared with nonusers, supplement users were also more likely to be edu-

TABLE 1. Characteristics by vitamin supplement use by men in 1982 in the Cancer Prevention Study II, 1982–1996

Characteristics	Vitamin A		Vitamin C		Vitamin E		Multivitamins	
	None	Regular users	None	Regular users	None	Regular users	None	Regular users
Use of vitamin supplements (%)	98.7	1.3	88.9	11.0	91.9	8.0	82.8	17.2
Average age at enrollment (years)	57.2	58.5	57.2	58.0	57.2	59.0	57.2	57.6
Age-adjusted means*								
Height (inches)†	70.0	70.2	70.0	70.2	70.0	70.2	70.0	70.2
Body mass index (kg/m^2)	26.0	25.5	26.1	25.5	26.0	25.7	26.1	25.5
Age-adjusted percentages*								
White race	94.0	96.8	93.8	97.2	93.9	96.8	93.6	96.9
Family history of non-Hodgkin's lymphoma	0.8	1.1	0.8	1.1	0.8	1.1	0.8	1.0
Current smoker‡	41.4	39.1	41.5	40.0	41.4	39.8	41.3	41.5
Religion§								
Protestant	60.8	61.2	60.7	62.0	60.8	60.8	60.3	63.6
Catholic	24.0	21.6	24.3	21.0	24.0	22.5	24.3	21.9
Jewish	4.7	5.3	4.5	6.9	4.6	6.7	4.6	5.5
Other	5.4	7.4	5.3	6.2	5.4	5.9	5.5	5.5
Education§								
Less than grade 12	37.6	23.5	38.6	25.4	38.0	28.4	39.3	26.1
Grade 12 or more	60.8	75.7	59.8	74.0	60.4	71.0	59.0	73.1
Geographic region§								
Northeast	28.3	25.9	28.2	28.4	28.2	28.4	28.3	28.0
Northwest	3.2	5.0	3.1	5.0	3.2	4.3	3.2	3.9
North central	4.2	3.3	4.3	3.3	4.3	3.1	4.3	3.6
Midwest	26.7	22.6	27.1	22.6	26.9	23.6	26.9	24.8
Southeast	17.1	12.9	17.4	12.9	17.2	13.9	17.4	14.4
Southwest	10.8	20.6	10.2	17.9	10.5	17.3	10.2	14.9
South central	7.5	7.0	7.5	7.1	7.5	6.6	7.4	7.8
Nonregional¶	0.6	0.7	0.6	0.8	0.6	0.7	0.6	0.7
Regular users of								
Vitamin A supplements			0.2	15.5	0.3	20.2	1.0	4.7
Vitamin C supplements	8.0	90.3			5.0	72.0	5.0	34.0
Vitamin E supplements	5.3	80.3	2.0	49.4			3.5	23.4
Multivitamins	14.4	44.8	10.8	54.8	12.1	55.1		

* Percentages are directly standardized according to age distribution of the entire study population.
† 1 inch = 2.54 cm.
‡ Percentages include pipe and cigar smoking.
§ Percentages do not sum to 100 because of missing data.
¶ Including Alaska, Hawaii, and Puerto Rico.

cated and White and less likely to be Catholic. Additionally, supplement users were more likely to live in the Southwest/California and less likely to live in the Midwest and the Southeast. Moreover, use of supplements was slightly inversely associated with current smoking and body mass index. We did not observe any other important differences in other potential risk factors for non-Hodgkin's lymphoma at baseline across status of vitamin supplement use (tables 1 and 2).

Among men, after adjustments for age and other potential confounders, regular use of individual supplements of vitamins A, C, and E only and multivitamins was not significantly associated with fatal non-Hodgkin's lymphoma; the multivariate relative risks for men who used supplements for 10 or more years were 1.03 (95 percent confidence interval (CI): 0.54, 2.00) for vitamin A supplements, 1.04 (95 percent CI: 0.78, 1.39) for vitamin C supplements, 1.06 (95 percent CI: 0.74, 1.51) for vitamin E supplements, and 1.14 (95 percent CI: 0.92, 1.40) for multivitamins (table 3). Although we observed a significant positive association between short-term use of multivitamins (0–4 years) and fatal non-Hodgkin's lymphoma (multivariate relative risk = 1.32, 95 percent CI: 1.01, 1.71), the association was greatly attenuated after further adjustments for individual supplements of vitamins A, C, and E only (multivariate relative risk = 1.18, 95 percent CI: 0.87, 1.59). All associations became weaker when vitamin supplements were mutually adjusted (table 3).

Among women, regular use of individual supplements of vitamins A, C, and E only and multivitamins was also not significantly associated with fatal non-Hodgkin's lymphoma; the multivariate relative risks for women who used supplements for 10 or more years were 1.40 (95 percent CI: 0.77, 2.54) for vitamin A supplements, 1.19 (95 percent CI: 0.89, 1.60) for vitamin C supplements, 1.27 (95 percent CI: 0.87, 1.84) for vitamin E supplements, and 1.21 (95 percent CI: 0.98, 1.50) for multivitamins (table 4). Mutual adjust-

TABLE 2. Characteristics by vitamin supplement use by women in 1982 in the Cancer Prevention Study II, 1982–1996

Characteristics	Vitamin A		Vitamin C		Vitamin E		Multivitamins	
	None	Regular users	None	Regular users	None	Regular users	None	Regular users
Use of vitamin supplements (%)	96.9	3.1	86.8	13.2	89.9	10.1	80.2	19.8
Average age at enrollment (years)	56.5	56.5	56.5	56.4	56.5	56.5	56.7	55.8
Age-adjusted means*								
Height (inches)†	64.2	64.4	64.2	64.4	64.2	64.3	64.2	64.3
Body mass index (kg/m^2)	24.8	23.8	24.9	23.9	24.9	24.1	24.9	24.0
Age-adjusted percentages*								
White race	92.5	95.5	92.1	96.4	92.2	96.4	91.6	96.5
Family history of non-Hodgkin's lymphoma	0.9	1.1	0.9	1.1	0.9	1.1	0.9	1.1
Current smoker	20.5	16.9	20.7	18.8	20.7	18.0	20.7	19.3
Religion‡								
Protestant	61.0	62.8	60.8	62.8	60.9	62.1	60.2	64.3
Catholic	25.5	22.4	25.8	22.6	25.7	23.4	25.9	23.5
Jewish	4.3	4.3	4.1	6.2	4.1	6.2	4.2	4.9
Other	3.5	5.4	3.4	6.1	3.5	4.2	3.3	3.9
Education‡								
Less than grade 12	46.1	34.1	47.1	36.0	46.4	39.6	47.9	37.0
Grade 12 or more	52.2	65.0	51.0	63.3	51.8	59.6	50.0	62.2
Geographic region‡								
Northeast	28.9	24.9	28.8	28.3	28.8	28.4	28.9	28.1
Northwest	3.1	5.3	2.9	5.0	3.0	4.6	2.9	4.1
North central	3.9	3.4	3.9	3.5	3.9	3.1	3.9	3.7
Midwest	26.3	21.9	26.8	22.1	26.6	22.6	26.6	24.6
Southeast	17.9	13.6	18.4	12.9	18.1	14.7	18.5	14.6
Southwest	10.3	19.9	9.5	18.1	9.8	17.5	9.5	14.7
South central	7.4	7.5	7.4	7.1	7.5	6.3	7.3	7.6
Nonregional§	0.7	1.1	0.6	0.8	0.7	0.8	0.7	0.6
Regular users of								
Vitamin A supplements			0.3	16.7	0.5	20.4	1.3	5.6
Vitamin C supplements	9.8	88.8			6.0	69.4	5.9	34.2
Vitamin E supplements	7.0	80.2	3.0	51.7			4.6	25.2
Multivitamins	18.8	50.5	14.4	58.5	15.9	57.4		

* Percentages are directly standardized according to age distribution of the entire study population.
† 1 inch = 2.54 cm.
‡ Percentages do no sum to 100 because of missing data.
§ Including Alaska, Hawaii, and Puerto Rico.

ments of these supplements also weakened all associations. Although short-term use of vitamin A supplements was significantly associated with an elevated risk of fatal non-Hodgkin's lymphoma after adjustments for age and other potential confounders (multivariate relative risk = 1.88, 95 percent CI: 1.11, 3.19), the positive association was not significant after further adjustments for individual supplements of vitamins C and E only and multivitamins (multivariate relative risk = 1.68, 95 percent CI: 0.88, 3.22) (table 4).

To address the potential bias that subjects might have changed their supplement use due to clinical symptoms of non-Hodgkin's lymphoma before they were diagnosed or due to other sicknesses, we further examined the associations after excluding each of the following: 1) non-Hodgkin's lymphoma deaths that occurred during the first 4 years of follow-up (plus relevant person-years); 2) participants who lost 10 or more pounds (≥4.54 kg) in the year preceding study enrollment; and 3) participants who reported that they were sick at study enrollment. The relative risks did not change appreciably in most of these analyses (data not shown).

Because participants might have changed their supplement use during the follow-up period, misclassification of exposure might be greater during the later years of follow-up. We investigated this possibility among multivitamin users of 10 or more years duration by dividing the follow-up period into two segments, 1982–1989 and 1989–1996. The multivariate relative risks for men who took multivitamins for 10 or more years were 1.26 (95 percent CI: 0.84, 1.87) for the period of 1982–1989 and 1.10 (95 percent CI: 0.86, 1.41) for the period of 1989–1996. The comparable multivariate relative risks for women were 0.94 (95 percent CI: 0.58, 1.53) for the period of 1982–1989 and 1.29 (95 percent CI: 1.02, 1.64) for the period of 1989–1996.

DISCUSSION

In this large cohort of US men and women, use of individual supplements of vitamins A, C, and E only and multivitamins was not significantly related to fatal non-Hodgkin's lymphoma. These results are consistent with the

TABLE 3. Relative risks and 95% confidence intervals of fatal non-Hodgkin's lymphoma by duration of vitamin supplement use in the Cancer Prevention Study II among men, 1982–1996

	Nonusers	Duration of regular current users						*p* for trend
		0–4 years		5–9 years		≥10 years		
		RR*	95% CI*	RR	95% CI	RR	95% CI	
Vitamin A supplements								
No. of deaths	1,152		5		2		9	
Age-adjusted RR†	1.00	0.76	0.31, 1.82	0.48	0.12, 1.92	1.02	0.53, 1.97	0.82
Multivariate RR‡	1.00	0.76	0.32, 1.84	0.48	0.12, 1.92	1.03	0.54, 2.00	0.84
Multivariate RR§	1.00	0.55	0.20, 1.52	0.34	0.05, 2.53	0.83	0.37, 1.88	0.45
Vitamin C supplements								
No. of deaths	967		39		24		49	
Age-adjusted RR†	1.00	1.17	0.85, 1.61	0.89	0.59, 1.33	1.03	0.77, 1.37	0.92
Multivariate RR‡	1.00	1.17	0.85, 1.61	0.89	0.59, 1.33	1.04	0.78, 1.39	0.85
Multivariate RR§	1.00	1.16	0.79, 1.70	1.19	0.73, 1.93	1.03	0.69, 1.55	0.71
Vitamin E supplements								
No. of deaths	1,050		37		14		31	
Age-adjustedRR†	1.00	1.29	0.93, 1.79	0.66	0.39, 1.12	1.06	0.74, 1.51	0.95
Multivariate RR‡	1.00	1.29	0.93, 1.79	0.66	0.39, 1.12	1.06	0.74, 1.51	0.94
Multivariate RR§	1.00	1.29	0.87, 1.92	0.59	0.30, 1.15	1.18	0.73, 1.92	0.79
Multivitamins								
No. of deaths	852		60		33		102	
Age-adjusted RR†	1.00	1.30	1.00, 1.69	0.95	0.67, 1.35	1.13	0.92, 1.38	0.27
Multivariate RR‡	1.00	1.32	1.01, 1.71	0.95	0.67, 1.35	1.14	0.92, 1.40	0.25
Multivariate RR§	1.00	1.18	0.87, 1.59	1.10	0.74, 1.62	1.09	0.85, 1.40	0.45

* RR, relative risk; CI, confidence interval.
† Stratified according to single year of age at enrollment.
‡ Adjusted for age at enrollment, race, religion, education, geographic region, family history of non-Hodgkin's lymphoma, height, body mass index, and smoking.
§ Additionally adjusted for other vitamin supplements in the table.

findings of previous studies on incidence of non-Hodgkin's lymphoma and individual supplements of vitamins A, C, and E only (8–10). In a case-control study with 171 cases and 573 controls among men and 144 cases and 532 controls among women, no association was found with duration of vitamin C supplements (8). In a large cohort study among older women, with 104 incident non-Hodgkin's lymphoma cases, supplemental vitamins C and E did not differ among cases and noncases (9). In a large cohort study among women with 261 incident case of non-Hodgkin's lymphoma and another large cohort among men with 111 incident cases, use of individual supplements of vitamins A, C, and E only was unrelated to risk (10). Consistent with these findings, we did not find a significant association of use of individual supplements of vitamins A, C, and E only with fatal non-Hodgkin's lymphoma.

The results of two previous studies of multivitamin use in relation to non-Hodgkin's lymphoma risk are mixed. In a case-control study by Ward et al. (8), multivitamin use for 9 years or more was significantly associated with a 50 percent lower risk of non-Hodgkin's lymphoma among men, but duration of multivitamin use was not associated with risk among women. Long-term and regular uses of multivitamins were associated with an increased risk of non-Hodgkin's lymphoma among women in the Nurses' Health Study but not among men in the Health Professionals Follow-Up Study (10). In the current prospective mortality study, long-term use of multivitamins was not significantly associated with non-Hodgkin's lymphoma in either men or women.

The prospective design and high follow-up rates of this study reduce the possibility that the results were due to methodological biases. We were also able to control for many risk factors for non-Hodgkin's lymphoma, thus minimizing potential confounding effects of other factors. However, the relative risks for each specific vitamin supplement were confounded by the use of other vitamin supplements and were attenuated after mutual adjustments.

Because we asked for information on vitamin supplement use in only the month preceding study enrollment, our measurements are subject to misclassification if the preceding month did not represent typical or long-term supplement use. Additionally, there was no information on change in vitamin supplement use during the follow-up period, which might also introduce some misclassification. However, the relative risks were similar during early and later follow-up periods (1982–1989 and 1989–1996). Moreover, among a subgroup of the Cancer Prevention Study II participants from 21 selected states, 174,832 participants also answered the 1992–1993 follow-up ques-

TABLE 4. Relative risks and 95% confidence intervals of fatal non-Hodgkin's lymphoma by duration of vitamin supplement use in the Cancer Prevention Study II among women, 1982–1996

	Nonusers	Duration of regular current users						*p* for trend
		0–4 years		5–9 years		≥10 years		
		RR*	95% CI*	RR	95% CI	RR	95% CI	
Vitamin A supplements								
No. of deaths	957		14		3		11	
Age-adjusted RR†	1.00	1.83	1.08, 3.11	0.78	0.25, 2.44	1.37	0.76, 2.49	0.24
Multivariate RR‡	1.00	1.88	1.11, 3.19	0.81	0.26, 2.52	1.40	0.77, 2.54	0.21
Multivariate RR§	1.00	1.68	0.88, 3.22	0.99	0.30, 3.32	1.05	0.48, 2.29	0.81
Vitamin C supplements								
No. of deaths	760		39		23		48	
Age-adjusted RR†	1.00	1.13	0.82, 1.56	0.96	0.63, 1.45	1.15	0.86, 1.55	0.36
Multivariate RR‡	1.00	1.15	0.84, 1.60	0.98	0.65, 1.48	1.19	0.89, 1.60	0.26
Multivariate RR§	1.00	1.03	0.68, 1.54	1.00	0.59, 1.70	1.14	0.75, 1.74	0.56
Vitamin E supplements								
No. of deaths	840		38		20		29	
Age-adjusted RR†	1.00	1.14	0.82, 1.58	1.05	0.67, 1.64	1.26	0.87, 1.82	0.20
Multivariate RR‡	1.00	1.16	0.84, 1.61	1.07	0.69, 1.67	1.27	0.87, 1.84	0.17
Multivariate RR§	1.00	1.06	0.70, 1.60	1.01	0.56, 1.81	1.17	0.69, 1.99	0.59
Multivitamins								
No. of deaths	672		54		64		102	
Age-adjusted RR†	1.00	1.07	0.81, 1.41	1.05	0.75, 1.49	1.19	0.97, 1.47	0.10
Multivariate RR‡	1.00	1.08	0.81, 1.42	1.06	0.75, 1.50	1.21	0.98, 1.50	0.07
Multivariate RR§	1.00	1.03	0.75, 1.42	0.99	0.65, 1.51	1.04	0.80, 1.36	0.78

* RR, relative risk; CI, confidence interval.
† Stratified according to single year of age at enrollment.
‡ Adjusted for age at enrollment, race, religion, education, geographic region, family history of non-Hodgkin's lymphoma, height, body mass index, and smoking.
§ Additionally adjusted for other vitamin supplements in the table.

tionnaire. The proportions of regular users of vitamin supplements in 1982 who were also regular users in 1992–1993 were 24 percent for vitamin A supplements, 54 percent for vitamin C supplements, 50 percent for vitamin E supplements, and 57 percent for multivitamins. The proportions of nonusers of vitamin supplements in 1982 who became regular users in 1992–1993 were 2 percent for vitamin A supplements, 9 percent for vitamin C supplements, 8 percent for vitamin E supplements, and 16 percent for multivitamins. The proportions were similar among men and women. These suggested that most of the people in this cohort did not substantially change their use of vitamins C and E supplements and multivitamins. Misclassification would tend to weaken any true associations and would have obscured a weak association between the use of vitamin supplements and fatal non-Hodgkin's lymphoma in this population.

One other potential source of bias in this study is that participants might have changed their supplement use due to symptoms of non-Hodgkin's lymphoma. However, the fact that results did not appreciably change after we excluded non-Hodgkin's lymphoma deaths that occurred during the first 4 years of follow-up, those who reported sickness at study enrollment, or participants who lost 10 or more pounds (≥4.54 kg) during the year preceding study enrollment suggests that this is an unlikely source of bias.

One limitation of this study is that we examined mortality due to non-Hodgkin's lymphoma rather than incidence. Thus, the associations we observed could reflect the effects of vitamin supplement use on incidence, survival, or both. However, our results on use of individual supplements of vitamins A, C, and E only in relation to mortality from non-Hodgkin's lymphoma are consistent with those of previous studies relating to incidence, suggesting that our findings do not reflect survival only.

In summary, data from the Cancer Prevention Study II did not suggest that use of individual supplements of vitamins A, C, and E only and multivitamins was significantly related to either increased or decreased mortality rates from non-Hodgkin's lymphoma among either men or women. These findings are mostly consistent with those of several other studies relating to incidence of non-Hodgkin's lymphoma (8–10). Although data are still limited, they suggest that the use of individual supplements of vitamins A, C, and E only and multivitamins is neither protective nor detrimental with respect to mortality rates from non-Hodgkin's lymphoma. The initiation of studies designed to investigate the association between use of vitamin supplements and fatal non-Hodgkin's lymphoma is not warranted.

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