α-Linolenic acid intake is not beneficially associated with 10-y risk of coronary artery disease incidence: the Zutphen Elderly Study[1–3]

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ABSTRACT

Background: Data on the relation between α-linolenic acid intake and coronary artery disease (CAD) are limited. Other dietary components appear to modify the reported relation between α-linolenic acid intake and CAD.

Objective: We examined whether dietary α-linolenic acid intake was inversely associated with risk of CAD.

Design: We prospectively studied 667 men aged 64–84 y from the Zutphen Elderly Study who were free of CAD at baseline. Dietary intake was assessed by using a cross-check dietary history method.

Results: During the 10-y follow-up, we documented 98 cases of CAD. After adjustment for age, standard coronary risk factors, and intake of *trans* fatty acids and other nutrients, α-linolenic acid intake was not significantly associated with CAD risk. The relative risk of CAD for the highest compared with the lowest tertile of α-linolenic acid intake was 1.68 (95% CI: 0.86, 3.29). α-Linolenic acid intake from sources containing *trans* fatty acids was also nonsignificantly, yet positively, associated with CAD risk. α-Linolenic acid intake from foods that did not contain *trans* fatty acids was not associated with CAD risk, the relative risk of CAD for the highest compared with the lowest tertile was 1.15 (95% CI: 0.63, 2.11).

Conclusion: We did not observe a beneficial effect of dietary α-linolenic acid intake on the risk of 10-y CAD incidence. Investigating this hypothesis was complicated by the association between intakes of α-linolenic acid and *trans* fatty acids. Given the results of current prospective studies, a protective cardiac effect of α-linolenic acid is questionable. *Am J Clin Nutr* 2001;74:457–63.

KEY WORDS Coronary artery disease, diet, fatty acids, unsaturated fatty acids, cohort studies, α-linolenic acid, *trans* fatty acids, Zutphen Elderly Study, men

INTRODUCTION

Diets enriched with α-linolenic acid (18:3n−3) have been reported to increase the blood concentrations of α-linolenic acid and n−3 long-chain polyunsaturated fatty acids, especially eicosapentaenoic acid (EPA; 20:5n−3), in humans (1–8). n−3 Long-chain polyunsaturated fatty acids are considered to have a variety of favorable physiologic cardiac effects (9). Although the efficiency of the conversion of α-linolenic acid to EPA is relatively low (1, 2, 10, 11), dietary intervention trials reported that consuming α-linolenic acid beneficially affects eicosanoid metabolism, platelet aggregation (2–4, 12), and arterial compliance (7). In contrast, no consensus exists on the effect of α-linolenic acid on serum lipid concentrations (12–14) and blood pressure (3, 7, 8, 12, 13).

The results of case-control studies on the association of markers for α-linolenic acid intake and risk of myocardial infarction (15–17), angina pectoris (18), or sudden cardiac death (19) are conflicting. In addition, in nested case-control studies, platelet or plasma α-linolenic acid contents were inconsistently associated with the risk of coronary artery disease (CAD) (20–22).

Until now, only a few prospective studies have focused on the association between intake of α-linolenic acid and CAD incidence. In 2 dietary intervention trials, a remarkable reduction in the risk of cardiac events occurred in survivors of myocardial infarction who consumed an α-linolenic acid–enriched Mediterranean-type diet (23) or mustard oil (containing α-linolenic acid) (24). Previously reported cohort studies suggested that a higher intake of α-linolenic acid may reduce CAD risk (25–28). However, in most population-based studies, other dietary factors, such as intake of total or *trans* fatty acids, were potentially associated with α-linolenic acid and could have influenced the results of the study (17, 23, 25–28).

As a result, insight into the relation between α-linolenic acid intake and CAD risk in different populations who have characteristic dietary habits is needed. We previously reported the intake and sources of α-linolenic acid for men participating in the Zutphen Elderly Study (29). In the present study we examined the relation between α-linolenic acid intake and CAD incidence, carefully accounting for the intake of several other fatty acids.

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SUBJECTS AND METHODS

Study population

The study population consisted of men who had participated in the Zutphen Elderly Study, an extension of the Zutphen Study. In 1960 the Zutphen Study was initiated as the Dutch contribution to the Seven Countries Study (30) with a cohort of 878 men from Zutphen, Netherlands, who were born between 1900 and 1919. In 1985, 367 of the 555 participants who were still alive were re-examined. In addition, 711 other men from Zutphen in the same age category were asked to participate in the study. A total of 939 men (response rate of 74%) were examined in 1985 (31) and complete information on diet and CAD risk factors were available for 824 of these men. Men with previously diagnosed CAD were excluded from the present analyses (n = 157), which left 667 men for study at baseline in 1985.

Data collection

Dietary and medical examinations were completed between March and June 1985. Information about habitual food consumption was collected by using the cross-check, dietary history method, adapted to the Dutch habitual food consumption pattern (32). Each subject, and if possible, his wife, was interviewed about his average food consumption pattern of the previous month. A checklist of foods and food quantities bought per week was used to calculate and verify the subject's food consumption.

Nutrient intake data were calculated by using the corresponding Dutch food table (33), which was partly updated (34) and completed with data for α-linolenic acid (29), *trans* fatty acids (35), linoleic acid, EPA, docosahexaenoic acid (36), β-carotene, and vitamin E (37).

Venous blood samples were drawn from nonfasting subjects. Serum total and HDL-cholesterol concentrations were determined enzymatically (38, 39). Weight and height were measured while subjects wore light clothing without shoes, and body mass index (BMI) was calculated (weight/height^2). Information on cigarette smoking (eg, never smoked, former smoker, or current smoker) was obtained from subjects by use of a standardized questionnaire. The total minutes of physical activity per week was calculated by using information from a self-administered questionnaire designed for retired men (40).

Follow-up

Incident cases included fatal CAD plus nonfatal myocardial infarction (whichever occurred first) that occurred between the baseline assessment in 1985 and January 1995. Information on the vital status of the participants was obtained from municipal registries. Three participants were lost at follow-up. Information on the cause of death was obtained between 1985 and June 1990 from Statistics Netherlands. Information on deaths that occurred after June 1990 or that was not available from Statistics Netherlands was obtained from hospital discharge data or from general practitioners. Causes of death were coded according to the 9th revision of the *International Classification of Diseases* (41). CAD refers to codes 410–414. Because the underlying cause of death in elderly persons is often difficult to establish, CAD as both a primary (n = 46) and a secondary (n = 3) cause of death was considered in the analyses.

Data on the prevalence of CAD was obtained by both the Dutch translation of the Rose Questionnaire (42) and by a standardized medical questionnaire (after 1990). In cases of nonresponse, information on major chronic diseases was obtained from a short questionnaire that was completed either by subjects or their closest relative or caretaker. Diagnosis of each disease was confirmed with hospital discharge data. In addition, for subjects who had died, information on disease history was obtained from the general practitioner. Incidence of CAD at baseline was considered when either myocardial infarction or angina pectoris was diagnosed. For myocardial infarction (between baseline through January 1995), final diagnosis required ≥2 of the following criteria: *1*) a specific medical history, *2*) characteristic electrocardiographic changes, or *3*) specific enzyme elevations. During the 10 y of follow-up, we documented 98 CAD cases in subjects without previously diagnosed CAD (14.7% of the baseline population), 49 of which were fatal.

Statistical methods

Men were divided into tertiles based on the contribution of α-linolenic acid to energy intake at baseline. To test for differences in major risk and dietary factors across categories of α-linolenic acid intake at baseline, we used analysis of variance for normally distributed variables, the Kruskal-Wallis test for skewed distributed variables, and the chi-square test for categorical variables. Spearman's rank-order correlation coefficients (r_s) were calculated between α-linolenic acid and other dietary fatty acids. Cox proportional hazards regression analysis was performed to calculate relative risks (RRs) with the lowest α-linolenic acid tertile used as the reference group or by using α-linolenic acid intake as a continuous variable. Additional analyses were conducted to examine the associations between CAD incidence and intake of α-linolenic acid from sources with and without *trans* fatty acids, separately, in addition to the consumption of oil and salad dressing plus mayonnaise (foods rich in α-linolenic acid). Adjustments were made for age, energy intake, BMI, smoking, alcohol consumption, vitamin supplement use, and dietary factors (in the analyses of α-linolenic acid) or food groups (in the food analyses) potentially associated with CAD incidence. Other risk factors were not included in the model because they were viewed as an intermediate variable (eg, cholesterol or blood pressure) or were not associated with α-linolenic acid intake (ie, physical activity and history of diabetes mellitus or hypertension). All statistical analyses were conducted by using the SAS statistical analysis computer package (version 6.12; SAS Institute, Inc, Cary, NC).

RESULTS

The mean (±SD) daily intake of α-linolenic acid was 1.32 ± 0.47 g, which contributed 0.53 ± 0.15% to total energy intake. The main sources of α-linolenic acid in the diets of subjects were margarine, meat, bread, and vegetables, which contributed >50% of the total intake of α-linolenic acid.

The daily intake of α-linolenic acid at baseline, when expressed as a percentage of total energy, was positively associated with cigarette smoking and the daily intake of total, saturated, and unsaturated fat; cholesterol; fiber; vitamin E; and β-carotene, and inversely associated with systolic blood pressure, use of vitamin supplements, and daily intake of carbohydrates and alcohol (**Table 1**). α-Linolenic acid intake correlated strongly with intakes of total fat (r_s = 0.40), *trans* fatty acids (r_s = 0.61), and *cis* monounsaturated fatty acids (r_s = 0.44), and correlated weakly with linoleic acid (r_s = 0.19) and saturated fat (r_s = 0.08). The correlation coefficient between the intake of

TABLE 1
Characteristics at baseline by tertiles of α-linolenic acid intake[1]

	Total group (n = 667)	α-Linolenic acid tertile (% of energy) <0.45% (n = 222)	0.45–0.58% (n = 223)	≥0.58% (n = 222)	P^2
Age (y)	71.1 ± 5.2[3]	71.3	71.4	70.8	0.48
BMI (kg/m^2)	25.5 ± 3.2	25.3	25.3	25.8	0.13
Physical activity (min/wk)	611 ± 533	581	633	620	0.85
Systolic blood pressure (mm Hg)	151 ± 21	154	149	150	0.02
Serum total cholesterol (mmol/L)	6.08 ± 1.11	6.05	6.00	6.19	0.18
Serum HDL cholesterol (mmol/L)	1.14 ± 0.30	1.15	1.12	1.14	0.58
Smoking (%)					
Current	32.4	26.6	34.1	36.5	0.07
Past	48.7	55.4	42.6	48.2	0.03
Use of vitamin supplements (%)	15.9	22.3	12.6	13.1	0.007
Daily intake					
Energy (MJ)	9.2 ± 2.0	9.1	9.4	9.1	0.24
Total fat (% of energy)	40.3 ± 6.4	37.2	40.9	42.9	0.0001
Saturated fat (% of energy)	18.0 ± 3.6	17.3	18.8	17.9	0.0001
trans Fatty acids (% of energy)	4.3 ± 2.2	2.8	4.4	5.8	0.0001
cis Unsaturated fat (% of energy)	18.0 ± 3.9	17.1	17.7	19.2	0.0001
Linoleic acid (% of energy)	5.0 ± 2.4	5.1	4.6	5.4	0.0001
EPA and DHA (% of energy)	0.08 ± 0.14	0.05	0.09	0.09	0.22
Cholesterol (mg)	273 ± 97.0	253	289	274	0.0004
Carbohydrate (% of energy)	41.0 ± 7.3	42.5	41.0	39.4	0.0001
Protein (% of energy)	14.3 ± 2.6	14.3	14.2	14.3	0.92
Alcohol (g)	13.8 ± 17.3	18.3	12.5	10.7	0.001
Nondrinkers (%)	23.5	20.3	23.8	26.6	0.29
≥20 g (%)	26.7	34.7	24.2	21.2	0.003
Fiber (g)	24.9 ± 7.1	23.8	25.7	25.1	0.01
Vitamin E (mg)	8.5 ± 2.6	8.0	8.7	8.9	0.0001
Vitamin C (mg)	90.3 ± 39.5	92.9	89.7	88.2	0.54
β-Carotene (mg)	1.4 ± 0.6	1.3	1.4	1.4	0.02

[1] EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.
[2] Significance between α-linolenic acid categories (ANOVA for normally distributed variables, Kruskal-Wallis test for skewed variables, chi-square test for dichotomous variables).
[3] $\bar{x}$ ± SD.

α-linolenic acid and that of n−3 fatty acids from fish was not significant (r_s = 0.03).

The crude relative risk of 10-y fatal plus nonfatal CAD was 2.24 (95% CI: 1.33, 3.77) for the highest compared with the lowest tertile of α-linolenic acid intake (**Table 2**). After adjustment for age, BMI, smoking, use of vitamin supplements and dietary vitamin intake, and intakes of energy, alcohol, dietary cholesterol, fiber, and specific fatty acids (including *trans* fatty acids), the association between α-linolenic acid intake and CAD was minimized and no longer significant. The adjusted relative risk of CAD incidence for the highest compared with the lowest tertile of α-linolenic acid intake was 1.68 (95% CI: 0.86, 3.29). In addition, the adjusted relative risk of CAD incidence with an increase in α-linolenic acid intake of 0.5% of energy was 1.58 (95% CI: 0.67, 3.74). The association was similar for fatal CAD. The adjusted relative risk of fatal CAD for the highest compared with the lowest tertile of α-linolenic acid intake was 1.59 (95% CI: 0.62, 4.08). In addition, for an increase in α-linolenic acid intake of 0.5% of energy, the adjusted relative risk of fatal CAD was 1.40 (95% CI: 0.36, 5.41).

In the present study, consumption of foods that contained *trans* fatty acids, eg, margarines and meat, contributed most to α-linolenic acid intake and thus may have been associated with the possible increased risk of CAD. We therefore examined α-linolenic acid sources with *trans* fatty acids (eg, margarine, cooking fat, butter, cookies, pastries, meat, dairy products, and bread) and without *trans* fatty acids (eg, cereals, legumes, vegetables, and fruit) separately in their relation to CAD risk. There was a significant, positive association between CAD risk and α-linolenic acid intake from sources containing *trans* fatty acids, which became nonsignificant after additional adjustment for *trans* fatty acid intake (**Table 3**). In contrast, the intake of α-linolenic acid from foods without *trans* fatty acids was not associated with CAD risk.

The main sources of α-linolenic acid in the present study differed from those in other studies, ie, vegetable oils (43, 44) or salad dressings and mayonnaise (28). We also examined the relations of the consumption of oil, creamy salad dressings, and mayonnaise with CAD risk. The most significant oils consumed by the elderly population in the present study were sunflower oil (n = 50; 41% of the total oil consumption), soybean oil (n = 46; 33% of the total oil consumption), olive oil (8%), and safflower oil (8%). Subjects who consumed these oils were younger, consumed more alcohol and vegetables, and had a lower *trans* fatty acids intake than did nonconsumers.

A crude, significant, inverse association was observed between oil consumption and CAD incidence (**Table 4**). After adjustment for potential confounders, the relative risk for those who consumed oil compared with those who did not was 0.53 (95% CI: 0.26, 1.06).

TABLE 2
Relative risks (RR) and 95% CIs of fatal plus nonfatal coronary artery disease and fatal coronary artery disease according to tertiles of α-linolenic acid intake[1]

	α-Linolenic acid tertile (% of energy)[2]			
	<0.45%	0.45–0.58%	≥0.58%	*P* for trend
Fatal plus nonfatal coronary artery disease				
Percentage of cases (%)	9.5 [21]	15.3 [34]	19.4 [43]	
Crude RR	1	1.68 (0.97, 2.89)	2.24 (1.33, 3.77)	0.003
Age- and energy-adjusted RR	1	1.69 (0.98, 2.92)	2.23 (1.32, 3.76)	0.003
Fully adjusted RR	1	1.49 (0.82, 2.70)	1.68 (0.86, 3.29)	0.17
Fatal coronary artery disease				
Percentage of cases (%)	5.4 [12]	6.7 [15]	9.9 [22]	
Crude RR	1	1.27 (0.59, 2.71)	1.97 (0.97, 3.98)	0.05
Age- and energy-adjusted RR	1	1.26 (0.59, 2.69)	1.95 (0.96, 3.94)	0.05
Fully adjusted RR	1	0.99 (0.43, 2.28)	1.59 (0.62, 4.08)	0.26

[1] 95% CI in parentheses. *n* in brackets. Models included the following variables: age; BMI; ex-smoking (yes or no); current smoking (yes or no); alcohol intake; use of vitamin supplements (yes or no); intake of saturated fatty acids, *trans* fatty acids, linoleic acid, eicosapentaenoic and docosahexaenoic acids, other *cis* unsaturated fatty acids, and protein (as a percentage of energy); and intake of energy, dietary cholesterol, fiber, vitamin E, vitamin C, and β-carotene. Alcohol intake (0, 1–19, ≥20 g/d) was used as a categorical variable (included as 2 dummies in the model, with the nondrinkers as a reference).
[2] Median intakes for the tertiles were 0.40%, 0.51%, and 0.67% of energy, respectively.

Additional adjustment for intakes of α-linolenic acid, linoleic acid, *trans* fatty acids, or vitamin E did not appreciably change the results (data not shown). Furthermore, no association was observed between the intake of creamy salad dressings and mayonnaise and CAD.

DISCUSSION

In the present study, we observed a nonsignificant, positive association between α-linolenic acid intake and CAD risk that seems to be the result of the strong association between intakes of α-linolenic acid and *trans* fatty acids. It is likely that in other populations with dietary sources of α-linolenic acid, comparable to those of the present study population, intake of α-linolenic acid is also strongly associated with intake of *trans* fatty acids. In a Norwegian case-control study, contents of *trans* fatty and α-linolenic acids in adipose tissue were also intercorrelated and associated with increased CAD risk (17). This emphasizes the importance of adjusting for other dietary factors and the difficulty in pursuing this hypothesis (of whether α-linolenic acid intake is beneficially associated with CAD incidence) epidemiologically or to generalize the epidemiologic findings to other populations.

TABLE 3
Relative risks (RR) and 95% CIs of fatal plus nonfatal coronary artery disease according to tertiles of α-linolenic acid intake from food sources with and without *trans* fatty acids[1]

	Tertile			
	1	2	3	*P* for trend
α-Linolenic acid from sources with *trans* fatty acids				
Range (% of energy)	<0.40	0.40–0.52	>0.52	
Median intake (% of energy)	0.35	0.46	0.61	
Percentage of cases (%)	9.5 [21]	15.7 [35]	18.9 [42]	
Crude RR	1	1.71 (0.99, 2.94)	2.18 (1.29, 3.68)	0.004
Age- and energy-adjusted RR	1	1.71 (1.00, 2.95)	2.20 (1.30, 3.71)	0.004
Adjusted RR[2]	1	1.56 (0.88, 2.77)	1.90 (1.06, 3.40)	0.04
Fully adjusted RR[3]	1	1.42 (0.78, 2.57)	1.51 (0.75, 3.04)	0.31
α-Linolenic acid from souces without *trans* fatty acids				
Range (% of energy)	<0.04	0.04–0.06	>0.06	
Median intake (% of energy)	0.03	0.05	0.07	
Percentage of cases (%)	14.4 [32]	13.9 [31]	15.8 [35]	
Crude RR	1	0.93 (0.57, 1.52)	1.08 (0.67, 1.75)	0.77
Age- and energy-adjusted RR	1	0.90 (0.55, 1.48)	0.97 (0.58, 1.63)	0.90
Adjusted RR[2]	1	1.06 (0.62, 1.81)	1.17 (0.63, 2.15)	0.63
Fully adjusted RR[3]	1	1.06 (0.62, 1.81)	1.15 (0.63, 2.11)	0.67

[1] 95% CI in parentheses. *n* in brackets.
[2] Models included the following variables: age; BMI; ex-smoking (yes or no); current smoking (yes or no); alcohol intake; use of vitamin supplements (yes or no); intakes of saturated fatty acids, linoleic acid, eicosapentaenoic and docosahexaenoic acids, other *cis* unsaturated fatty acids; and protein (as a percentage of energy); intakes of energy, dietary cholesterol, fiber, vitamin E, vitamin C, and β-carotene; and intakes of α-linolenic acid from sources with (in model with α-linolenic acid from food sources without *trans* fatty acids) or without (in model with α-linolenic acid from food sources with *trans* fatty acids) *trans* fatty acids. Alcohol intake (0, 1–19, ≥20 g/d) was used as a categorical variable (included as 2 dummies in the model, with the nondrinkers as a reference).
[3] Additional adjustment for *trans* fatty acid intake.

TABLE 4
Relative risks (RR) and 95% CIs of fatal plus nonfatal coronary artery disease according to consumption of oil and salad dressings[1]

	Oil[2]	Mayonnaise and creamy dressings[3]
Consumers		
Median intake (g/d)	2.0	3.0
Percentage of cases (%)	7.8 [9]	15.6 [35]
Crude RR	0.47 (0.23, 0.92)	1.0 (0.66, 1.51)
Fully adjusted RR	0.53 (0.26, 1.06)	1.09 (0.71, 1.66)
Nonconsumers (reference group)		
Median intake (g/d)	0	0
Percentage of cases (%)	16.1 [89]	14.3 [63]
Crude RR	1.0	1.0
Fully adjusted RR	1.0	1.0

[1] 95% CI in parentheses. *n* in brackets. Models included the following variables: age, BMI, ex-smoking (yes or no), current smoking (yes or no), alcohol intake, use of vitamin supplements (yes or no), intakes of energy, vegetables, fruit, meat, fish, and fats for household use (eg, margarine, butter, cooking fat, and frying fat). Alcohol intake (0, 1–19, ≥20 g/d) was used as a categorical variable (included as 2 dummies in the model, with nondrinkers as a reference).

[2] *n* = 115 consumers and 552 nonconsumers.

[3] *n* = 225 consumers and 442 nonconsumers.

Imprecision in estimating α-linolenic acid intake could have obscured an association with CAD. Habitual food composition was measured by use of the cross-check dietary history method, which is acknowledged as a valid method of measurement in an epidemiologic setting (32). The α-linolenic acid content of ≈1000 products consumed by the participants of the Zutphen Elderly Study was used to calculate the intake of α-linolenic acid (29). Random misclassification of dietary exposure, due to error in the quantification of food composition data, including α-linolenic acid, cannot be excluded as a possible means of imprecision. However, values in the nutrient database were updated as much as possible, accounting for improvements in the quality of analytic methods and changes in food composition over time (34, 44). Intercorrelation between α-linolenic acid and other dietary factors, mainly *trans* fatty acids, complicated the estimation of the independent effect of α-linolenic acid. We confirmed the results of our analyses by relating the α-linolenic acid intake of foods with and without *trans* fatty acids to CAD risk. However, because of the strong association between intake of α-linolenic acid and *trans* fatty acids, residual confounding cannot be totally excluded. It might be that the effects of consuming α-linolenic acid on CAD risk are especially evident when large amounts of α-linolenic acid from sources without *trans* fatty acids are consumed.

A limitation of the present study was that it included only men aged 64–84 y at baseline. The etiology of CAD in elderly persons may be altered because of advanced coronary atherosclerosis. The beneficial effects of α-linolenic acid on platelet aggregation or arterial compliance might be greater in young populations; however, there are no data available on whether age affects the association between α-linolenic acid intake and CAD risk or risk factors. Our results were consistent when we used either fatal CAD or fatal CAD plus nonfatal myocardial infarction. Because of power, we mainly focused on the association of fatal plus nonfatal CAD.

A few prospective cohort studies previously reported on the association between α-linolenic acid intake and CAD (25–28). A strong inverse association was observed in the Nurses' Health Study (28). In other cohort studies, however, the results were less clear (25–27). First, the results of other cohort studies were strongly affected by adjustment for other dietary factors. Adjustment for total fat in the Health Professionals Study (26), or adjustment for *trans*-unsaturated, *cis*-monounsaturated, and saturated fatty acids in the α-Tocopherol β-Carotene Cancer Prevention Study (27), strengthened the associations between α-linolenic acid and CAD risk. In the Multiple Risk Factor Intervention Trial (MRFIT), the association may have been confounded by other dietary factors because such adjustments were not made (25). Second, there was no suggestion of a linear dose-response relation for quintiles of intake of α-linolenic acid in data of the MRFIT and the Health Professionals Study. In MRFIT, the adjusted relative risks for the lowest, second, third, fourth, and highest quintiles of α-linolenic acid intake were 1, 0.98, 0.57, 0.98, and 0.68, respectively (25). In the Health Professionals Study, the relative risk of fatal CAD was not reduced in the highest quintile; however, a reduced risk of fatal CAD was observed in the analyses when α-linolenic acid was used as a continuous variable (26). Thus, prospective studies do not provide enough evidence to support the hypothesis that a high intake of α-linolenic acid will reduce the risk of CAD.

Our results on α-linolenic acid intake and CAD risk are not consistent with those observed in the Nurses' Health Study. The range of α-linolenic acid intake in our cohort is comparable with that in the Nurses' Health Study; however, in the Nurses' Health Study, ≈70% of the α-linolenic acid intake was derived from vegetable or plant sources, of which salad dressings were the most significant food source (30%) (28). In the present study, a borderline, significant inverse association was observed between the intake of oils and CAD incidence. In addition, no association was observed between the intake of salad dressings and CAD. Neither α-linolenic acid, linoleic acid, or vitamin E, all of which are abundant in these oils, seem to be responsible for the protective effect of oil because the results were similar when these components were included in the model. The results of the present study could have been biased because oil consumption was limited in these Dutch elderly men and may be a marker for healthier lifestyles. However, adjustment for potential confounders, or additionally for physical activity and history of hypertension and diabetes mellitus (data not shown), did not change the relative risks appreciably. Therefore, the potential protective effect of oil consumption, including the responsible components, deserves further research.

In a secondary prevention trial, recurrence of cardiac events was substantially lower among patients randomly assigned to consume a Mediterranean diet enriched with α-linolenic acid than among those in a control group (23); however, other dietary changes occurred simultaneously in this trial. In another secondary prevention trial, cardiac events were significantly lower after a 1-y treatment with mustard oil compared with placebo (24). However, the experimental and control groups differed in other characteristics relevant to cardiovascular health (eg, smoking habits) and these were not accounted for in the final risk estimates. Therefore, also on the basis of these trials, it cannot be deduced that the protective effect against cardiac events was solely due to the intake of α-linolenic acid.

In conclusion, we observed no beneficial association between dietary α-linolenic acid intake and risk of 10-y CAD incidence in elderly Dutch men. The substantial differences between crude and adjusted relative risks of CAD in association with α-linolenic acid intake in prospective studies, together with the

limited evidence on the mechanisms, indicates that the protective cardiac effect of α-linolenic acid is questionable.

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