Fat Consumption and Its Association With Age-Related Macular Degeneration

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Objective: To evaluate associations between past dietary fat intake and the prevalence of age-related macular degeneration (AMD).

Methods: Six thousand seven hundred thirty-four participants aged 58 to 69 years in 1990-1994 took part in this cohort study. Participants' nutrient intakes were estimated from a food frequency questionnaire at baseline. At follow-up from 2003 to 2006, digital macula photographs of both eyes were evaluated for early and late AMD signs. Logistic regression was used to estimate odds ratios, with adjustment for age, smoking, and other potential confounders.

Results: Higher *trans*-unsaturated fat intake was associated with an increased prevalence of late AMD; the odds ratio comparing the highest with the lowest quartile of *trans* fat was 1.76 (95% confidence interval, 0.92-3.37; $P=.02$). Higher ω-3 fatty acid intake (highest quartile vs lowest quartile) was inversely associated with early AMD (odds ratio, 0.85; 95% confidence interval, 0.71-1.02; $P=.03$). Olive oil intake (≥100 mL/week vs <1 mL/week) was associated with decreased prevalence of late AMD (odds ratio, 0.48; 95% confidence interval, 0.22-1.04; $P=.03$). No significant associations with AMD were observed for intakes of fish, total fat, butter, or margarine.

Conclusion: A diet low in *trans*-unsaturated fat and rich in ω-3 fatty acids and olive oil may reduce the risk of AMD.

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AGE-RELATED MACULAR DEgeneration (AMD) is the leading cause of severe visual loss among people aged older than 65 years in the developed world.[1,2] This progressive late-onset degenerative disease affects central vision, which can impair important activities, such as driving and reading. The ensuing disability not only results in significant personal costs but also places a large burden on health resources.[3,4] With the aging population, it is estimated that by 2020, the number of Americans with late (end-stage) AMD will increase by 50% to 3 million[1]; similarly, in Australia, AMD prevalence is expected to double, with direct costs to the community reaching to more than A$1 billion (>US $668 million) by the year 2020.[3] For these reasons, research into AMD prevention is important. Established risk factors for AMD include age, genetic markers,[5] and smoking, with the latter being the only consistently reported modifiable risk factor.[6] To date, the pathogenesis of AMD remains unknown, and with treatment only available for neovascular complications of AMD,[7] the identification of modifiable risk factors would have enormous implications.

Thus far, the evidence from published studies has been inconsistent, with some studies suggesting that higher intakes of vegetable fat and *trans* fat increase the risk of AMD[8,9] and others not finding such risks.[10] Some studies have also suggested that diets rich in ω-3 or fish, as a proxy for ω-3 fatty acids, are protective against AMD.[11,12] As recommended by recent reviews in this area,[12-14] with only 3 published prospective cohort studies evaluating the associations between dietary fat, its subtypes,[10,11] or fish[15] and AMD and 1 cohort study evaluating AMD progression thus far,[9] more evidence from cohort studies is clearly needed. Therefore, we investigated these associations prospectively in a large cohort of Melbourne residents aged between 58 and 69 years at baseline examination.

METHODS

STUDY DESIGN AND PARTICIPANTS

Participants were selected from the Melbourne Collaborative Cohort Study, a prospective cohort study of 41 528 Melbourne residents (17 049 men) aged 40 to 69 years at the time of recruitment from 1990 to 1994. Participants were recruited via the electoral register (registration to vote is compulsory for Aus-

tralian citizens) and advertisements, details of which have been described else where.[16,17] We focused this study on participants who were aged between 58 and 69 years at baseline and were Australian or British born. Of 13 217 participants who satisfied these eligibility criteria, 11 617 were alive and residing in Victoria, Australia on May 1, 2003. Of these participants, 6734 (58%) attended follow-up between May 2003 and July 2006. During the follow-up period from May 2003 to July 2006, an additional 638 participants died and another 157 participants left Victoria. Despite higher attrition rates in an elderly cohort, our follow-up rate during a 13- to 16-year period was comparable with other well-conducted, long-term cohort studies with a younger age range of participants. The 15-year response rate in the Beaver Dam Eye Study was 43% (2119 participated at year 15 of 4926 participants aged 43-84 years at baseline)[18]; and the 10-year follow-up rate for the Blue Mountains Eye Study was 53% (1952 participated at year 10 of 3654 participants aged ≥49 years at baseline).[19]

Participants were excluded if they reported extreme energy intakes, indicating that food frequency questionnaires (FFQs) were improperly filled in (n=110; <1st percentile and >99th percentile); if they reported acute myocardial infarction, angina, or diabetes at baseline and thus were likely to have changed their diet (n=624); if they had missing dietary data (n=1); or if they had missing or nongradable macula photographs owing to refusal, loss of an eye, or poor photograph quality secondary to cataract or small pupils (n=395). After these exclusions, data from 5604 participants were available for analysis.

BASELINE DIETARY ASSESSMENT

Dietary intake from the year before baseline was estimated using a 121-item FFQ. The food list in the FFQ was derived from weighed food records in a sample of 810 Melbourne residents of similar age and ethnic origin to the Melbourne Collaborative Cohort Study cohort.[20] The FFQ included questions about the use of vitamins, fish oil, and cod liver oil supplements and was optically scanned into the database. Only yes/no answers were collected on fish and cod liver supplements without further detail on brand and dosage; hence, nutrients derived from supplements were not included in total nutrient intake. Nutrient intakes were calculated using standard sex-specific portion sizes from the weighed food records. The energy and fat contents in food were derived from Australian food composition tables.[21] Fatty acid composition of foods data were obtained from the Royal Melbourne Institute of Technology fatty acid database.[22] Carotenoid data were obtained from the 1998 US Department of Agriculture database.[23] In a random sample of 4439 Melbourne Collaborative Cohort Study participants, plasma phospholipid fatty acid levels were correlated with those estimated from the FFQ.[24] Similar to the correlation coefficients of other studies of nutrition using FFQs,[25-27] the corrected correlation coefficients in our study ranged from 0.38 to 0.78 for most fatty acids with weaker associations observed for saturated fatty acids. The reliability coefficients for estimates of intake obtained from the FFQ in a subset of 272 participants who completed the FFQ again after 12 months ranged from 0.33 to 0.56 for fatty acids and from 0.68 to 0.73 for food categories.

A structured interview was used to obtain demographic and lifestyle information, which included age, sex, smoking, and country of birth. Height, weight, and blood pressure were directly measured.

OPHTHALMIC DATA

At follow-up from May 2003 to July 2006, participants had both eyes photographed using a digital camera. Four 45° nonstereoscopic retinal photographs of the disc and macula of each eye were taken in each participant. The images were viewed immediately and taken again if unsatisfactory. Graders were physicians who had additional training in AMD grading. The 2 graders were masked and disagreements between them were resolved by a senior grader/ophthalmologist. Intergrader and intragrader reliability ranged from 0.64 to 0.76 and 0.60 to 1.00, respectively. To test the robustness of our readings and because there are many definitions of AMD, the 2 most commonly used definitions of early AMD were used: presence of drusen 63 μm or larger, with or without the presence of hyperpigmentation/hypopigmentation (International Classification of Age-Related Maculopathy[28]); and presence of large drusen, 125 μm or larger,[29] with or without the presence of hyperpigmentation/hypopigmentation. Late AMD was defined as evidence of choroidal neovascularization or geographic atrophy.

STATISTICAL ANALYSIS

Multiple logistic regression was used to calculate odds ratios (ORs) for intakes of different fats and foods at baseline, with the presence or absence of AMD at follow-up as the outcome, adjusting for age; sex; smoking (never-, former, or current smoker at baseline); intakes of energy (using the nutrient density adjustment method[30]), vitamins C and E, β-carotene, and zinc; and use of supplements (ascorbic acid, vitamin E, cod liver oil, and fish oil) at baseline. These variables were retained, as they changed the β coefficients by more than 5%. Dietary intake of nutrients was categorized into quartile groupings, with the first quartile used as the reference category. Food frequency distributions used to construct quartiles were based on the baseline data of all participants in the Melbourne Collaborative Cohort Study. Tests for trend across categories of nutrient intake were calculated by using the medians within each category as pseudocontinuous variables. Analyses stratified by median age of participants were also performed, and a test for interaction assessed using a multiplicative term and the likelihood ratio test. Analyses were performed using Stata, version 9.1 (Stata Corp, College Station, Texas).

ETHICS APPROVAL

Cancer Council Victoria's Human Research Ethics Committee and the Royal Victorian Eye and Ear Hospital Human Research Ethics Committee approved the study protocols. Study participants gave written consent for the investigators to access their medical records and to collect and store their macula photographs, anthropometric measurements, and biologic samples. They also consented to passive follow-up conducted through record linkage to electoral rolls, electronic telephone books, the Victorian Cancer Registry, and death records. The study was carried out in accordance with the principles outlined in the Declaration of Helsinki.

RESULTS

Of the 6734 eligible participants who attended the follow-up sessions, 6339 (94.1%) had gradable macula photographs. At the time when retinal photographs were taken, participants had a median age of 74 years (range, 66-85 years). We identified 1861 cases of early AMD (drusen ≥63 μm; 29.4%), 1011 cases of early AMD (large drusen, ≥125 μm; 16.0%), and 88 cases of late AMD (1.4%), including 36 cases of exudative AMD and 52 cases of geographic atrophy. After excluding participants with outlier energy intakes and those with a history of acute myo-

Table 1. Demographic and Dietary Characteristics in Participants vs Nonparticipants From Melbourne, Australia, 1990-1994

Characteristic	Mean (SD)	
	Participants (n=5999)	Nonparticipants (n=4150)
Demographics		
Age at baseline, y	63.7 (3.3)	64.5 (3.4)
Age at follow-up, y	74.4 (3.5)	NA
Female sex, No. (%)	3666 (61)	2762 (67)
Smoking, No. (%)		
Current	336 (6)	382 (9)
Past	1921 (32)	1362 (32)
Completed high school, No. (%)	1454 (24)	936 (23)
Systolic blood pressure, mm Hg	142.3 (19.5)	145.7 (21.4)
Body mass index[a]	26.2 (3.9)	26.8 (4.3)
Does not exercise, No. (%)	910 (15)	736 (17)
Dietary intake		
Energy, kcal/d	2260.6 (729.7)	2193.4 (739.8)
Fat, g/d	82.7 (30.5)	81.1 (31.4)
Fat, mean % of total energy	32.2	32.5
Polyunsaturated fat, g/d	13.1 (5.8)	13.0 (6.0)
Trans fat, g/d	0.08 (0.08)	0.08 (0.09)
ω-3 Fatty acid, g/d	1.2 (0.4)	1.2 (0.4)
Olive oil, median (IQR), mL/wk	33.3 (0.0-58.3)	0.0 (0.0-58.3)
Fish, ≤1.5 times/wk, No. (%)	2763 (63)	2509 (60)
Vitamin C, mg/d	215.8 (109.6)	202.9 (110.0)
Vitamin E, mg/d	8.5 (3.3)	8.0 (3.2)
Lutein and zeaxanthin, mg/d	1778.8 (964.3)	1654.4 (916.5)
Zinc, mg/d	13.0 (5.1)	12.6 (5.1)
Alcohol, g/d	12.4 (18.8)	10.9 (20.0)

Abbreviations: IQR, interquartile range; NA, not applicable.
[a]Calculated as weight in kilograms divided by height in meters squared.

cardial infarct, angina, or diabetes at baseline, 1680 cases of early AMD (drusen ≥63 µm; 30%), 910 cases of early AMD (large drusen, ≥125 µm; 16.3%), and 77 cases of late AMD (1.4%) were included in our analyses.

Table 1 describes the characteristics of the participants and nonparticipants who were eligible to take part in this study. The distributions of age, smoking habits, education level, systolic blood pressure, and fatty acid and fish intakes were similar in the 2 groups. Participants had higher median olive oil intake compared with nonparticipants; however, the interquartile range was the same for the 2 groups.

Table 2 summarizes the ORs for AMD at follow-up associated with baseline nutrient intakes. A higher *trans*-unsaturated fatty acid (TFA) intake tended to be directly associated with the prevalence of late AMD; the OR comparing the highest with the lowest quartile of TFA intake was 1.76 (95% confidence interval [CI], 0.92-3.37; $P=.02$). However, there was no evidence of a dose response across the quartile groupings (Table 2). No associations were seen between TFA intake and early AMD. Higher ω-3 fatty acid intake was weakly negatively associated with prevalence of early AMD (drusen ≥63 µm: OR, 0.85; 95% CI, 0.71-1.02; $P=.03$; large drusen, ≥125 µm: OR, 0.87; 95% CI, 0.70-1.08; $P=.24$). No other associations were observed between any grouping of fats or for any individual fatty acid and either early or late AMD. Further adjustment for other fat subtypes did not materially change the results.

Table 3 summarizes the ORs for AMD in relation to intake of specific foods that have a high fat content. Higher intake of olive oil, which contains large amounts of oleic acid (monounsaturated fatty acid), was inversely associated with late AMD ($P<.03$). Fish intake (high marine ω-3 fatty acid source), cooked in various ways, showed no significant associations with AMD. No associations were seen between margarine (high TFA content) or butter (saturated fat) and AMD. Further analyses stratified by median age into younger and older groups revealed ORs in similar directions across fatty acid and food group intake; there was no evidence of effect modification by median age groups (results not shown).

COMMENT

In this cohort study of persons aged 58 to 69 years at baseline, we observed a direct association between baseline TFA intake and prevalence of late AMD; an inverse association between ω-3 fatty acids and prevalence of early AMD; and an inverse association between olive oil intake and late AMD. *Trans*-unsaturated fatty acids are formed when liquid vegetable fats are hardened through a process of partial hydrogenation and are commonly found in shortenings and processed foods.[14] Prospective epidemiological studies and case-control studies have shown TFA to increase the risk of coronary heart disease as a result of its adverse effects on lipids[31] and possibly owing to an association with inflammation.[32] A positive association between TFA and late AMD was found in our study. Two American cohort studies similarly reported TFA intake to be associated with an increased risk of AMD. In the first study of 261 participants with early AMD, TFA intake in the highest quartile compared with the lowest quartile was associated with an increased risk of AMD progression (relative risk, 2.39; 95% CI, 1.10-5.17; $P=.008$).[9] In the second, a pooled analysis of the Nurses' Health and the Health Professionals Follow-up studies, TFA intake in the highest compared with the lowest quintile was associated with an increased risk of any AMD (relative risk, 1.35; 95% CI, 1.02-1.80; $P=.02$).[11]

Various studies have shown ω-3 fatty acids and fish to be inversely associated with AMD,[8-11,15,33,34] resulting in a growing interest in the role of long-chain ω-3 fatty acids in the prevention of AMD. High levels of docosahexaenoic acid, a marine long-chain ω-3 fatty acid, is found in the rod outer segments of the retina.[35] These outer segments are constantly shed and turned over in the normal visual cycle. It has been suggested that deficiency of these fatty acids may initiate the onset of AMD. ω-3 Fatty acids have also been suggested to protect against oxidative-, inflammatory-, and age-associated damage to the retina,[36] postulated to be key pathogenic processes in AMD development.[37-39] Two recent systematic reviews evaluating ω-3 fatty acids in the prevention of AMD acknowledged that there was some evidence that ω-3 fatty acids might offer some protection toward AMD and that further cohort studies addressing this area were required.[12,40] Our study found ω-3 fatty acids, which

Table 2. Association of AMD With Energy-Adjusted Dietary Fat Intake[a]

Baseline Dietary Intake				AMD Status at Follow-up								
				Early AMD[b]			Early AMD[c]			Late AMD		
Dietary Measure	Median, g/d	Quartile	No. of People	No. of Cases	OR (95% CI)	*P* Value	No. of Cases	OR (95% CI)	*P* Value	No. of Cases	OR (95% CI)	*P* Value
Total fat	60.1	1	1342	410	1 [Reference]		225	1 [Reference]		20	1 [Reference]	
	75.1	2	1414	411	0.94 (0.79-1.12)	.98	226	0.97 (0.79-1.19)	.71	17	0.85 (0.44-1.65)	.87
	83.0	3	1406	424	0.99 (0.83-1.18)		215	0.92 (0.75-1.15)		19	0.95 (0.49-1.86)	
	96.9	4	1442	435	0.98 (0.82-1.18)		244	1.05 (0.85-1.32)		21	1.03 (0.52-2.04)	
Polyunsaturated fat	8.3	1	1416	422	1 [Reference]		233	1 [Reference]		22	1 [Reference]	
	10.6	2	1395	417	0.99 (0.84-1.17)	.55	217	0.93 (0.75-1.14)	.82	17	0.78 (0.41-1.51)	.9
	14.0	3	1406	419	0.94 (0.79-1.12)		229	0.97 (0.78-1.20)		16	0.74 (0.37-1.47)	
	17.1	4	1387	422	0.95 (0.79-1.15)		231	1.01 (0.80-1.27)		22	1.02 (0.51-2.06)	
Monounsaturated fat	21.0	1	1353	407	1 [Reference]		227	1 [Reference]		18	1 [Reference]	
	25.8	2	1427	421	1.00 (0.85-1.19)	.62	229	0.97 (0.79-1.19)	.88	13	0.73 (0.35-1.51)	.33
	29.0	3	1401	422	1.05 (0.89-1.25)		219	0.96 (0.78-1.19)		25	1.44 (0.76-2.75)	
	33.3	4	1423	430	1.03 (0.86-1.24)		235	1.02 (0.82-1.27)		21	1.19 (0.60-2.39)	
Saturated fat	22.0	1	1336	415	1 [Reference]		221	1 [Reference]		22	1 [Reference]	
	29.7	2	1383	394	0.92 (0.77-1.09)	.89	211	0.94 (0.76-1.16)	.65	18	0.89 (0.46-1.68)	.94
	35.5	3	1426	434	0.99 (0.83-1.18)		246	1.10 (0.89-1.36)		15	0.72 (0.36-1.44)	
	42.8	4	1459	437	0.99 (0.83-1.18)		232	1.01 (0.82-1.26)		22	1.00 (0.52-1.90)	
Trans fat	0.02	1	1426	430	1 [Reference]		236	1 [Reference]		15	1 [Reference]	
	0.03	2	1373	420	0.96 (0.81-1.13)	.42	226	0.96 (0.78-1.18)	.94	16	0.93 (0.45-1.95)	.02
	0.08	3	1388	428	1.02 (0.87-1.21)		217	0.92 (0.75-1.13)		17	1.08 (0.53-2.19)	
	0.10	4	1417	402	0.92 (0.78-1.09)		231	0.98 (0.80-1.20)		29	1.76 (0.92-3.37)	
Cholesterol	0.21	1	1362	414	1 [Reference]		223	1 [Reference]		17	1 [Reference]	
	0.26	2	1391	407	0.92 (0.78-1.09)	.48	225	0.97 (0.79-1.19)	.72	23	1.32 (0.70-2.51)	.96
	0.30	3	1440	453	1.03 (0.87-1.22)		243	1.03 (0.84-1.26)		16	0.84 (0.42-1.70)	
	0.37	4	1411	406	0.91 (0.77-1.09)		219	0.95 (0.77-1.17)		21	1.11 (0.57-2.18)	
Oleic acid	19.5	1	1367	416	1 [Reference]		230	1 [Reference]		17	1 [Reference]	
	22.9	2	1407	412	0.96 (0.81-1.14)	.94	222	0.94 (0.76-1.15)	.88	14	0.80 (0.39-1.66)	.45
	25.8	3	1401	419	0.99 (0.84-1.18)		219	0.94 (0.76-1.16)		27	1.63 (0.86-3.09)	
	29.6	4	1429	433	1.00 (0.84-1.19)		239	1.01 (0.82-1.260		19	1.09 (0.54-2.22)	
Linoleic acid	7.3	1	1415	423	1 [Reference]	.24	232	1 [Reference]	.54	21	1 [Reference]	
	9.6	2	1398	417	0.97 (0.82-1.15)		225	0.96 (0.78-1.18)		19	0.92 (0.48-1.73)	.72
	12.5	3	1414	430	0.95 (0.80-1.12)		234	0.97 (0.78-1.20)		13	0.63 (0.30-1.30)	
	15.2	4	1377	410	0.90 (0.74-1.08)		219	0.93 (0.74-1.16)		24	1.19 (0.60-2.35)	
Arachidonic acid	0.02	1	1404	431	1 [Reference]		231	1 [Reference]		20	1 [Reference]	
	0.03	2	1413	423	0.94 (0.80-1.11)	.08	227	0.96 (0.78-1.18)	.94	19	0.87 (0.46-1.65)	.46
	0.04	3	1410	431	0.96 (0.81-1.13)		225	0.96 (0.78-1.18)		20	0.89 (0.47-1.67)	
	0.06	4	1377	395	0.85 (0.72-1.01)		227	0.98 (0.79-1.21)		18	0.76 (0.39-1.48)	
ω-3 Fatty acids[d]	1.0	1	1396	412	1 [Reference]		231	1 [Reference]		21	1 [Reference]	
	1.1	2	1407	445	1.02 (0.87-1.21)	.03	229	0.94 (0.76-1.16)	.24	17	0.74 (0.38-1.42)	.89
	1.2	3	1410	419	0.90 (0.76-1.08)		235	0.97 (0.78-1.19)		15	0.63 (0.31-1.26)	
	1.4	4	1391	404	0.85 (0.71-1.02)		215	0.87 (0.70-1.08)		24	0.98 (0.52-1.86)	
Marine ω-3 fatty acids[e]	0.13	1	1417	420	1 [Reference]		221	1 [Reference]		21	1 [Reference]	
	0.21	2	1415	426	0.99 (0.84-1.17)	.08	244	1.12 (0.92-1.37)	.30	19	0.87 (0.46-1.63)	.92
	0.28	3	1392	435	1.00 (0.85-1.18)		234	1.07 (0.87-1.31)		15	0.65 (0.33-1.28)	
	0.57	4	1380	399	0.87 (0.73-1.03)		211	0.94 (0.76-1.17)		22	0.92 (0.49-1.74)	
Eicosapentaenoic acid	0.04	1	1410	412	1 [Reference]		218	1 [Reference]	.19	21	1 [Reference]	
	0.07	2	1418	439	1.03 (0.87-1.22)	.08	250	1.16 (0.95-1.42)		21	0.95 (0.51-1.75)	.94
	0.09	3	1396	429	0.98 (0.83-1.16)		235	1.07 (0.87-1.32)		12	0.50 (0.24-1.04)	
	0.18	4	1380	400	0.88 (0.74-1.05)		207	0.92 (0.74-1.15)		23	0.95 (0.51-1.79)	
Docosahexaenoic acid	0.07	1	1415	416	1 [Reference]		222	1 [Reference]		23	1 [Reference]	
	0.12	2	1418	433	1.02 (0.86-1.20)	.06	238	1.07 (0.87-1.31)	.29	15	0.61 (0.32-1.18)	.90
	0.16	3	1394	438	1.02 (0.86-1.20)		242	1.10 (0.89-1.35)		16	0.64 (0.33-1.22)	
	0.32	4	1377	393	0.87 (0.73-1.03)		208	0.92 (0.74-1.14)		23	0.89 (0.48-1.64)	
α-Linolenic acid	0.76	1	1393	429	1 [Reference]		237	1 [Reference]		22	1 [Reference]	
	0.86	2	1402	411	0.85 (0.72-1.01)	.14	215	0.84 (0.68-1.04)	.71	11	0.48 (0.23-1.01)	.48
	0.94	3	1412	422	0.86 (0.72-1.02)		227	0.89 (0.72-1.10)		19	0.82 (0.42-1.58)	
	1.06	4	1397	418	0.86 (0.71-1.03)		231	0.94 (0.75-1.17)		25	1.11 (0.58-2.13)	

Abbreviations: AMD, age-related macular degeneration; CI, confidence interval; OR, odds ratio.

[a] Adjusted for age, sex, smoking (current, past, or never), energy, dietary vitamin C, vitamin E, β-carotene, zinc, lutein, zeaxanthin, and supplements (vitamin C, vitamin E, cod liver oil, and fish oil [yes/no]).

[b] Drusen 63 μm or larger.

[c] Drusen 125 μm or larger.

[d] Includes α-linolenic acid, docosahexaenoic acid, and eicosapentaenoic acid.

[e] Includes only docosahexaenoic acid and eicosapentaenoic acid.

included docosahexaenoic acid, eicosapentaenoic acid, and α-linolenic acid, to be inversely associated with early AMD (drusen ≥63 μm). However, when the other definition of early AMD was used, because there were approximately half the number of cases, the results were not statistically significant, though the point estimates

Table 3. Association of AMD With Increasing Frequencies of Food Intake[a]

Baseline Dietary Intake		AMD Status at Follow-up								
		Early AMD[b]			Early AMD[c]			Late AMD		
Dietary Measure	No. of People	No. of Cases	OR (95% CI)	*P* Value	No. of Cases	OR (95% CI)	*P* Value	No. of Cases	OR (95% CI)	*P* Value
Fish, servings/wk										
0-0.5	1043	315	1 [Reference]		164	1 [Reference]		20	1 [Reference]	
1-1.5	2459	750	0.98 (0.83-1.15)	.13	425	1.09 (0.90-1.34)	.23	28	0.59 (0.33-1.07)	.51
≥2	2102	615	0.89 (0.75-1.05)		321	0.92 (0.74-1.14)		29	0.76 (0.42-1.38)	
Steamed, grilled, or baked fish										
Never or <1/mo	1434	438	1 [Reference]		232	1 [Reference]		27	1 [Reference]	
1-3 Times/mo	1659	492	0.94 (0.80-1.10)	.31	265	0.98 (0.81-1.19)	.99	18	0.59 (0.32-1.09)	.25
≥1/wk	2509	750	0.92 (0.80-1.07)		413	1.00 (0.83-1.20)		32	0.71 (0.41-1.21)	
Fried fish										
Never or <1/mo	3493	1077	1 [Reference]		581	1 [Reference]		44	1 [Reference]	
1-3 Times/mo	1376	396	0.96 (0.83-1.10)	.36	212	0.95 (0.79-1.13)	.64	23	1.49 (0.88-2.50)	.33
≥1/wk	735	207	0.93 (0.78-1.11)		117	0.97 (0.78-1.21)		10	1.18 (0.58-2.41)	
Canned fish										
Never or <1/mo	1764	510	1 [Reference]		280	1 [Reference]		30	1 [Reference]	
1-3 Times/mo	2252	696	1.04 (0.90-1.19)	.47	380	1.04 (0.87-1.23)	.44	23	0.59 (0.34-1.03)	.60
≥1/wk	1587	473	0.94 (0.81-1.10)		249	0.92 (0.76-1.12)		24	0.89 (0.51-1.57)	
Smoked fish										
Never or <1/mo	5119	1530	1 [Reference]		831	1 [Reference]		74	1 [Reference]	
1-3 Times/mo	400	128	1.12 (0.90-1.40)	.72	69	1.09 (0.83-1.44)	.88	2	0.39 (0.10-1.63)	.30
≥1/wk	85	22	0.88 (0.53-1.44)		10	0.73 (0.37-1.43)		1	0.85 (0.11-6.39)	
Olive oil, mL/wk										
0-0.5	2607	753	1 [Reference]		408	1 [Reference]		47	1 [Reference]	
1-49.5	561	172	1.20 (0.98-1.47)	.23	99	1.31 (1.02-1.67)	.68	5	0.67 (0.26-1.72)	.03
50-99.5	1504	464	1.08 (0.94-1.25)		256	1.09 (0.92-1.30)		17	0.66 (0.37-1.16)	
≥100	932	291	1.09 (0.92-1.29)		147	1.00 (0.81-1.24)		8	0.48 (0.22-1.04)	
Margarine, times/wk										
0	1016	295	1 [Reference]		160	1 [Reference]		16	1 [Reference]	
0.5-6.5	1126	337	1.03 (0.86-1.25)	.99	174	0.97 (0.77-1.23)	.65	13	0.72 (0.34-1.52)	.78
7-17	1508	463	1.05 (0.88-1.25)		254	1.05 (0.84-1.30)		19	0.80 (0.40-1.60)	
≥17.5	1954	585	1.00 (0.84-1.20)		322	1.03 (0.83-1.29)		29	1.05 (0.53-2.07)	
Butter, times/wk										
0	3188	942	1 [Reference]		498	1 [Reference]		47	1 [Reference]	
0.5	518	148	0.95 (0.77-1.17)	.22	87	1.10 (0.85-1.41)	.21	4	0.59 (0.21-1.66)	.78
1-6.5	727	230	1.09 (0.92-1.31)		135	1.25 (1.01-1.55)		12	1.19 (0.62-2.27)	
≥7	1171	360	1.08 (0.93-1.26)		190	1.06 (0.88-1.29)		14	0.85 (0.45-1.58)	

Abbreviations: AMD, age-related macular degeneration; CI, confidence interval; OR, odds ratio.
[a] Adjusted for age, sex, smoking (current, past, or never), energy, vitamin C, vitamin E, β-carotene, zinc, lutein, zeaxanthin, and supplements (vitamin C, vitamin E, cod liver oil, and fish oil [yes/no]).
[b] Drusen 63 μm or larger.
[c] Drusen 125 μm or larger.

for the ORs were similar. Although associations with long-chain marine ω-3 fatty acids, which have been postulated to be more relevant in reducing retinal damage (docosahexaenoic acid and eicosapentaenoic acid), and α-linolenic acid, individually, were not statistically significant, their ORs were in the protective direction. It should be noted that ω-3 fatty acid intakes from fish and cod liver oil supplementation were not included in the total dietary intake, which may or may not have resulted in an underestimation of the OR.

We found olive oil intake to be inversely associated with the prevalence of late AMD. Although olive oil contains approximately 85% oleic acid, neither monounsaturated fatty acids nor oleic acid intakes were associated with late AMD. In the Australian diet, meat and dairy products contribute similar amounts of monounsaturated fats as oils[41]; meat intake in our study was similarly not inversely associated with AMD. Thus, it is possible that other nonfat components of olive oil may contribute to this apparent protective effect.[42] Olive oil is rich in vitamin E, polyphenols, and oleocanthal; the first 2 substances are powerful antioxidants,[43] while the latter is a potent anti-inflammatory compound likened to ibuprofen.[44] Olive oil may also be a proxy for certain healthy lifestyles that may be associated with a decreased risk of AMD. Together with the association seen only with late AMD, our results need to be interpreted contextually. As ORs in the positive direction were seen in 1 cohort[11] and 2 case-control studies[8,45] that investigated monounsaturated fatty acids and AMD, though not statistically significant, this inverse relationship demands further confirmation in other cohort studies. Thus far, a significant inverse association between olive oil and AMD has not been reported in previous studies.

The strengths of our study include its large size and collection of dietary data in the early 1990s, when there was little interest in the association between dietary fatty acid intake and AMD. Our study had reasonably good follow-up during a 13-year period, with little evidence that participants and nonparticipants had different characteristics. However, our study does have limitations. First, although our FFQ showed good correlations with serum measurements,[24] limitations exist in all dietary stud-

ies that use the FFQ, as it is an imperfect instrument. Measurement errors of dietary factors estimated by the FFQ, administered only once at baseline, could have occurred. However, such errors are likely to be nondifferential, therefore attenuating our results. Another limitation with the FFQ was that it did not differentiate between nonoily and oily fish (rich in marine ω-3 fatty acids), which may have resulted in the lack of associations seen with fish in our analyses. Second, the issue of multiple comparisons in analyses of diet and disease should be considered, as most FFQs measure a large number of food items. Some proponents argue that the *P* value should be adjusted according to the number of variables examined; however, the consensus in epidemiology is that this unduly reduces power, and individual associations should be evaluated on their own merits and conclusions drawn in light of consistency with information both internal and external to the study.[46-50] Similar to other studies evaluating dietary fat and AMD,[10,11] we did not adjust for multiple comparisons because our hypotheses were generated a priori; we interpreted our findings in the context of systematic reviews of the currently available literature[12]; and we checked for internal consistency using 2 definitions of early AMD. Nevertheless, in interpreting our results, the possibility of chance findings must be considered. Additionally, as few cases of late AMD were present, the study may lack power in evaluating the dietary associations with late AMD. Last, we were unable to exclude residual confounding due to inaccurately measured or unmeasured confounders.

In summary, we found that higher TFA intake was associated with an increased prevalence of late AMD, while ω-3 fatty acids and olive oil were associated with a reduced prevalence of early and late AMD, respectively. Our findings suggest that people who follow a diet low in processed foods high in TFA and rich in ω-3 fatty acids and olive oil might enjoy some protection from developing AMD.

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From the Archives of the Archives

140 Years Ago . . .

It was therefore now the main question to judge, whether the power of the air-gun was great enough to drive the ball forward into the brain. For this purpose I sent to the owner of the gun, in order to obtain a statement of the charge usually employed. But as he could not give me the information I desired, I tried the same gun myself. We shot against a deal door at a distance of 4 paces. The usual lead ball, which had a diameter of somewhat more than three lines, was thrown back by the soft wood, and only left a superficial mark. By this trial I was convinced that the ball had not force enough to pass twice through the membranes of the eyeball and also to penetrate through the contents of the orbit and its bones.

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