Dietary Fatty Acids and the 5-Year Incidence of Age-Related Maculopathy

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Objective: To assess longitudinal associations between dietary fat and incident age-related maculopathy (ARM) in an older, population-based, historical cohort.

Methods: A total of 3654 persons, 49 years or older, participated in the Blue Mountains Eye Study (1992-1994); 2335 (75.1% of survivors) were reexamined after 5 years (1997-1999). Dietary data were collected from 2895 people (79%) at baseline by means of a semiquantitative food frequency questionnaire to calculate dietary fat intakes. Presence of ARM was graded from retinal photographs (Wisconsin ARM Grading System). Logistic regression adjusted for age, sex, vitamin C intake, and smoking.

Results: Participants with the highest vs lowest quintiles of n-3 polyunsaturated fat intake had lower risk of incident early ARM (odds ratio [95% confidence interval], 0.41 [0.22-0.75). A 40% reduction of incident early ARM was associated with fish consumption at least once a week (odds ratio [95% confidence interval], 0.58 [0.37-0.90]), whereas fish consumption at least 3 times per week could reduce the incidence of late ARM (odds ratio [95% confidence interval], 0.25 [0.06-1.00]). We found no association between incident ARM and butter, margarine, or nut consumption.

Conclusions: A regular diet high in n-3 polyunsaturated fat, especially from fish, suggests protection against early and late ARM in this older Australian cohort. Our study could not confirm deleterious effects of higher polyunsaturated fat intakes reported by other clinic-based studies.

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AGE-RELATED MACULOPATHY (ARM) is the most frequent cause of severe vision loss in elderly people.[1-3] We currently lack effective treatments for early ARM and a high proportion of late ARM cases. Risk factor identification and preventive strategies therefore have the potential to reduce the impact and burden of ARM on the global aging population.

Several recent articles have examined possible associations between dietary fat and progression of ARM,[4-6] based on a proposed atherosclerotic pathogenesis of ARM.[7,8] Dietary fat modification appeared to provide a method for ARM prevention. These articles reported that high dietary intake of fat and all its subtypes, including vegetable and unsaturated fats, increased the risk of ARM progression. These results have caused concern in the lay, medical, and ophthalmic communities because it challenged current clinical evidence and practice advice regarding the benefits of vegetable and unsaturated fats on cardiovascular health.[9] Additionally, current explanations associating unsaturated fat intakes with ARM risk remain unconvincing. Assuming a hypothesis that atherosclerosis is common to the pathogenesis of ARM and cardiovascular disease, clinical evidence has shown that diets high in unsaturated fats reduce cardiovascular events.[9] Furthermore, although polyunsaturated fatty acids, concentrated in photoreceptor outer segments, are suggested to cause macular damage through lipid peroxidation,[10] reports from animal studies show that certain polyunsaturated fats, particularly docosahexaenoic acid, protect against retinal oxidation and degeneration.[11-14]

In light of these reports and the ensuing controversy, we aimed to examine the association between intakes of dietary fat and fatty acid components and the 5-year incidence of ARM, using population-based data from the Blue Mountains Eye Study[1] (BMES) cohort.

METHODS

The BMES is a population-based study of vision and common eye diseases of noninstitutionalized residents, 49 years or older, living in 2 urban postal codes west of Sydney, Australia. We used a historical cohort study design to examine the association between dietary fat intake, collected at baseline, and risk of 5-year incident ARM. The study was approved by both the Western Sydney Area Health Service and the University of Sydney Human Ethics Committees, and written informed consent was obtained from all participants. Survey methods and procedures have been described previously.[1] Briefly, the baseline survey (BMES I) was conducted from 1992 to 1994 and included 3654 participants (82.4% of those eligible); 5-year follow-up (BMES II) conducted from 1997 to 1999 examined 2335 participants from the original cohort (75.1% of survivors). A detailed interviewer-administered questionnaire was administered, and a comprehensive eye examination, including dilated 30° stereoscopic retinal photographs (Zeiss FF3; Carl Zeiss, Oberkochen, Germany), was performed.

Photographic grading for ARM lesions closely followed the Wisconsin ARM grading system.[15] All retinal photographs underwent initial masked grading followed by concurrent grading of baseline and 5-year photographs in cases where ARM lesions were identified at either examination. Incident early ARM was defined by the appearance of indistinct soft drusen, reticular drusen, or concurrent distinct soft drusen and retinal pigmentary abnormalities at follow-up in either eye of persons without early or late ARM at baseline. Incident late ARM was defined by the appearance of neovascular ARM or generalized atrophy involving the foveal center at follow-up in either eye of persons in whom no late ARM had been present at baseline.[15]

Dietary data were collected from 2895 people at baseline (79% of those examined) by means of a semiquantitative 145-item self-administered food frequency questionnaire (FFQ), modified from a Willet questionnaire for Australian diet and vernacular.[16] Dietary data collected included portion size, frequency estimates, and details about margarines, butters, oils, and supplements to permit more detailed analysis of fatty acids. The FFQ was validated with 79 participants on 3 occasions during 1 year by using 4-day weighed food records.[17,18] The FFQ showed moderate to good agreement (total fat, $r=0.68$; saturated fatty acids [SFAs], $r=0.67$; monounsaturated fatty acids [MUFAs], $r=0.54$; and polyunsaturated fatty acids [PUFAs], $r=0.44$), correctly classifying more than 70% of people within 1 quintile for all types of fat.[17,19] Dietary intakes were estimated by means of the Australian Tables of Food Composition (NUTTAB95),[19] with fatty acid composition of foods compiled by the Royal Melbourne Institute of Technology.[20] Dietary fat intakes were expressed as contribution to percentage of energy intake. Long-chain n-3 PUFAs were calculated from addition of fatty acids: eicosapentaenoic (EPA) (20:5, n-3), docosapentaenoic (DPA) (22:5, n-3), and docosahexaenoic (DHA) (22:6, n-3).

Characteristics of participants examined and not examined in the BMES II and participants who completed and did not complete the FFQ have been reported.[21,22] The BMES I participants not examined in the BMES II were more likely at baseline to be older (age ≥80 years, 9.3% vs 5.1%), to have reported difficulty in walking (7.9% vs 3.2%), and to be a current smoker (18.2% vs 13.0%). There were no significant differences between the 2 groups with respect to history of systemic diseases or perceived global health status.[21] Older persons (mean age, 66.6 years vs 64.2 years), those with early ARM (6.5% vs 4.0%), and current smokers (16.0% vs 12.4%) were less likely to have returned the FFQ.[22]

Statistical analyses were performed with SAS statistical software (SAS Institute Inc, Cary, NC), using the χ^2 test for comparison of proportions and the unpaired *t* test to compare means between groups, to examine characteristics of participants in different quintiles of dietary fat intake. Logistic regression examined the likelihood of early or late ARM incidence in the presence of different levels of dietary fat intake at baseline, adjusting for significant confounders, including age, sex, current smoking status, and vitamin C intake (diet and/or supplement). Potential confounders found not significant in our multivariable-adjusted models included hypertension, body mass index, and intakes of zinc (diet and/or supplement), retinol (diet), beta carotene (diet), and vitamin E (supplement). Odds ratios (ORs) and 95% confidence intervals (CIs) are reported. Statistical significance was defined as $P<.05$.

We estimate that for a power of 80% and $\alpha=.05$, the smallest detectable ORs for investigating protective associations with incident early and late ARM from this study were 0.6 and 0.25, respectively. The smallest detectable ORs for investigating increased risk of early and late ARM were 1.7 and 4.0, respectively.

RESULTS

After a mean 5.1-year follow-up period from the BMES I to the BMES II, 543 (14.9%) of 3654 participants had died, 383 (10.5%) had moved away, and 393 (10.8%) refused further participation, leaving 2335 (75.1% of survivors) of our baseline cohort for reexamination. Stereoscopic retinal photographs were available for 1 eye in 98.8% and for both eyes in 97.5% of participants in the BMES II.

After exclusion of participants with prevalent late ARM at baseline and those with missing retinal photographs at the BMES II, the person-specific 5-year incidence rates for early and late ARM in our cohort were 158 (7.4%) of 2145 and 26 (1.2%) of 2258,[21] respectively. Further exclusion of persons with missing FFQ data resulted in 5-year incidence rates for early ARM of 130 (7.1%) of 1839 and for late ARM of 22 (1.1%) of 1925. There were no significant differences in the incidence of early or late ARM by sex ($P>.05$), but the incidence of both early and late ARM increased significantly with age (*P* for trend, $<.001$).

Initial analysis compared the odds of incident ARM with increasing quintiles of dietary fat intake, using the lowest quintile as reference. After adjusting for age, sex, current smoking, and vitamin C intake, participants with the highest quintiles of total fat, SFA, MUFA, and *trans*-fat intakes had around 50% lower odds of incident early ARM compared with persons within the lowest quintiles of fat intake (total fat: OR, 0.49; 95% CI, 0.27-0.88; SFA: OR, 0.54; 95% CI, 0.29-0.98; MUFA: OR, 0.46; 95% CI, 0.25-0.84; *trans*-fat: OR, 0.46; 95% CI, 0.25-0.85). Participants within the highest quintile of dietary n-3 PUFA intake (OR, 0.41; 95% CI, 0.22-0.75) and those within the highest quintile of α-linolenic acid intake (18:3, n-3) (OR, 0.45; 95% CI, 0.25-0.84) had significantly reduced odds of incident early ARM compared with those in the lowest quintile.

Significant differences were found across groups reporting different levels of dietary fat intake (**Table 1**). Participants with the lowest quintile of total dietary fat intake were found to be slightly older, to have lower body mass index but greater prevalence of hypertension, and also to report lower intakes of zinc and retinol

Table 1. Characteristics of Participants Stratified by Quintile of Total Dietary Fat

	Total Dietary Fat Intake*		
	Quintile 1 (n = 397)	Quintiles 2-4 (n = 1194)	Quintile 5 (n = 397)
Age, y	65.2 ± 7.8†	64.1 ± 8.6	63.4 ± 8.6
Sex, No. (%) F	237 (59.7)	663 (55.5)	231 (58.2)
Hypertension, No. (%)	196 (49.5)‡	509 (42.7)	161 (40.6)
Current smoker, No. (%)	38 (9.9)	132 (11.3)	70 (18.2)‡
BMI	25.6 ± 4.2†	26.5 ± 4.3	26.1 ± 4.4
Zinc, mg (diet and supplements)	11.6 ± 5.4†	13.5 ± 8.4	14.3 ± 10.0
Beta carotene, µg (diet)	8013.7 ± 4741.4†	7298.1 ± 4235.2	6246.6 ± 3756.9†
Retinol, µg (diet)	490.1 ± 494.1†	818.9 ± 925.3	1106.4 ± 1337.5†
Vitamin C, mg (diet and supplements)	394.3 ± 399.8†	342.8 ± 380.1	279.1 ± 314.2†
Vitamin E, mg (supplements only)	38.3 ± 115.5†	26.7 ± 104.8	23.4 ± 91.3

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).

*Quintile 1, 9.9% to <27.3% of total energy; quintiles 2 to 4, 27.3% to 37.7% of total energy; quintile 5, 37.8% to 60.5% of total energy. Values are presented as mean ± SD unless otherwise stated.

†$P<.05$ by t test when compared with quintiles 2 through 4.

‡$P<.05$ by χ^2 test when compared with quintiles 2 through 4.

Table 2. ORs and CIs of 5-Year Incidence of ARM in BMES Participants With Lowest (Q1) and Highest (Q5) 20% of Dietary Fat Intake Compared With Middle 60% (Q2-4)*

	5-y Incidence, OR (95% CI)	
	Early ARM (n = 130)	Late ARM (n = 22)
Total dietary fat		
Q1 (9.9-<27.3)	1.71 (1.11-2.64)	1.27 (0.43-3.74)
Q2-4 (27.3-37.7)	1.00 (Reference)	1.00 (Reference)
Q5 (37.8-60.5)	0.92 (0.53-1.59)	1.19 (0.36-3.94)
Saturated fat		
Q1 (2.5-9.6)	0.99 (0.56-1.73)	0.37 (0.09-1.62)
Q2-4 (9.7-15.4)	1.00 (Reference)	1.00 (Reference)
Q5 (15.5-28.1)	1.01 (0.55-1.86)	1.90 (0.53-6.80)
Monounsaturated fat		
Q1 (2.8-9.6)	1.67 (0.93-3.00)	2.46 (0.67-9.06)
Q2-4 (9.7-13.4)	1.00 (Reference)	1.00 (Reference)
Q5 (13.5-21.1)	0.84 (0.45-1.58)	0.43 (0.08-2.32)
Polyunsaturated fat		
Q1 (1.0-3.8)	0.99 (0.60-1.63)	1.05 (0.34-3.22)
Q2-4 (3.9-7.1)	1.00 (Reference)	1.00 (Reference)
Q5 (7.2-15.5)	1.24 (0.73-2.12)	1.10 (0.27-4.48)
Trans-unsaturated fat		
Q1 (0-0.002)	1.15 (0.73-1.80)	1.51 (0.48-4.81)
Q2-4 (0.003-0.2)	1.00 (Reference)	1.00 (Reference)
Q5 (0.3-1.4)	0.64 (0.36-1.13)	1.76 (0.60-5.18)

Abbreviations: ARM, age-related maculopathy; BMES, Blue Mountains Eye Study[1]; CI, confidence interval; OR, odds ratio; Q, quintile.

*Quintiles represent dietary fat intake as a percentage of total energy intake. Models for subtypes of dietary fat are adjusted for age, sex, current smoking, vitamin C intake (diet and supplements), and other subtypes of dietary fat.

and higher intakes of vitamin C, beta carotene, and vitamin E than participants in the middle 3 quintiles. Participants with the highest level of dietary fat intake were more likely to smoke and to have significantly higher intakes of retinol and significantly lower intakes of beta carotene and vitamin C than participants in the middle 3 quintiles. To avoid potential bias and overestimating associations by using an unusual reference group, we used the middle 3 quintiles (population with "moderate" fat intakes) as the reference group to compare the risk of incident ARM for participants at either end of the dietary fat intake spectrum.

Table 2 summarizes the multivariable-adjusted odds of incident early and late ARM for persons having either the lowest or the highest intake compared with those within the middle 3 quintiles but taking into account concurrent intakes of other dietary fat subtypes (ie, SFAs, MUFAs, PUFAs, and *trans*-fats). Participants reporting the lowest quintile of total fat intake had a 70% higher risk of incident early ARM (OR, 1.71; 95% CI, 1.11-2.64). Participants with the lowest quintile of MUFA had a marginally nonsignificant increased likelihood of incident early ARM (OR, 1.67; 95% CI, 0.93-3.00). No significant association was found between dietary intakes of SFA, PUFA, and *trans*-fats and 5-year incident ARM.

Table 3 shows the odds of incident ARM for different components of dietary PUFA while adjusting for age, sex, current smoking, and vitamin C intake. We found that, compared with participants reporting moderate intakes, those within the lowest quintile of dietary n-3 PUFA intake had a marginally nonsignificant greater risk of 5-year incident early ARM (OR, 1.51; 95% CI, 0.98-2.33). Participants within the highest quintile of dietary n-3 PUFA intake did not have a significant association with either incident early or late ARM. Participants reporting the lowest quintile of intake of the essential fatty acid α-linolenic acid had a nonsignificant higher incidence of early ARM (OR, 1.48; 95% CI, 0.96-2.28). We did not find any association between intakes of n-6 PUFA, linoleic acid, or long-chain n-3 and incident ARM. There appeared, however, to be a nonsignificant, protective influence of long-chain n-3 PUFA for late ARM for those reporting the highest quintile of intake (OR, 0.18; 95% CI, 0.02-1.38).

We found no significant difference in the incidence of either early or late ARM by intakes of butter or margarine, rich sources of both dietary saturated and unsaturated fats, or with higher dietary intakes of nuts (**Table 4**). In contrast, compared with participants who reported no fish consumption or reported eating fish less than once a month, we found that those who reported eating at least 1 fish serving per week had a 40% lower risk of 5-year incident early ARM (OR, 0.58; 95% CI, 0.37-0.90). Significant risk reduction for incident late ARM, however, became apparent only for participants who reported consuming at least 3 servings of fish per week (OR, 0.25; 95% CI, 0.06-1.00).

Table 3. ORs and CIs of 5-Year Incidence of ARM in BMES Participants With Lowest (Q1) and Highest (Q5) 20% of Dietary Polyunsaturated Fat Components Compared With Middle 60% (Q2-4)*

	5-y Incidence, OR (95% CI)	
	Early ARM (n = 130)	Late ARM (n = 22)
Total n-3 polyunsaturated fatty acids		
Q1 (0.05-0.26)	1.51 (0.98-2.33)	0.95 (0.33-2.74)
Q2-4 (0.27-0.51)	1.00 (Reference)	1.00 (Reference)
Q5 (0.52-2.11)	0.65 (0.38-1.14)	0.39 (0.09-1.77)
α-Linolenic acid (18:3, n-3)		
Q1 (0.04-0.19)	1.48 (0.96-2.28)	0.68 (0.22-2.13)
Q2-4 (0.20-0.38)	1.00 (Reference)	1.00 (Reference)
Q5 (0.39-1.39)	0.73 (0.42-1.29)	0.44 (0.10-1.98)
Long-chain n-3 polyunsaturated fatty acids		
Q1 (0-0.033)	1.31 (0.82-2.09)	0.93 (0.32-2.69)
Q2-4 (0.033-0.148)	1.00 (Reference)	1.00 (Reference)
Q5 (0.149-1.456)	0.92 (0.57-1.51)	0.18 (0.02-1.38)
Total n-6 polyunsaturated fatty acids		
Q1 (0.66-2.12)	1.19 (0.75-1.88)	1.70 (0.64-4.52)
Q2-4 (2.13-4.29)	1.00 (Reference)	1.00 (Reference)
Q5 (4.30-11.09)	0.81 (0.48-1.38)	0.58 (0.13-2.64)
Linoleic acid (18:2, n-6)		
Q1 (0.66-2.11)	1.19 (0.75-1.88)	1.70 (0.64-4.52)
Q2-4 (2.12-4.28)	1.00 (Reference)	1.00 (Reference)
Q5 (4.29-11.03)	0.81 (0.48-1.38)	0.58 (0.13-2.64)
Arachidonic acid (20:4, n-6)		
Q1 (0-0.002)	1.22 (0.78-1.93)	1.02 (0.34-3.07)
Q2-4 (0.002-0.010)	1.00 (Reference)	1.00 (Reference)
Q5 (0.011-0.059)	0.75 (0.46-1.28)	1.04 (0.32-3.34)

Abbreviations: ARM, age-related maculopathy; BMES, Blue Mountains Eye Study[1]; CI, confidence interval; OR, odds ratio; Q, quintile.

*Quintiles represent dietary fat intake as a percentage of total energy intake. Components are adjusted for age, sex, current smoking, and vitamin C intake (diet and supplements).

Table 4. ORs and CIs of Early and Late ARM With Increasing Frequency of Certain Food Types in BMES Participants*

	5-y Incidence, OR (95% CI)	
	Early ARM (n = 130)	Late ARM (n = 22)
Margarine		
<1/wk	1.00 (Reference)	1.00 (Reference)
1-6/wk	0.89 (0.57-1.38)	1.55 (0.44-5.40)
Daily	0.87 (0.58-1.29)	0.85 (0.33-2.22)
Butter		
<1/wk	1.00 (Reference)	1.00 (Reference)
1-6/wk	0.48 (0.22-1.02)	0.82 (0.18-3.76)
Daily	0.77 (0.48-1.24)	0.85 (0.27-2.66)
Total fish†		
<1/mo	1.00 (Reference)	1.00 (Reference)
≥1/wk	0.58 (0.37-0.90)	0.44 (0.16-1.21)
≥3/wk	0.62 (0.38-1.03)	0.25 (0.06-1.00)
Nuts		
Never	1.00 (Reference)	1.00 (Reference)
<1/wk	0.80 (0.52-1.25)	0.82 (0.29-2.34)
≥1/wk	0.79 (0.46-1.34)	0.55 (0.14-2.16)

Abbreviations: ARM, age-related maculopathy; BMES, Blue Mountains Eye Study[1]; CI, confidence interval; OR, odds ratio.

*Food types are categorized by frequency of servings.

†Includes sardines, tuna, and other fish.

COMMENT

To our knowledge, this is the first cohort study of longitudinal association between dietary fat intakes and incident ARM in a representative older population. Our findings indicate that participants reporting total dietary fat intake in the lowest quintile of the population had around a 70% increased likelihood of incident early ARM after 5 years, compared with most of the population reporting a moderate intake. We also found that participants within the lowest intake of dietary MUFA and n-3 PUFA, particularly the n-3 essential fatty acid α-linolenic acid, may be at increased risk of incident early ARM after simultaneously adjusting for the intakes of other fatty acid subtypes. A weekly intake of fish was found to protect against development of both early and late ARM in this older Australian cohort.

The current American dietary guidelines recommend dietary fat intakes between 20% and 35% of energy intake.[23] Individuals whose dietary fat consumption is less than 20% of total energy intake may have inadequate intakes of essential fatty acids. Considering that (1) participants in our study reporting the lowest quintile of total dietary fat intake had different risk profiles for ARM than other intake groups, (2) a high proportion of this group also had less than 20% of energy intake from fat, and (3) our FFQ was previously shown to overestimate total dietary fat,[17] we decided to use the middle 3 quintiles of intake as our reference group to determine the risk of incident ARM among participants at either end of the dietary fat intake spectrum. We believe that this was a reasonable and conservative approach, leading only to underestimates of associations examined in this study.

To explain our findings, we suggest that insufficient essential fatty acid intake could result in abnormal retinal metabolism and cell renewal. Studies have shown cardioprotective benefits of MUFA in the Mediterranean diet and that diets high in n-3 fatty acids, particularly docosahexaenoic acid, derived largely from fish, may protect against retinal oxidation and degeneration.[11-14] Our finding that at least weekly fish consumption was protective against incident early ARM provides support for this hypothesis. It is also in keeping with our group's earlier cross-sectional report.[24]

We could not confirm the previously reported[4-6] increased risk of incident ARM from high dietary intakes of unsaturated fat, including MUFAs and PUFAs. Our findings from a representative older population caution against altering current advice regarding dietary fat recommendations to the community.

Previous reports examining associations between dietary fat and ARM require further discussion. Seddon et al[5] examined a highly selected cohort of hospital-based older patients and found that higher total dietary fats, SFAs, MUFAs, PUFAs, *trans*-fats, and vegetable oils increased the risk of ARM progression. Their study reported findings from 261 of 366 participants (71.3% of enrollment), where 101 (38.7%) of the 261 individuals showed evidence of ARM progression. This rate of progression is significantly higher than that in reports from general populations[1,25] and may not be directly applicable to general older populations. Second, their recruitment period spanned almost 9 years (1989-1998), and data from 22% of participants were obtained more than 7 years after recruitment, potentially biasing (dietary) behavior after disease diagnosis. Third, models used in that study did not simultaneously adjust for intakes of the other types or subclasses of dietary fat. Because participants with high total fat intakes are more likely to have high intakes of all fat subtypes, it can be difficult to separate influences of one subclass from that of the total fat intake. This may account for the similarity in the findings of increased risk of ARM progression across increasing intakes of all types and subclasses of dietary fats.

Cho et al[6] reported results from a series of 567 participants derived from a total pool of 71 486 women and 41 474 men older than 50 years from the Nurses Health Study and the Health Professionals Follow-up Study, 2 highly selected health professional cohort populations. The 10-year late ARM incidence was 0.5%, significantly lower than the 1% incidence reported from both the Beaver Dam Eye Study[2] and BMES populations (J.J.W., E.R., A. J. Lee, MBBS, E.-M. Chia, MBBS, W.S., R. G. Cumming, MBBS, PhD, and P.M., unpublished data, 2005). The lower incidence of late ARM could be due to younger age (56-57 years in women and 60-61 years in men compared with a mean of 64 years in the BMES) and a much healthier population in these 2 studies than in either the Beaver Dam Eye Study or the BMES. Alternatively, it suggests underreporting or misclassification of incident cases and controls, as incident ARM cases were initially self-reported and only later confirmed by the treating ophthalmologist. Interestingly, the analyses in the article by Cho et al[6] also adjusted simultaneously for intakes of other types of dietary fat and did not show significant association between incident late ARM and increasing dietary intakes of vegetable or unsaturated fats.

Direct comparisons between our study and the studies by Seddon et al[5] and Cho et al[6] were limited by different definitions of early and late ARM and differences in fatty acid composition between Australian and US food products. The contribution of *trans*-fats in the United States has been estimated as 1% to 2% of total energy intake,[16,26] compared with 0.15% in the BMES. Food-processing changes during the last decade have reduced the proportion of *trans*-fats in processed foods in Australia[27,28] while similar *trans*-fats trends are occurring in the United States.[23] Additionally, we chose to compare the risk from excessive or insufficient intakes of dietary fats with that of the moderate or normal intakes to minimize potential confounding effects or overestimation of the association, avoiding potential misleading results.

Key strengths of our study include its representative, population-based sample with relatively high participation, minimizing selection bias. Second, study participants were unaware of the study question and our dietary data were collected before detection of 5-year incident ARM, reducing indication bias arising from behavioral change after the disease was diagnosed. Third, our definition of ARM was defined from retinal photographic grading. Fourth, we attempted to examine association between each dietary fat component and ARM incidence, and we simultaneously adjusted for dietary intakes of other classes. Finally, we examined the risk of incident ARM in participants with the lowest and highest quintiles of dietary fat intakes with respect to the middle 60% of the population, who represent a moderate or normal intake. Our decision to use the middle 3 quintiles as the reference group was likely to underestimate the associations and thus to bias our findings only toward the null. On the other hand, our study was limited by a much smaller number of incident late ARM cases than in the reported case series and hospital-based cohorts. Further research using 10-year incident data will provide greater study power to investigate any potential protective effects of long-chain n-3 PUFA against the development of late ARM.

In summary, our findings do not support any adverse associations between high intakes of dietary fats or subtypes and the incidence of either early or late ARM, but they support a previous finding that weekly dietary intake of fish protects against the development of both early and late ARM. Consumption of nuts was not shown to be protective. Butter and margarine were not found to be significantly associated with risk of incident ARM. We found an apparent, although nonsignificant, increased risk of incident early ARM with low intakes of monounsaturated and n-3 polyunsaturated fat, contrary to data from some recent studies. Future collaboration and pooling of data from other population-based cohort studies will be useful to further examine potentially significant modifiable dietary risk factors for ARM.

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