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Overall diet quality and age-related macular degeneration

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Abstract

Objective—To examine overall diet quality in relation to advanced age-related macular degeneration (AMD).

Methods—This case-control study identified 437 advanced AMD patients and 259 unrelated controls using stereoscopic color fundus photographs. Participants were predominantly non-Hispanic white men and women from North Carolina and Tennessee. A 97-item Block food frequency questionnaire was used to gather diet information, and overall diet quality was measured using the Healthy Eating Index (HEI) and Alternate Healthy Eating Index (AHEI).

Results—Participants in the highest quartile of diet quality had significantly reduced odds of AMD according to the AHEI score (0.54, 95% confidence interval 0.30 – 0.99) and non-significantly reduced odds of AMD according to the HEI (0.75, 0.41 – 1.38). Odds of AMD were also 51% lower in the highest quartile of fish intake compared to the lowest quartile (odds ratio = 0.49, 0.26 – 0.90).

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Conclusions—We found that advanced AMD was significantly related to overall diet quality. The AHEI score may be a useful instrument for assessing AMD risk due to diet, and it could potentially be improved by incorporating more specific information regarding micronutrient intake.

INTRODUCTION

Identifying modifiable risk factors for age-related macular degeneration (AMD), the most common cause of blindness in developed countries,¹ is becoming increasingly important as many of these countries confront aging demographic profiles. Diet is one potentially modifiable risk factor, and different nutritional factors, including antioxidants and lipids, are believed to influence the development and/or progression of AMD. Different dietary components, however, are not entirely independent since the elimination of one food often leads to substitution with another food. Rather than focus on one particular component of diet, we decided to examine AMD risk in relation to overall diet quality. The advantage to using a composite score for overall diet quality is that it can better account for inherent relationships among different diet components and could serve as a tool to guide diet patterns of patients in early stages or at high risk of AMD. There is one individual food component, grams of fish intake, that we considered because it has been consistently cited in other dietary studies of AMD.^{2–5}

Several composite dietary scores have been designed and adapted to reflect current guidelines and understandings of how nutrition is related to morbidity and mortality. Our goal was to identify a pre-defined score that would emphasize dietary factors believed to be related to AMD. Based on a literature review^{6–17} we chose the Healthy Eating Index (HEI) and the Alternate Healthy Eating Index (AHEI). The HEI was developed as a general measure of diet quality while the AHEI was adjusted to capture dietary factors specifically related to cardiovascular disease risk. Both scores have been shown to be predictive of cardiovascular disease risk.^{18–20} Because AMD shares many risk factors with cardiovascular disease,²¹ we hypothesized that these measures of diet quality may also be associated with AMD risk. We tested this hypothesis using data from a case-control study conducted by two centers in the Southeastern U. S. designed to study genetic and environmental factors associated with AMD.

METHODS

Population

The study population included 840 predominantly non-Hispanic white men and women over the age of 55 who were recruited between July 2000 and October 2007. Participants were examined at Duke University Eye Center (DUEC), Vanderbilt University Medical Center (VUMC), or collaborating retinal specialty clinics. AMD patients who attended these clinics were recruited as cases. Study advertisements in center-specific newsletters, AMD-related seminars for the general public, and presentations at local retirement centers were used to recruit controls who were at least 55 years old and likely to receive eye exams at DUEC or VUMC. The study was approved by the institutional review boards of Duke University Medical Center, Vanderbilt University Medical Center, and the University of Miami Miller School of Medicine. All study participants provided informed consent prior to participation.

Outcome

The primary outcome of the study was the presence or absence of advanced AMD. Stereoscopic color fundus photographs obtained on all cases and controls were used to assign an AMD grade of 1 through 5 in the more severely affected eye using a slightly

modified Age-Related Eye Disease Study grading system as described previously.²² Advanced AMD cases were defined as grades 4 (geographic atrophy- area of retinal pigment epithelium atrophy with sharp margins, usually visible choroidal vessels, at least 175 μ m in diameter) and 5 (exudative AMD including nondrusenoid retinal pigment epithelium detachment, choroidal neovascularization, subretinal hemorrhage or fibrosis, or photocoagulation scar consistent with treatment of AMD). Controls included grades 1 (no drusen or nonextensive small (<63 μ m) drusen without retinal pigment epithelium abnormalities) and 2 (extensive small drusen or nonextensive intermediate (>63 μ m and <125 μ m) drusen and/or retinal pigment epithelium hyper- or hypopigmentation). A sensitivity analysis excluding grade 2 participants from the control group was conducted. Participants identified as grade 3 (extensive intermediate drusen or any large (>125 μ m), soft drusen, including drusenoid RPE detachment) were not included in the analysis.

Dietary information

Participants completed a 97-item Block food frequency questionnaire, slightly modified for regional preferences from the original 97-item questionnaire,²³ to collect information on dietary history over the year prior to study enrollment. Participants reported how often and how much of each food they consumed. There were nine options for frequency, ranging from never or less than once per month to two or more times per day. Participants indicated quantity according to either small, medium, or large portions, and the definition for a medium serving size was listed on the questionnaire.

Daily food group frequencies and daily nutrient intake were calculated using HHHQ-DietSys Analysis Software version 4.02 (National Cancer Institute, Bethesda, MD). Food groups were defined for each diet score as described by the references cited.^{10, 11} Mixed foods were permitted to contribute to multiple food groups. Participants also completed a self-administered health and activities survey which included information on level of education, frequency and duration of smoking, and use of vitamin and mineral supplements.

We calculated diet scores using both the Healthy Eating Index¹⁰ and an updated version, the Alternate Healthy Eating Index.¹¹ In short, the HEI includes ten components, each of which ranged from 0 to 10 for a total score ranging from 0 (poorest quality) to 100 (highest quality). The components were based on five food groups (grains, vegetables, fruits, milk, and meat) and five dietary guidelines (total fat, saturated fat, cholesterol, sodium, and variety). We followed the cited cutoff values for high and low intake in each component and scored intermediate intake values linearly. The variety component was calculated according to the 1999–2000 HEI scoring system²⁴ in which the minimum criterion was three or fewer different items consumed in a day and the maximum criterion was 8 or more different items consumed in a day.

The AHEI was based on the HEI with the following modifications. First, the milk group was removed and a nuts and soy group was added. Second, a ratio of white to red meat replaced the meat group in the original score. Because our questionnaire contained a disproportionate number of red meat compared to white meat items, grams of meat consumed were divided by the total number of items before taking the ratio. Third, instead of separate components for total fat and saturated fat, the AHEI used a polyunsaturated to saturated fat ratio and added a component for *trans*-unsaturated fats. Because *trans*-unsaturated fats were not calculated automatically in the DietSys software, we collected this information primarily from the U.S. Department of Agriculture Nutrient Data Laboratory.²⁵ Lastly, the AHEI accounted for duration of multivitamin use and alcohol consumption for a total of nine components and an overall range from 2.5 (poorest) to 87.5 (highest).

Statistical analyses

Statistical analyses were conducted using SAS version 9.1 (SAS Institute Inc., Cary, NC). Pearson correlation coefficients were used to estimate correlation. Odds ratios and 95% confidence intervals were estimated using multiple logistic regression. Age (under 65, 65–69, 70–74, 75–79, 80–84, 85 and older), smoking (ever/never), study site, sex, total energy intake (quartiles) and education (less than high school, high school graduate or GED, some college, college graduate) were included as covariates in fully adjusted models. Age and smoking were included *a priori* because of their strong relationship with AMD, and total energy intake was included because it is a standard approach in diet analyses.²⁶ All other covariates were selected because in linear regression analyses they were related to diet scores in both cases and controls. Body mass index was associated with diet scores but had no appreciable effect on the results. Because body mass index was missing for 10% of participants, it was not included in final models.

We excluded participants who were missing more than 25 items on the food frequency questionnaire (N = 48, 6%) or who reported unusually low (<500 Kcal for women; <800 Kcal for men) or high (>3,500 Kcal for women; >4000 Kcal for men) daily energy intake (N = 70, 8%). Controls who were spouses of the cases (N = 17, 2%) and participants who were missing essential covariate information (N = 9, 1%) were also excluded.

RESULTS

Final analyses included a total of 437 advanced AMD cases (75 grade 4; 362 grade 5) and 259 controls (181 grade 1; 78 grade 2). AMD was positively associated with both age and smoking and inversely associated with level of education (Table 1). There was no significant association of AMD with either body mass index or total energy intake. There was also no significant difference between cases and controls in reporting a change in diet in the past 10 years.

The distributions of both scores for our study population compared to the populations used to develop the scores are shown in Table 2. The current study population had an average HEI score similar to that of the HEI cohort, and the distribution of scores was comparable. In contrast, the AHEI distribution was lower for the current study compared to both the male and female cohorts used in the AHEI score development.

For overall diet quality, participants in the present study had an average HEI score of 65.0 (standard deviation 13.7), which ranged from 30.8 to 95.0. For the AHEI, participants had an average score of 30.7 (standard deviation 9.0) ranging from 10.4 to 61.2. Significantly decreased odds of AMD were observed in the highest quartile compared to the lowest quartile of diet quality using the AHEI score but not using the HEI (Table 3). Restricting the control group to only grade 1 participants decreased the precision of the estimates but did not alter the conclusions drawn.

Based on other published findings in the literature,^{2–5} we examined one individual diet component, which was daily grams of fish intake. The odds of AMD were 51% lower in the highest compared to lowest quartile of fish intake (Table 3).

DISCUSSION

This analysis is one of the first attempts to evaluate the association between overall diet quality and age-related macular degeneration. After adjusting for potential confounding factors, we found that the odds of AMD were halved for participants in the highest quartile compared to the lowest quartile of AHEI-measured diet quality. Odds of AMD were also

reduced when comparing the highest and lowest quartiles of the HEI, but the difference was not statistically significant and there was no strong indication of dose-response. Thus, for AMD as for cardiovascular disease,^{11, 19} there was an inverse relationship between overall diet quality and risk of disease.

We found that the distribution of the HEI was similar to and that of the AHEI was slightly lower than the original populations used to develop the scores. In the case of the HEI, the AMD population had slightly higher diet quality than the participants of the 1989 and 1990 Continuing Survey of Food Intake by Individuals,¹⁰ which included persons 2 years of age and older and was intended to be a nationally representative sample of the U.S. population. In comparison, the AHEI was developed based on the Health Professional's Follow-up Study for men and the Nurses' Health Study for women,¹¹ both of which were populations whose dietary habits were likely to be healthier than the population average. It was not surprising, therefore, that our study population scored lower on the AHEI than either of these cohorts. Nevertheless, the distribution of both scores across the AMD sample showed sufficient variability to be able to distinguish between different levels of diet quality.

The Healthy Eating Index was developed to measure how closely a person's diet followed recommendations put forth in the U.S. Dietary Guidelines for Americans. Modeled after the HEI, the AHEI made specific modifications to incorporate nutritional parameters related to chronic disease risk, particularly cardiovascular disease. As a result, researchers found that the AHEI performed better for predicting cardiovascular disease risk than the HEI.^{11, 19} Similarly, in our study the larger reduction in odds of AMD associated with dietary quality measured by the AHEI as compared to the HEI suggests that the AHEI score reflects dietary factors that are more relevant to AMD risk. One of the major differences between the HEI and the AHEI was the emphasis on fat quality in addition to fat quantity. This was reflected in two particular modifications. The first was the change of the meat group component to a ratio of white to red meat. The second was the incorporation of a polysaturated to saturated fat ratio. The larger difference in odds of AMD between high and low diet qualities in the AHEI score compared to the HEI score indicates that recognizing a difference in fat type may be important in evaluating AMD risk with respect to diet quality.

Although reports on specific subtypes of lipids have not always been consistent, several cross-sectional studies have reported an inverse association of AMD with omega-3 fatty acids.^{2, 27, 28} One of the most consistent findings suggesting that lipid type may play a role in AMD is an inverse association with the number of servings of fish,^{2-5, 29} which would support a protective effect of omega-3 fatty acids. Our finding that participants in the highest quartile of fish intake had a 51% reduced odds of AMD compared to the lowest quartile supports this hypothesis. Furthermore, fish intake was more highly correlated with the AHEI score (0.26, $p < 0.0001$) than the HEI score (0.06, $p = 0.1136$) indicating that the AHEI score was better adapted to capture differences in participants' levels of fish intake. This may partially explain the stronger correlation between the AHEI score and AMD.

Another aspect of nutrition believed to play a role in AMD risk is consumption of micronutrients, particularly antioxidants. In randomized clinical trials, for example, a daily supplement of vitamin C, vitamin E, beta-carotene, and zinc (the AREDS combination) significantly slowed the progression of AMD.³⁰ Studies in both animals^{31, 32} and humans^{33, 34} suggest a potential benefit from the macular carotenoids, lutein and zeaxanthin, although other studies have found no such association.³⁵⁻³⁷ Many authors have argued that current evidence to establish the effect of these nutrients is insufficient,^{38, 39} and further studies are in progress to investigate this question.⁴⁰ Although none of these micronutrients were directly incorporated into either the HEI or the AHEI, higher HEI scores have been shown to correlate with higher plasma concentrations of beta-carotene, vitamin C, and

lutein.⁴¹ The number of participants in our study who had taken the AREDS combination for a minimum of five years was too small to conduct an adequately powered analysis. Incorporating specific micronutrients known to be protective for AMD into future diet scores may improve the ability of diet scores to predict AMD risk.

These findings are preliminary in nature due to the relatively small sample size and retrospective design (where dietary habits were reported after diagnosis). However, it is reassuring to note that cases were not more likely than controls to report having changed their diet in the past ten years. Furthermore, when analyses were restricted to the population which reported no change in diet in the past ten years, the results were either similar or stronger, albeit with wider confidence intervals owing to the reduced sample size. Another potential limitation is that the average age of cases was older than that of controls. Age, therefore, could be a potential confounder of the association between diet and AMD if it was associated with both diet and AMD. Age was positively associated with the HEI score (older participants had a higher average diet score) but was not significantly associated with the AHEI score. Because age was positively associated with both diet score and AMD, it could potentially have led to an underestimation of the association, but residual confounding by age is unlikely to have created a spurious inverse association.

In conclusion, this study provides evidence that overall diet quality may play an important role in modulating the risk of AMD. Our results also support the general hypothesis that AMD shares multiple risk factors with cardiovascular disease. Finally, this study suggests that the Alternate Healthy Eating Index may be a useful instrument for identifying diet patterns associated with lower AMD risk.

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Abbreviations

AHEI	alternate healthy eating index
AMD	age-related macular degeneration
HEI	healthy eating index

REFERENCES

1. Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. *Bull World Health Organ.* 2004; 82:844–851. [PubMed: 15640920]
2. Seddon JM, Rosner B, Sperduto RD, et al. Dietary fat and risk for advanced age-related macular degeneration. *Arch Ophthalmol.* 2001; 119:1191–1199. [PubMed: 11483088]
3. Smith W, Mitchell P, Leeder SR. Dietary fat and fish intake and age-related maculopathy. *Arch Ophthalmol.* 2000; 118:401–404. [PubMed: 10721964]
4. Cho E, Hung S, Willett WC, et al. Prospective study of dietary fat and the risk of age-related macular degeneration. *Am J Clin Nutr.* 2001; 73:209–218. [PubMed: 11157315]

5. Seddon JM, Cote J, Rosner B. Progression of age-related macular degeneration: association with dietary fat, transunsaturated fat, nuts, and fish intake. *Arch Ophthalmol*. 2003; 121:1728–1737. [PubMed: 14662593]
6. Patterson RE, Haines PS, Popkin BM. Diet quality index: capturing a multidimensional behavior. *J Am Diet Assoc*. 1994; 94:57–64. [PubMed: 8270756]
7. Gerber MJ, Scali JD, Michaud A, et al. Profiles of a healthful diet and its relationship to biomarkers in a population sample from Mediterranean southern France. *J Am Diet Assoc*. 2000; 100:1164–1171. [PubMed: 11043701]
8. Haines PS, Siega-Riz AM, Popkin BM. The Diet Quality Index revised: a measurement instrument for populations. *J Am Diet Assoc*. 1999; 99:697–704. [PubMed: 10361532]
9. Kim S, Haines PS, Siega-Riz AM, Popkin BM. The Diet Quality Index-International (DQI-I) provides an effective tool for cross-national comparison of diet quality as illustrated by China and the United States. *J Nutr*. 2003; 133:3476–3484. [PubMed: 14608061]
10. Kennedy ET, Ohls J, Carlson S, Fleming K. The Healthy Eating Index: design and applications. *J Am Diet Assoc*. 1995; 95:1103–1108. [PubMed: 7560680]
11. McCullough ML, Feskanich D, Stampfer MJ, et al. Diet quality and major chronic disease risk in men and women: moving toward improved dietary guidance. *Am J Clin Nutr*. 2002; 76:1261–1271. [PubMed: 12450892]
12. Trichopoulou A, Kouris-Blazos A, Wahlqvist ML, et al. Diet and overall survival in elderly people. *BMJ*. 1995; 311:1457–1460. [PubMed: 8520331]
13. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med*. 2003; 348:2599–2608. [PubMed: 12826634]
14. Trichopoulou A, Orfanos P, Norat T, et al. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. *BMJ*. 2005; 330:991. [PubMed: 15820966]
15. Fung TT, McCullough ML, Newby PK, et al. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. *Am J Clin Nutr*. 2005; 82:163–173. [PubMed: 16002815]
16. Dubois L, Girard M, Bergeron N. The choice of a diet quality indicator to evaluate the nutritional health of populations. *Public Health Nutr*. 2000; 3:357–365. [PubMed: 10979155]
17. Waijers PM, Feskens EJ, Ocke MC. A critical review of predefined diet quality scores. *Br J Nutr*. 2007; 97:219–231. [PubMed: 17298689]
18. McCullough ML, Feskanich D, Stampfer MJ, et al. Adherence to the Dietary Guidelines for Americans and risk of major chronic disease in women. *Am J Clin Nutr*. 2000; 72:1214–1222. [PubMed: 11063452]
19. McCullough ML, Willett WC. Evaluating adherence to recommended diets in adults: the Alternate Healthy Eating Index. *Public Health Nutr*. 2006; 9:152–157. [PubMed: 16512963]
20. McCullough ML, Feskanich D, Rimm EB, et al. Adherence to the Dietary Guidelines for Americans and risk of major chronic disease in men. *Am J Clin Nutr*. 2000; 72:1223–1231. [PubMed: 11063453]
21. Guymer RH, Chong EW. Modifiable risk factors for age-related macular degeneration. *Med J Aust*. 2006; 184:455–458. [PubMed: 16646746]
22. Schmidt S, Saunders AM, De La Paz MA, et al. Association of the apolipoprotein E gene with age-related macular degeneration: possible effect modification by family history, age, and gender. *Mol Vis*. 2000; 6:287–293. [PubMed: 11141572]
23. Block G, Hartman AM, Dresser CM, Carroll MD, Gannon J, Gardner L. A data-based approach to diet questionnaire design and testing. *Am J Epidemiol*. 1986; 124:453–469. [PubMed: 3740045]
24. Basiotis PP, Carlson A, Gerrior SA, Juan WY, Lino M. The Healthy Eating Index: 1999–2000. Center for Nutrition Policy and Promotion. U. S. Department of Agriculture. 2002
25. U.S. Department of Agriculture. Fat and Fatty Acid Content of Selected Foods Containing Trans-Fatty Acids. 1993.
26. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr*. 1997; 65:1220S–1228S. discussion 1229S–1231S. [PubMed: 9094926]

27. Seddon JM, George S, Rosner B. Cigarette smoking, fish consumption, omega-3 fatty acid intake, and associations with age-related macular degeneration: the US Twin Study of Age-Related Macular Degeneration. *Arch Ophthalmol*. 2006; 124:995–1001. [PubMed: 16832023]
28. AREDS. The Relationship of Dietary Lipid Intake and Age-Related Macular Degeneration in a Case-Control Study: AREDS Report No. 20. *Arch Ophthalmol*. 2007; 125:671–679. [PubMed: 17502507]
29. Chua B, Flood V, Rochtchina E, Wang JJ, Smith W, Mitchell P. Dietary fatty acids and the 5-year incidence of age-related maculopathy. *Arch Ophthalmol*. 2006; 124:981–986. [PubMed: 16832021]
30. AREDS. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. *Arch Ophthalmol*. 2001; 119:1417–1436. [PubMed: 11594942]
31. Izumi-Nagai K, Nagai N, Ohgami K, et al. Macular Pigment Lutein Is Antiinflammatory in Preventing Choroidal Neovascularization. *Arterioscler Thromb Vasc Biol*. 2007
32. Chucair AJ, Rotstein NP, Sangiovanni JP, During A, Chew EY, Politi LE. Lutein and zeaxanthin protect photoreceptors from apoptosis induced by oxidative stress: relation with docosahexaenoic acid. *Invest Ophthalmol Vis Sci*. 2007; 48:5168–5177. [PubMed: 17962470]
33. Parisi V, Tedeschi M, Gallinaro G, Varano M, Saviano S, Piermarocchi S. Carotenoids and Antioxidants in Age-Related Maculopathy Italian Study Multifocal Electoretinogram Modifications after 1 Year. *Ophthalmology*. 2007
34. Richer S, Stiles W, Statkute L, et al. Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial). *Optometry*. 2004; 75:216–230. [PubMed: 15117055]
35. Dasch B, Fuhs A, Schmidt J, et al. Serum levels of macular carotenoids in relation to age-related maculopathy: the Muenster Aging and Retina Study (MARS). *Graefes Arch Clin Exp Ophthalmol*. 2005; 243:1028–1035. [PubMed: 15909159]
36. Bartlett HE, Eperjesi F. Effect of lutein and antioxidant dietary supplementation on contrast sensitivity in age-related macular disease: a randomized controlled trial. *Eur J Clin Nutr*. 2007
37. Morris MS, Jacques PF, Chylack LT, et al. Intake of zinc and antioxidant micronutrients and early age-related maculopathy lesions. *Ophthalmic Epidemiol*. 2007; 14:288–298. [PubMed: 17994438]
38. Mozaffarieh M, Sacu S, Wedrich A. The role of the carotenoids, lutein and zeaxanthin, in protecting against age-related macular degeneration: a review based on controversial evidence. *Nutr J*. 2003; 2:20. [PubMed: 14670087]
39. Chong EW, Wong TY, Kreis AJ, Simpson JA, Guymer RH. Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis. *BMJ*. 2007; 335:755. [PubMed: 17923720]
40. Seddon JM. Multivitamin-multimineral supplements and eye disease: age-related macular degeneration and cataract. *Am J Clin Nutr*. 2007; 85:304S–307S. [PubMed: 17209215]
41. Hann CS, Rock CL, King I, Drewnowski A. Validation of the Healthy Eating Index with use of plasma biomarkers in a clinical sample of women. *Am J Clin Nutr*. 2001; 74:479–486. [PubMed: 11566646]

Table 1

General study population characteristics of age-related macular degeneration cases and controls.

Characteristic	Cases	%	Controls	%	Age-adjusted OR, 95% CI		Fully adjusted* OR, 95% CI	
Age at exam								
Under 65	21	5	126	49	0.2	0.1	0.1	0.2
65-69	51	12	48	19	1.0	Referent	1.0	Referent
70-74	96	22	36	14	2.5	1.4	2.2	1.2
75-79	106	24	38	15	2.6	1.5	2.6	1.4
80-84	95	22	7	3	12.8	5.4	11.9	4.9
85 and older	68	16	4	2	16.0	5.4	16.7	5.5
Smoke								
Never	172	39	133	51	1.0	Referent	1.0	Referent
Ever	265	61	126	49	2.2	1.5	2.9	1.9
Years of smoking								
Never	172	42	133	54	1.0	Referent	1.0	Referent
Up to 12	32	8	33	13	1.1	0.6	1.4	0.7
12 to 30	54	13	38	15	1.8	1.0	2.6	1.4
30 to 44	70	17	29	12	3.0	1.6	4.2	2.2
More than 44	86	21	15	6	4.2	2.1	4.9	2.4
Sex								
Male	153	35	103	40	1.0	Referent	1.0	Referent
Female	284	65	156	60	1.4	0.9	1.5	1.0
Education								
< High school	115	26	39	15	1.0	Referent	1.0	Referent
High school or GED	110	25	40	15	1.1	0.6	1.1	0.6
Some college	91	21	50	19	0.7	0.4	0.6	0.3
College graduate	121	28	130	50	0.4	0.2	0.3	0.2
Body mass index (kg/m ²)								
Less than 25	160	41	90	38	0.7	0.4	0.8	0.5
								1.3

Characteristic	Cases	%	Controls	%	Age-adjusted OR, 95% CI		Fully adjusted* OR, 95% CI	
25 to 30	161	42	87	37	1.0	Referent	1.0	Referent
30 or more	66	17	59	25	0.8	0.5	0.8	0.4
Study site								
Vanderbilt	210	48	110	42	1.0	Referent	1.0	Referent
Duke	227	52	149	58	1.0	0.7	1.2	0.8
Diet change 10y								
No	155	37	71	28	1.0	Referent	1.0	Referent
Yes	264	63	182	72	0.9	0.6	0.9	0.6
Total energy intake, sex-specific								
1st quartile	117	27	57	22	1.0	Referent	1.0	Referent
2nd quartile	109	25	65	25	1.1	0.6	1.1	0.6
3rd quartile	102	23	72	28	0.8	0.5	0.9	0.5
4th quartile	109	25	65	25	0.9	0.5	0.8	0.5

* Adjusted for age (under 65, 65–69, 70–74, 75–79, 80–84, 85 and older), smoking (ever/never), study site, sex, education (<high school, high school or GED, some college, college grad), and sex-specific total energy intake (quartiles)

Table 2

Comparison of diet scores in the current study population and the populations used to design the scores.

	Healthy Eating Index			Alternate Healthy Eating Index		
				McCullough 2002	Current study	
	Kennedy 1995	Current study		Men	Women	
Overall mean score	63.9	65.0	Overall mean (standard deviation)	45.0 (+/- 11.1)	38.4 (+/- 10.3)	30.7 (+/- 9.0)
Distribution of scores by percent:						
<30	<0.5	0.0	Range	8.8 – 86.0	9.8 – 83.6	10.4 – 61.2
31 – 40	2.3	3.6				
41 – 50	11.8	14.1	Median score by quintile			
51 – 60	24.4	18.4	1st	31.0	25.4	19.8
61 – 70	28.7	25.7	2nd	38.5	32.3	25.0
71 – 80	21.3	22.7	3rd	44.4	37.7	29.8
81 – 90	10.0	13.9	4th	50.1	43.5	34.8
>90	1.4	1.6	5th	59.9	52.3	42.8

Table 3

Odds ratios for advanced AMD by diet scores and fish consumption.

Quartiles	Cases	%	Controls	%	Age-adjusted OR, 95% CI	Fully adjusted* OR, 95% CI	p-value [†]
Healthy Eating Index							
1st (poor)	115	26	59	23	1.00	Referent	
2nd	107	24	63	24	0.68	0.39 1.19	0.40 1.31
3rd	101	23	77	30	0.43	0.25 0.74	0.25 0.81
4th (good)	114	26	60	23	0.64	0.37 1.11	0.41 1.38
Alternate Healthy Eating Index							
1st (poor)	114	26	60	23	1.00	Referent	
2nd	109	25	63	24	0.56	0.32 0.97	0.32 1.04
3rd	116	27	59	23	0.53	0.30 0.93	0.30 1.01
4th (good)	98	22	77	30	0.49	0.28 0.86	0.30 0.99
Fish intake (daily grams)							
1st (lowest)	125	29	46	18	1.00	Referent	
2nd	111	25	64	25	0.55	0.31 0.97	0.30 0.99
3rd	106	24	67	26	0.63	0.35 1.11	0.32 1.09
4th (highest)	95	22	82	32	0.46	0.26 0.80	0.26 0.90

* Adjusted for age (under 65, 65–69, 70–74, 75–79, 80–84, 85 and older), smoking (ever/never), study site, sex, education (<high school, high school or GED, some college, college grad), and sex-specific total energy intake (quartiles)

[†] Chi-square test for trend