

Published in final edited form as:

Am J Ophthalmol. 2014 July ; 158(1): 118–127.e1. doi:10.1016/j.ajo.2014.04.016.

The Relationship of Major American Dietary Patterns to Age-related Macular Degeneration

Chung-Jung Chiu, DDS, PhD, Min-Lee Chang, MS, Fang Fang Zhang, PhD, Tricia Li, MS, Gary Gensler, MS, Molly Schleicher, BS, and Allen Taylor, PhD

Jean Mayer United States Department of Agriculture Human Nutrition Research Center on Aging (C-J.C., M-L.C., M.S., A.T.), Department of Ophthalmology, School of Medicine (C-J.C. A.T.), and Friedman School of Nutrition Science and Policy (F.F.Z.), Tufts University, Boston, Massachusetts; Channing Division of Network Medicine, Brigham and Women's Hospital, Harvard Medical School (T.L.); Age-Related Eye Disease Study Coordinating Center, The EMMES Corporation, Rockville, Maryland (G.G.).

Abstract

PURPOSE—We hypothesized that major American dietary patterns are associated with age-related macular degeneration (AMD) risk.

DESIGN—Cross-sectional study

METHODS—8,103 eyes from 4,088 eligible participants in the baseline Age-Related Eye Disease Study (AREDS) were classified into control ($n=2,739$), early AMD ($n=4,599$), and advanced AMD ($n=765$) by AREDS AMD Classification System. Food consumption data were collected by a 90-item food frequency questionnaire.

RESULTS—Two major dietary patterns were identified by factor (principle component) analysis based on 37 food groups and named Oriental and Western patterns. The Oriental pattern was characterized by higher intake of vegetables, legumes, fruit, whole grains, tomatoes, and seafood. The Western pattern was characterized by higher intake of red meat, processed meat, high-fat dairy products, French fries, refined grains, and eggs. We ranked our participants according to how closely their diets line up with the two patterns by calculating the two factor scores for each participant. For early AMD, multivariate-adjusted odds ratio (OR) from generalized estimating equation logistic analysis comparing the highest to lowest quintile of the Oriental pattern score was $OR_{E5O}=0.74$ (95% confidence interval (CI): 0.59–0.91; $P_{trend}=0.01$), and the OR comparing the highest to lowest quintile of the Western pattern score was $OR_{E5W}=1.56$ (1.18–2.06; $P_{trend}=0.01$). For advanced AMD, the OR_{A5O} was 0.38 (0.27–0.54; $P_{trend}<0.0001$), and the OR_{A5W} was 3.70 (2.31–5.92; $P_{trend}<0.0001$).

© 2014 Elsevier Inc. All rights reserved.

Correspondence and reprint requests to Chung-Jung Chiu, Jean Mayer United States Department of Agriculture Human Nutrition Research Center on Aging at Tufts University, 711 Washington Street, Boston, Massachusetts 02111, C.J.Chiu@tufts.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

No financial disclosures.

CONCLUSIONS—Our data indicate that overall diet is significantly associated with the odds of AMD and that dietary management as an AMD prevention strategy warrants further study.

Keywords

retina; nutrition; diet; aging; dietary pattern; epidemiology; principle component analysis; factor analysis

INTRODUCTION

Age-related macular degeneration (**AMD**) is the major cause of blindness in persons aged 65+ yrs in developed countries. In the US, advanced AMD accounts for over 50% of the legal blindness and, with people living longer, it is estimated that the number of advanced AMD cases will reach 3 million in 2020.¹ Vision impairment due to advanced AMD significantly reduces quality of life and consumes a large portion of the Medicare budget.² Currently, clinical treatments for AMD are costly and limited to arresting neovascular type of the disease and cannot prevent progression of visual loss. For geographic atrophy, the major cause of visual loss in eyes with late AMD, there is no treatment.³ Therefore, there is a high premium to design strategies to prevent AMD or delaying its progress to advanced stages that result in vision loss. Nutritional intervention seems to hold some promise toward these ends and this was recently corroborated by trials from the Age-Related Eye Disease Study (**AREDS**) and AREDS2 that show that use of a supplement containing vitamins C and E, lutein/zeaxanthin, and zinc delays progression of advanced AMD in persons with intermediate AMD.^{4, 5}

Most of the previous attempts to determine relationships between diet and AMD have focused on how intake of nutrients can be used to prolong retinal function and diminish risk for AMD. Interestingly, nutrient-nutrient interactions were recently observed. For example, we recently found that the benefits of omega-3 fatty acids from foods may depend on the stage of AMD and the status of other nutrients.⁶ These findings indicate that intake of one food, with its many nutrients, might affect the bioavailability and nutrition value of another food or nutrient. Our previous studies also suggested that the overall quality of carbohydrate in diet measured by dietary glycemic index affects the risk for AMD.^{6–10} These data emphasize the importance of studying diet as a whole to understand how it can be optimized to promote health.

In this study using data from the AREDS, we conducted factor (principle component) analysis to identify major dietary patterns. Factor analysis is a statistical method which can summarize two or more food items (groups) into a single factor which represents a major dietary pattern.¹¹ Thus, we can describe dietary patterns in terms of such factors. Then, we related the major dietary patterns to AMD.

METHODS

This case-control study is an analysis of preexisting data from the AREDS, and data were analyzed anonymously. The Tufts Health Sciences Campus Institutional Review Board certified the current study an exempt from institutional review board approval. This study

has been conducted according to the principles expressed in the Declaration of Helsinki and all federal or state laws in the United States.

Age-Related Eye Disease Study (AREDS)

AREDS of the National Eye Institute (NEI) of the National Institutes of Health (NIH) is a long-term multicenter, prospective study dedicated to assess the clinical course, prognosis, risk factors, and prevention strategy of both AMD and cataract.¹² The protocol was adherent to the Declaration of Helsinki and approved by a Data and Safety Monitoring Committee and by each Institutional Review Board for the 11 participating ophthalmic centers before initiation of the study. Participants were 55 to 80 years of age at enrollment. A total of 4757 participants were enrolled from November 1992 to January 1998. Informed consent was obtained from participants prior to enrollment.

Data on possible risk factors for AMD was obtained from a baseline general physical and ophthalmic examination and a detailed questionnaire on basic characteristics and demographic data.¹³ Stereoscopic fundus photographs of the macula and slit lamp and red reflex lens photographs were taken, and graded at a central ophthalmic photograph reading center, where the various lesions associated with AMD and the degree of lens opacities by type were assessed using AREDS grading procedures adapted from the Wisconsin age-related maculopathy grading system and the Wisconsin System for Classifying Cataracts from Photographs, respectively.^{14, 15}

For AMD grading, eyes were classified into one of five groups (see below) according to the size and extent of drusen, presence of geographic atrophy, and neovascular changes of AMD.¹⁶ The five groups, numbered serially and based on increasing severity of drusen or type of AMD, were defined as follows. The baseline characteristics for the five study groups have been published previously.⁸

Group 1 (Control): Eyes had no drusen or non-extensive small drusen.

Group 2 (Intermediate Drusen): Eyes had one or more intermediate drusen, extensive small drusen, or pigment abnormalities associated with AMD.

Group 3 (Large Drusen): Eyes had one or more large drusen or extensive intermediate drusen.

Group 4 (Geographic Atrophy): Eyes had geographic atrophy.

Group 5 (Neovascular): Eyes had choroidal neovascularization or retinal pigment epithelium (RPE) detachment.

A 90-item modified Block food frequency questionnaire (FFQ) was administered to AREDS participants at baseline. The FFQ was validated in relation to 24-hour recall using a subset (n = 192) of the AREDS volunteers (Kurini N, Gensler G, Milton R, AREDS Research Group. Development and valuation of a food frequency questionnaire in a randomized trial of eye diseases. Paper presented at: International Conference on Dietary Assessment Measures; May 7, 1998; Phoenix, Arizona). The FFQ collected information

about average frequency and serving sizes of consumption over the previous year. For each food item, participants indicated their average frequency of consumption in terms of the specified serving size (small=0.5 medium, medium, or large=1.5 medium) by checking 1 of 9 frequency categories ranging from “never or less than once per month” to “two or more times per day.” The medium serving sizes are described by using natural portions (eg, 1 banana and 2 slices of pizza) or standard weight and volume measures of the servings commonly consumed in American population. The selected frequency category and serving sizes for each food item was converted to a daily intake in terms of medium servings. For example, a response of “2–4 servings/wk” in large servings was converted to 4.5 ($=3 \times 1.5$) medium servings/wk ($=4.5/7=0.643$ medium servings/d).

More details about the AREDS can be found in the AREDS report series.

Statistical methods

We derived dietary patterns by using food consumption data from the FFQ. We first classified 90 food items in the FFQ into 37 predefined food groups (Table 1) to minimize within-person variations in intakes of individual foods. Individual food items were preserved if they constituted a distinct item on their own (e.g., eggs, pizza, coffee or tea, etc) or if they were thought to represent a particular dietary pattern (e.g., liquor, wine, beer, and French fries, etc). In order to determine the “structure” or “components” of diet and determine if the dietary components were associated with AMD, we conducted factor analysis using principal component analysis (PCA) to derive dietary patterns based on the 37 food groups. The goals of PCA are to extract the most important information from a data set and to reduce the number of variables by keeping only important information. PCA computes new variables called principal components (factors) which are obtained as linear combinations of the original variables (i.e. food groups).¹⁷ The first principal component is required to have the largest possible variance (i.e., inertia and therefore this component will “explain” or “extract” the largest part of the inertia of the data set). The second component is computed under the constraint of being orthogonal to the first component and to have the largest possible variance (inertia). In determining the number of factors to retain, we considered their eigenvalues, the Scree plot (the principle components as the X axis and the corresponding eigenvalues as the Y-axis), and the interpretability of the factors. The eigenvalues are also known as characteristic values or proper values and the factor with the largest eigenvalue has the most variance. We did not use the percentage of variance explained by each factor because this criterion depends largely on the total number of variables included in the analyses. The two major patterns identified in our factor analysis were similar to those described in many previous American studies,^{18, 19} which were often named “prudent pattern” and “Western pattern.” Here, we named the first factor as “Oriental pattern” because it was characterized by higher intake of vegetables, legumes, fruit, whole grains, tomatoes, and seafood, etc. The second factor was named “Western pattern” because it was characterized by higher intake of red meat, processed meat, high-fat dairy products, French fries, refined grains, and eggs, etc. Because of the variability in diets, we did not simply classify our participants as “following” or “not following” a given dietary pattern (factor), but instead ranked them according to how closely their diets line up with the two patterns by calculating the two factor scores for each participant. The factor score for each

pattern was constructed by summing observed intakes of the component food items weighted by factor loadings. The analyses were conducted by using the PROC FACTOR in SAS® (version 9.3; SAS Institute Inc, Cary, NC).

To evaluate the baseline cross-sectional relationship between the two major dietary patterns and AMD, we used eyes with AMD lesions (Groups 2 through 5) as our cases and those in Group 1 as our controls. Odds ratios (**ORs**) were calculated by dividing the odds of AMD among eyes in the highest quintile of dietary pattern scores by the odds among eyes in the lowest quintile of dietary pattern scores. The following baseline characteristics were considered as covariates in our analyses: age, gender, education level (college graduate, and high school or less), race (white and others), body mass index (**BMI**, computed from weight and height; kg/m²), alcohol intake (g/d), calorie intake, multivitamin use, smoking status (ever and never), sunlight exposure (h/d),²⁰ hypertension history, lens opacity, and refractive error. Nutrient variables were energy-adjusted by the residual method.²¹

We estimated ORs and 95% confidence intervals (**CI**s) by logistic regression analysis using SAS® PROC GENMOD (version 9.3; SAS Institute Inc, Cary, NC). The procedure uses the generalized estimating equation (**GEE**) method to estimate the coefficients and adjust the standard errors (**SE**s) of the model terms for the correlated data resulting from repeated measurements (both eyes) on the same individual.²² This accounts for the lack of independence between two eyes from the same individual.

We used $P < 0.05$ to denote statistical significance and all tests were two-sided.

RESULTS

Of the original 4,757 subjects in the AREDS, we excluded those with diabetes, invalid calorie intake (valid intakes ranged from 400 to 3,000 Kcal/d for female and 600 to 3,500 Kcal/d for male), and missing covariate information. This left 4,088 persons contributing 8,103 eyes available for analysis. The 8,103 eyes consisted of 2,739 control eyes (Group 1), 4,599 early AMD eyes (1,801 eyes with intermediate drusen plus 2,798 eyes with large drusen, i.e., Group 2 plus Group 3), 765 advanced AMD eyes (164 eyes with geographic atrophy plus 601 eyes with choroidal neovascularization, i.e., Group 4 plus Group 5).

We entered food consumption data for the 37 predefined food groups (Table 1) into the factor analysis procedure. The Scree plot of eigenvalues indicated two major factors with an eigenvalue of 4.01 and 3.29, respectively. They were much higher than the third highest eigenvalue (1.58). Thus, we retained the two factors in the final model. Factor-loading matrixes for the 2 major factors are listed in Table 2. The larger the loading of a given food item or group to the factor, the greater the contribution of that food item or group to a specific factor. The first factor was loaded heavily with the following foods or food groups: vegetables, legumes, fruit, fish, tomatoes, whole grains, poultry, etc. The second factor was loaded heavily with red meat, processed meat, butter, high-fat dairy products, French fries, refined grains, eggs, sweets and dessert, potatoes, etc. The first factor explained 10.8% of the total variance of food consumption and the second factor explained 8.9% of the total

variance. We named the first factor as the “Oriental pattern” and the second factor as the “Western pattern.”

In general, our study subjects with a higher Oriental pattern score were younger ($P=0.03$), more likely to have higher levels of education ($P<0.0001$), less likely to be smokers ($P=0.002$) and to have hypertension history ($P=0.03$), and have higher intakes (all P values <0.0001) of dietary intakes of vitamin C, vitamin E, beta-carotene, zinc, lutein/zeaxanthin, docosahexaenoic acid (**DHA**) and eicosapentaenoic acid (**EPA**) (Table 3). Importantly, consumption of vegetables, legumes, fruit, whole-grain products, fish, poultry, low-fat dairy products, etc, was positively correlated with the Oriental pattern score, whereas consumption of processed meat, French fries, high energy drinks etc, was inversely correlated.

Subjects with a higher Western pattern score were younger ($P=0.0006$) and less educated ($P=0.03$), more likely to be male ($P<0.0001$), smokers ($P<0.0001$), and white ($P=0.02$), had higher BMI ($P<0.0001$) and sunlight exposure ($P<0.0001$), and drank more alcohol ($P<0.0001$). They also tended to have lower levels of dietary vitamin C ($P<0.0001$), beta-carotene ($P<0.0001$), lutein/zeaxanthin ($P<0.0001$), slightly lower DHA ($P=0.01$) and EPA ($P<0.0001$) intakes, but have higher intake of vitamin E ($P=0.04$) (Table 4). Consumption of red meat, processed meat, butter, high-fat dairy products, French fries, refined grain, sweets and dessert etc, was positively correlated with the Western pattern score, whereas consumption of whole grains, fruit, low-fat dairy products, vegetables etc, was inversely correlated. Interestingly, calorie intake was positively correlated with both pattern scores (P values <0.0001) (Table 3 and Table 4).

In our multivariate logistic analysis relating the two dietary pattern scores to AMD, we found that a higher Oriental pattern score was strongly associated with a lower odds for both early (OR=0.90 (95% CI: 0.84–0.97) per Oriental score unit increase, $P=0.003$) and advanced AMD (OR=0.73 (95% CI: 0.64–0.82) per Oriental score unit increase, $P<0.0001$) (left panels of Figure 1). Compared with eyes in the first quintile of the Oriental pattern score, there was an almost 30% reduction of early AMD odds and over 60% reduction of advanced AMD odds for eyes in the fourth and fifth quintiles. On the contrary, a higher Western pattern score was strongly associated with a monotonic higher odds for both early (OR=1.15 (95% CI: 1.05–1.27) per Western score unit increase, $P=0.004$) and advanced AMD (OR=1.55 (95% CI: 1.31–1.83) per Western score unit increase, $P<0.0001$) (right panels of Figure 1). Compared with eyes in the first quintile of the Western pattern score, there is an almost 60% increase of early AMD odds and almost 3 fold increase of advanced AMD odds for eyes in the fifth quintile. In addition to the point estimates, the linear trend tests also indicated that both Oriental and Western pattern scores were more strongly associated with advanced AMD (lower panels of Figure 1) than with early AMD (upper panels of Figure 1).

DISCUSSION

Using dietary data from the American AREDS cohort, we identified two major dietary patterns, named “Oriental” and “Western’ patterns.” The two patterns feature the same

characteristics with traditional American dietary patterns identified in previous studies. We also found that both patterns showed a significant association with odds for either early or advanced AMD. The Oriental pattern is associated with reduced odds and closer adherents to the Oriental pattern gain larger benefit. In contrast, people who consume the Western pattern are at markedly increased odds.

Relating diet as a whole to ocular outcomes is relatively new in ophthalmic epidemiology. To our knowledge, only one study from the European Eye study (**EUREYE**) Northern Irish cohort has used factor analysis to derive dietary patterns and related the patterns to retinal vessel caliber.²³ Notably, the major dietary patterns identified in that cohort and in many previous reports from other white populations^{18, 19, 24, 25} feature the same eating characteristics with the major dietary patterns identified in the current study. Because ethnic and cultural origin is the major determinant of dietary pattern, this consistency suggests the robustness of our findings on the derived major patterns in the AREDS cohort.

Foods and nutrients are not eaten in isolation. In contrast with the traditional analytic approach relating single nutrients or foods to disease risk, dietary pattern analysis considers overall diet and thus would more closely relate to and inform about the effects of actual eating patterns on risk for AMD. Importantly, our findings are consistent with associations between AMD risk and intakes of nutrients or foods identified in previous epidemiologic studies. For example, intakes of nutrients or foods that are directly correlated with the Oriental dietary pattern, including lutein/zeaxanthin,²⁶ carbohydrate containing foods with a low glycemic index (**GI**) and whole-grain products,^{6-10, 27-29} and fish³⁰ have been associated with a reduced risk of AMD. On the other hand, intakes of nutrients or foods that are directly correlated with the Western dietary pattern, including red meat³¹ and trans-unsaturated fat,^{32, 33} have been associated with an increased risk of AMD.

Our data also gives support to the opinion that dietary pattern analysis provides a better insight into human diet than single food/nutrient approach, which does not take into account the complex interactions among foods/nutrients. For example, while data from interventional trials have shown that eggs may offer protection against AMD because of their higher lutein content,^{34, 35} no data has shown an association between higher egg consumption and lower risk for AMD from observational studies of free-living people. Our dietary pattern analysis implies that, because higher egg consumption is one of the characteristics of the Western pattern (Table 2), the detrimental effects from the many other characteristic foods in the Western pattern may have counteracted the protective effect from eggs.

No study has investigated the detailed mechanisms by which the Oriental and Western dietary patterns reduced and increased, respectively, the likelihood of early and advanced AMD. However, the mechanisms must be the result of the complex interactions among different foods/nutrients in diet. A randomized controlled feeding trial testing biomarkers for postulated mechanisms, such as advanced glycation end products formation, oxidative stress, inflammatory responses, angiogenesis, etc,²⁷ will be helpful to determine the mechanisms. An understanding of the mechanisms can elucidate the conditions under which dietary intervention will be most effective, help to identify target populations who may

receive optimal benefits, help to define interactions or synergistic effects with other concurrent interventions, and suggest potential biomarkers for the prediction of AMD.^{36, 37} In addition, our results also suggest that nutritional disparity plays a role in the distribution of AMD. Studies to understand the causes behind this nutritional disparity may offer important information for policy interventions to reduce the occurrence of AMD and related health care burden.

It has been suggested that differences in the prevalence of late AMD in various ethnicities and geographic regions may reflect genetic variations, especially the single-nucleotide polymorphism (SNP) Y402H in the complement factor H (*CFH*) gene. Populations of European descent had both higher risk allele frequencies and prevalence of late AMD than did Chinese and Japanese descendants.³⁸ However, in this study mainly composed of white participants, we found that both Western diet and Oriental diet are associated with the odds of AMD. Compared with the Western diet, traditional Asian diets contain substantially more grains, legumes, vegetables, fruit, and fish and less red meat, high-fat dairy products, and other animal products, which feature the same eating characteristics with the Oriental diet.¹⁹ Therefore, the ecological relationship between ethnicities/geographic regions and prevalence of AMD may be at least partially explained by the difference in distinct dietary patterns and/or by gene-diet interaction.³⁹ This issue deserves further study.

The strengths of this study include a well-characterized cohort, standardized collection of risk factor information and photographic grading of maculopathy, as well as increased power by using eyes as the unit of analysis in relating dietary patterns to AMD. Recall and selection bias in the AREDS were unlikely to explain our findings because exposure information was collected before outcome evaluation and our retinal classifications were performed in an independent center, by graders masked to our nutrition data.⁴⁰ As noted above, consistency with prior data relating nutrients or foods to AMD risk reduced the possibility that the present findings are due to chance. Residual confounding is a concern but should be minimized because we evaluated diet as a whole and included all known non-dietary confounders in our analysis.

Like all observational studies, this study has some limitations. The cross-sectional nature of this study limits its strength in defining causality and our ability to make dietary recommendations. Residual confounding could still be a concern because dietary pattern may be just a component of life style in general which is responsible for the underlying relationship. When comparing dietary patterns across studies, it is also important to keep in mind that, because of changes in food preferences and food availability, the profile of a dietary pattern could change over time. However, several studies in American cohorts using the same procedures for defining food groups and deriving dietary patterns with the current study have shown reasonable reproducibility over time in characterizing dietary patterns.^{18, 19} Some may also be concerned that the method of factor analysis to define dietary patterns is subjective because decisions on grouping foods and the number of factors are usually based on empirical guidelines rather than on an exact quantitative solution. However, this should not become a limitation of our study because in determining food grouping and the number of factors, we adhered to established empirical guidelines as

closely as possible and, as noted above, the two major dietary patterns identified in this study are highly similar to the major dietary patterns in other white populations.

In summary, our data give further support to the opinion that diet plays an important role in the development of AMD and that the prevention of AMD may be achievable through dietary intervention.

Acknowledgments

Financial support for this project has been provided by the RO1EY021826 (C-J.C.) from the National Institutes of Health, the United States Department of Agriculture under agreements, 1950-5100-060-01A (C-J.C., A.T.), and RO1EY013250 and RO1EY021212 (A.T.).

Design and conduct of the study (C-J.C., A.T.); collection, management, analysis, and interpretation of the data (C-J.C., M-L.C., F.F.Z., T.L., G.G.); preparation, review, or approval of the manuscript (C-J.C., M-L.C., F.F.Z., G.G., M.S., A.T.); statistical expertise (C-J.C., F.F.Z., T.L., G.G.); administrative, technical, or logistic support (M-L.C., G.G., M.S.).

Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views or policies of the United States Department of Agriculture, nor does mention of trade names, commercial products, or organizations imply endorsement by the United States Government.

The funding sources had no role in the design and conduct of the study; the collection, analysis, and interpretation of the data; or the preparation, review, or approval of the manuscript.

REFERENCES

1. Congdon N, O'Colmain B, Klaver CC, et al. Causes and prevalence of visual impairment among adults in the United States. *Arch Ophthalmol*. 2004; 122(4):477–485. [PubMed: 15078664]
2. Klein R. Overview of progress in the epidemiology of age-related macular degeneration. *Ophthalmic Epidemiol*. 2007; 14(4):184–187. [PubMed: 17896295]
3. Miller JW. Age-related macular degeneration revisited--piecing the puzzle: the LXIX Edward Jackson memorial lecture. *Am J Ophthalmol*. 2013; 155(1):1–35. e13. [PubMed: 23245386]
4. Age-Related Eye Disease Study Research Group. 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(10):1417–1436. [PubMed: 11594942]
5. The Age-Related Eye Disease Study 2 (AREDS2) Research Group. Lutein + Zeaxanthin and Omega-3 Fatty Acids for Age-Related Macular Degeneration: The Age-Related Eye Disease Study 2 (AREDS2) Randomized Clinical Trial. *JAMA*. 2013; 309(19):2005–2015. [PubMed: 23644932]
6. Chiu CJ, Klein R, Milton RC, Gensler G, Taylor A. Does eating particular diets alter risk of age-related macular degeneration in users of the Age-Related Eye Disease Study supplements? *Br J Ophthalmol*. 2009; 93(9):1241–1246. [PubMed: 19508997]
7. Chiu CJ, Hubbard LD, Armstrong J, et al. Dietary glycemic index and carbohydrate in relation to early age-related macular degeneration. *Am J Clin Nutr*. 2006; 83(4):880–886. [PubMed: 16600942]
8. Chiu CJ, Milton RC, Gensler G, Taylor A. Association between dietary glycemic index and age-related macular degeneration in nondiabetic participants in the Age-Related Eye Disease Study. *Am J Clin Nutr*. 2007; 86(1):180–188. [PubMed: 17616779]
9. Chiu CJ, Milton RC, Klein R, Gensler G, Taylor A. Dietary carbohydrate and progression of age-related macular degeneration, a prospective study from the Age-Related Eye Disease Study. *Am J Clin Nutr*. 2007; 86(4):1210–1218. [PubMed: 17921404]
10. Chiu CJ, Milton RC, Klein R, Gensler G, Taylor A. Dietary compound score and risk of age-related macular degeneration in the Age-Related Eye Disease Study. *Ophthalmology*. 2009; 116(5):939–946. [PubMed: 19410952]

11. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol*. 2002; 13(1):3–9. [PubMed: 11790957]
12. The Age-Related Eye Disease Study Research Group. The Age-Related Eye Disease Study (AREDS): design implications AREDS report no. 1. *Control Clin Trials*. 1999; 20(6):573–600. [PubMed: 10588299]
13. Age-Related Eye Disease Study Research Group. Risk factors associated with age-related macular degeneration. A case-control study in the age-related eye disease study: age-related eye disease study report number 3. *Ophthalmology*. 2000; 107(12):2224–2232.
14. Klein R, Davis MD, Magli YL, Segal P, Klein BEK, Hubbard L. The Wisconsin age-related maculopathy grading system. *Ophthalmology*. 1991; 98(7):1128–1134. [PubMed: 1843453]
15. Klein BEK, Klein R, Linton KLP, Magli YL, Neidler MW. Assessment of cataracts from photographs in the Beaver Dam Eye Study. *Ophthalmology*. 1990; 97(4549):1428–1433. [PubMed: 2255515]
16. Age-Related Eye Disease Study Research Group. The Age-Related Eye Disease Study system for classifying age-related macular degeneration from stereoscopic color fundus photographs: the Age-Related Eye Disease Study Report Number 6. *Am J Ophthalmol*. 2001; 132(5):668–681. [PubMed: 11704028]
17. Abdi H, Williams LJ. Principal component analysis. *Wiley Interdisciplinary Reviews: Computational Statistics*. 2010; 2(4):433–459.
18. Hu FB, Rimm E, Smith-Warner SA, et al. Reproducibility and validity of dietary patterns assessed with a food-frequency questionnaire. *Am J Clin Nutr*. 1999; 69(2):243–249. [PubMed: 9989687]
19. Hu FB, Rimm EB, Stampfer MJ, Ascherio A, Spiegelman D, Willett WC. Prospective study of major dietary patterns and risk of coronary heart disease in men. *Am J Clin Nutr*. 2000; 72(4):912–921. [PubMed: 11010931]
20. McCarty CA, Lee SE, Livingston PM, Bissinella M, Taylor HR. Ocular exposure to UV-B in sunlight: the Melbourne visual impairment project model. *Bull World Health Organ*. 1996; 74(4):353–360. [PubMed: 8823956]
21. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. *Am J Epidemiol*. 1986; 124(1):17–27. [PubMed: 3521261]
22. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics*. 1986; 42(1):121–130. [PubMed: 3719049]
23. McEvoy CT, Cardwell CR, Chakravarthy U, et al. A posteriori-derived dietary patterns and retinal vessel caliber in an elderly population. *Invest Ophthalmol Vis Sci*. 2013; 54(2):1337–1344. [PubMed: 23322577]
24. Slattery ML, Boucher KM, Caan BJ, Potter JD, Ma KN. Eating patterns and risk of colon cancer. *Am J Epidemiol*. 1998; 148(1):4–16. [PubMed: 9663397]
25. Fung TT, Rimm EB, Spiegelman D, et al. Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk. *Am J Clin Nutr*. 2001; 73(1):61–67. [PubMed: 11124751]
26. Chiu CJ, Taylor A. Nutritional antioxidants and age-related cataract and maculopathy. *Exp Eye Res*. 2007; 84(2):229–245. [PubMed: 16879819]
27. Chiu CJ, Taylor A. Dietary hyperglycemia, glycemic index and metabolic retinal diseases. *Prog Retin Eye Res*. 2011; 30(1):18–53. [PubMed: 20868767]
28. Kaushik S, Wang JJ, Flood V, et al. Dietary glycemic index and the risk of age-related macular degeneration. *Am J Clin Nutr*. 2008; 88(4):1104–1110. [PubMed: 18842800]
29. Weikel KA, Chiu CJ, Taylor A. Nutritional modulation of age-related macular degeneration. *Mol Aspects Med*. 2012; 33(4):318–375. [PubMed: 22503690]
30. Chong EW, Kreis AJ, Wong TY, Simpson JA, Guymer RH. Dietary omega-3 fatty acid and fish intake in the primary prevention of age-related macular degeneration: a systematic review and meta-analysis. *Arch Ophthalmol*. 2008; 126(6):826–833.
31. Chong EW, Simpson JA, Robman LD, et al. Red meat and chicken consumption and its association with age-related macular degeneration. *Am J Epidemiol*. 2009; 169(7):867–876. [PubMed: 19234096]

32. 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(2):209–218. [PubMed: 11157315]
33. Chong EW, Robman LD, Simpson JA, et al. Fat consumption and its association with age-related macular degeneration. *Arch Ophthalmol.* 2009; 127(5):674–680. [PubMed: 19433719]
34. Vishwanathan R, Goodrow-Kotyla EF, Wooten BR, Wilson TA, Nicolosi RJ. Consumption of 2 and 4 egg yolks/d for 5 wk increases macular pigment concentrations in older adults with low macular pigment taking cholesterol-lowering statins. *Am J Clin Nutr.* 2009; 90(5):1272–1279. [PubMed: 19759170]
35. Vishwanathan R, Gendron CM, Goodrow-Kotyla EF, Wilson TA, Nicolosi RJ. Increased consumption of dietary cholesterol, lutein, and zeaxanthin as egg yolks does not decrease serum concentrations and lipoprotein distribution of other carotenoids, retinol, and tocopherols. *Nutr Res.* 2010; 30(11):747–755. [PubMed: 21130293]
36. Chiu CJ, Mitchell P, Klein R, et al. A Risk Score for the Prediction of Advanced Age-related Macular Degeneration: Development and Validation in Two Prospective Cohorts. *Ophthalmology.* 2014 Available online 18 March 2014. <http://dx.doi.org/10.1016/j.ophtha.2014.1001.1016>.
37. Chang ML, Chiu CJ, Shang F, Taylor A. High Glucose Activates ChREBP-Mediated HIF-1 α and VEGF Expression in Human RPE Cells Under Normoxia. *Adv Exp Med Biol.* 2014; 801:609–621. [PubMed: 24664750]
38. Nonyane BA, Nitsch D, Whittaker JC, et al. An ecological correlation study of late age-related macular degeneration and the complement factor H Y402H polymorphism. *Invest Ophthalmol Vis Sci.* 2010; 51(5):2393–2402. [PubMed: 20042653]
39. Wang JJ, Buitendijk GH, Rochtchina E, et al. Genetic susceptibility, dietary antioxidants, and long-term incidence of age-related macular degeneration in two populations. *Ophthalmology.* 2014; 121(3):667–675. [PubMed: 24290803]
40. Chiu CJ, Milton RC, Gensler G, Taylor A. Dietary carbohydrate and glycemic index in relation to cortical and nuclear lens opacities in the Age-Related Eye Disease Study. *Am J Clin Nutr.* 2006; 83(5):1177–1184. [PubMed: 16685063]

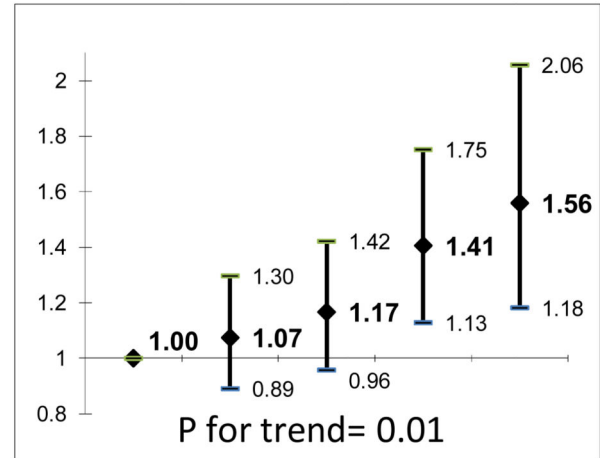
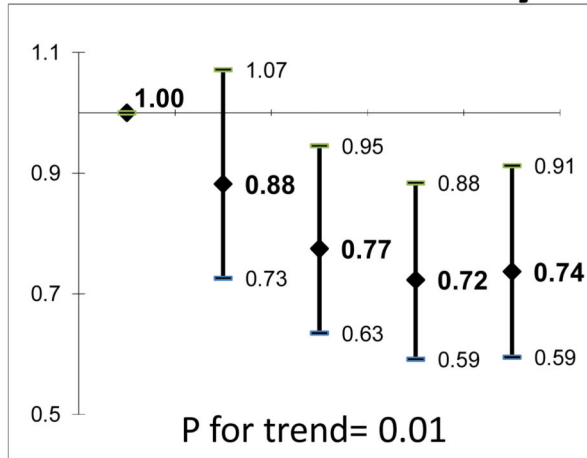
Biography



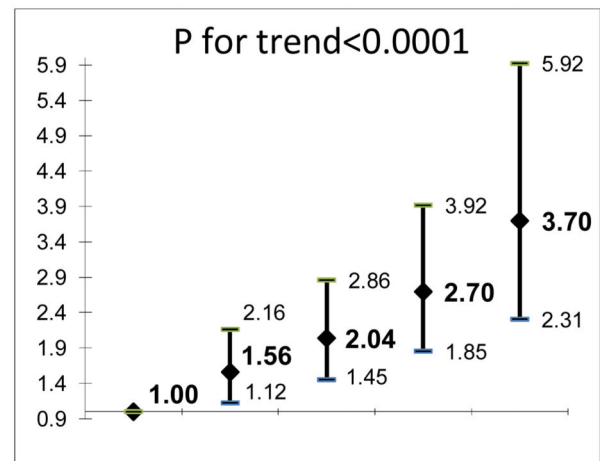
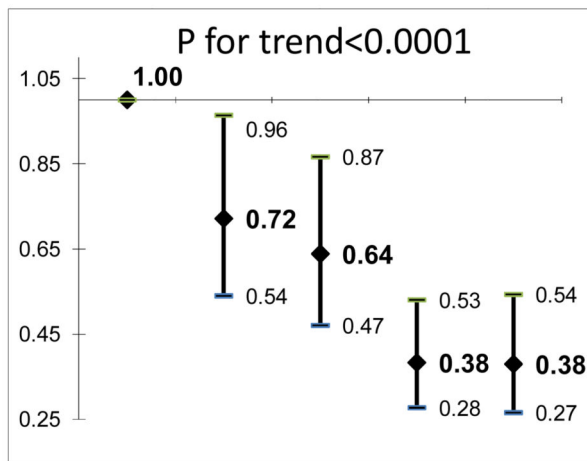
Chung-Jung Chiu DDS, PhD, is currently a scientist at the Jean Mayer United States Department of Agriculture Human Nutrition Research Center on Aging and an assistant professor at the Department of Ophthalmology School of Medicine, Tufts University. His research interest includes age-related eye diseases and their environmental, genetic, and nutritional risk factors, prediction, and pathogenesis.

OR (95% CI)

Early AMD Risk



Advanced AMD Risk



Low → High
Oriental Score Quintile Groups

Low → High
Western Score Quintile Groups

FIGURE 1.

Odds ratios (95% confidence intervals) of age-related macular degeneration according to quintile groups of two major American dietary pattern scores.

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

Participants were divided into quintile categories according to their dietary pattern score and those in the lowest 20% of the distribution comprised the referent category. The multivariate-adjusted logistic models using Group 1 (n = 2,739) as control were adjusted for age, sex, race, education, smoking status, alcohol intake, calorie intake, multivitamin use, body mass index, sunlight exposure, hypertension history, lens opacity, and refractive error. The analysis used 4,599 early AMD eyes (1,801 eyes with intermediate drusen plus 2,798 eyes with large drusen, i.e., Group 2 plus Group 3) and 765 advanced AMD eyes (164 eyes with geographic atrophy plus 601 eyes with choroidal neovascularization, i.e., Group 4 plus

Group 5). See **AMD grading procedures** in METHODS section for the five (Groups 1~5) AMD grouping criteria.

Table 1

The 90 food items in the food frequency questionnaire administered in the Age-Related Eye Disease Study were first grouped into 37 food groups, which were then entered into our factor analysis for deriving dietary patterns.

Food group		Food items in the AREDS FFQ
1.	Processed meats	Hotdogs, ham, bacon, sausage
2.	Red meats	Hamburgers, beef, beef stew, pork or lamb
3.	Organ meats	Liver, liverwurst
4.	Fish and other seafood	Fried fish, tuna, oysters, shrimp, other fish
5.	Poultry	Fried chicken, chicken or turkey
6.	Pizza	Pizza
7.	Soup	Vegetable and tomato soup, other soup
8.	Eggs	Eggs
9.	Butter or margarine	Butter added to vegetable, butter on bread, margarine on bread
10.	Peanuts	Peanuts or peanut butter
11.	Gravies	Gravies
12.	Cold breakfast cereal	Milk on cereal, other cold breakfast cereal
13.	Whole grains	High fiber cereals, fortified cereals, cooked cereals, dark bread
14.	Refined grains	Biscuits, white bread, corn bread, spaghetti, other noodle
15.	Rice	Rice
16.	Snacks	Chips
17.	High energy drinks	Regular soft drink, Fruit Drinks, Sugar in coffee or tea
18.	Sweets and desserts	doughnuts, chocolate candy, other candy
19.	French fries	French fries
20.	Liquor	Liquor
21.	Beer	Beer
22.	Wine	Wine
23.	High-fat dairy products	Whole milk, ice cream, other cheeses, macaroni and cheese, milk in coffee or tea
24.	Low-fat dairy products	2% milk, 1% milk, yogurt, Cottage cheese
25.	Condiments	Red chili sauce
26.	Salad dressings	Salad dressings
27.	Fruit	Apples, bananas, peaches, cantaloupe, watermelon, strawberries, oranges, grapefruit, other fruit
28.	Fruit juices	Orange or grapefruit juice
29.	Cruciferous vegetables	Broccoli, Cole slaw, cauliflower, cooked greens
30.	Dark-yellow vegetables	Winter squash, carrots, sweet potatoes
31.	Tomatoes	Tomatoes
32.	Green leafy vegetables	Raw spinach, cooked spinach, green salad
33.	Legumes	String beans, peas, other beans, chili with beans
34.	Other vegetables	Corn, any other vegetable

Food group		Food items in the AREDS FFQ
35.	Potatoes	Other potatoes
36.	Coffee or Tea	Coffee or tea
37.	Non-dairy creamer in coffee or tea	Non-dairy creamer in coffee or tea

Abbreviation: **AREDS**, Age-Related Eye Disease Study; **FFQ**, food frequency questionnaire.

Table 2

Factor-loading matrix for the 2 major factors (dietary patterns) identified by principle component analysis using food consumption data from the food frequency questionnaire administered in the Age-Related Eye Disease Study.¹

Food or food group ²	Factor 1 (Oriental pattern)	Factor 2 (Western pattern)
Dark-yellow vegetables	0.67	–
Cruciferous vegetables	0.65	–
Green leafy vegetables	0.60	–
Legumes	0.54	–
Fruit	0.54	–
Other vegetables	0.54	–
Whole grains	0.47	–
Tomatoes	0.46	–
Fish and other seafood	0.46	–
Rice	0.45	–
Poultry	0.45	–
Soup	0.39	–
Low-fat dairy products	0.39	–
Red meats	–	0.65
Processed meats	–	0.65
Butter or margarine	–	0.58
High-fat dairy products	–	0.53
Gravies	–	0.51
French fries	–	0.48
Refined grains	–	0.43
Eggs	–	0.43
Sweets and desserts	–	0.40
Potatoes	–	0.35
High energy drinks	–	0.32

¹ Foods or food groups with an absolute value for factor loading < 0.30 for both factors were not listed in the table for simplicity.

² See Table 1 for food groupings.

Table 3

Age-standardized characteristics and dietary consumptions by Oriental pattern score quintile groups (Q1-Q5 from low to high) in the Age-Related Eye Disease Study. Values are means (standard deviation) or proportions and are standardized to the age distribution of the study population.

	'Q1' (n=817)	'Q2' (n=818)	'Q3' (n=818)	'Q4' (n=818)	'Q5' (n=817)	P value ²
Age ¹	68.75 (5.32)	68.59 (5.18)	68.58 (5.09)	68.65 (4.85)	68.25 (4.98)	0.03
Male gender	0.45	0.42	0.41	0.44	0.39	0.13 ³
College or higher	0.49	0.62	0.66	0.72	0.77	<0.0001 ³
White	0.96	0.96	0.97	0.96	0.96	0.78 ³
BMI (Kg/m ²)	27.60 (4.76)	27.38 (4.78)	26.80 (4.49)	27.36 (4.63)	27.25 (5.05)	0.25
Sunlight exposure (h/d)	1.00 (1.08)	1.00 (1.07)	1.07 (1.18)	1.03 (1.12)	1.10 (1.12)	0.21
Ever smoke	0.59	0.58	0.53	0.54	0.50	0.002 ³
Alcohol intake (g/d)	5.95 (11.69)	6.04 (10.92)	7.42 (14.23)	6.36 (11.99)	6.20 (10.41)	0.81
Hypertension history	0.41	0.38	0.40	0.34	0.35	0.03 ³
Daily energy-adjusted nutrient intake						
Vitamin C (mg)	77.85 (42.79)	95.84 (42.61)	101.28 (46.77)	115.11 (50.51)	134.08 (59.00)	<0.0001
Vitamin E (µg)	8.71 (3.11)	9.57 (4.60)	9.78 (5.02)	10.39 (5.19)	9.99 (5.29)	<0.0001
Beta-carotene (mg)	1635.35 (787.70)	2000.15 (963.26)	2315.48 (1265.80)	2802.20 (1386.01)	4131.82 (2394.43)	<0.0001
Zinc (mg)	8.36 (3.24)	9.33 (3.75)	9.65 (4.40)	10.33 (4.69)	10.95 (5.09)	<0.0001
Lutein plus zeaxanthin (µg)	1113.09 (542.38)	1362.99 (713.04)	1511.08 (781.37)	1844.64 (970.46)	2493.65 (1554.72)	<0.0001
DHA (mg)	0.03 (0.02)	0.04 (0.03)	0.05 (0.03)	0.05 (0.04)	0.07 (0.05)	<0.0001
EPA (mg)	0.02 (0.02)	0.03 (0.02)	0.03 (0.03)	0.04 (0.03)	0.05 (0.04)	<0.0001
Calorie intake (Kcal/d)	1155.63 (486.88)	1329.22 (505.15)	1519.07 (505.58)	1632.48 (524.96)	1852.98 (546.81)	<0.0001
Daily intake of food or food group (medium servings/d)						
Dark-yellow vegetables	0.12 (0.11)	0.22 (0.18)	0.29 (0.21)	0.39 (0.24)	0.73 (0.48)	<0.0001
Cruciferous vegetables	0.16 (0.14)	0.26 (0.19)	0.35 (0.25)	0.49 (0.32)	0.81 (0.55)	<0.0001
Green leafy vegetables	0.22 (0.21)	0.39 (0.28)	0.53 (0.34)	0.67 (0.38)	0.93 (0.49)	<0.0001
Legumes	0.20 (0.15)	0.32 (0.21)	0.37 (0.23)	0.45 (0.27)	0.66 (0.42)	<0.0001
Fruit	0.85 (0.71)	1.31 (0.79)	1.58 (0.98)	1.97 (1.14)	2.72 (1.72)	<0.0001
Other vegetables	0.11 (0.10)	0.16 (0.15)	0.23 (0.19)	0.29 (0.23)	0.51 (0.45)	<0.0001
Whole grains	0.48 (0.48)	0.78 (0.59)	0.98 (0.67)	1.16 (0.72)	1.52 (0.95)	<0.0001

	'Q1' (n=817)	'Q2' (n=818)	'Q3' (n=818)	'Q4' (n=818)	'Q5' (n=817)	P value ²
Tomatoes	0.11 (0.14)	0.18 (0.19)	0.24 (0.24)	0.31 (0.30)	0.50 (0.39)	<0.0001
Fish and other seafood	0.14 (0.12)	0.21 (0.15)	0.26 (0.19)	0.32 (0.22)	0.44 (0.33)	<0.0001
Rice	0.06 (0.07)	0.10 (0.10)	0.14 (0.14)	0.19 (0.18)	0.27 (0.24)	<0.0001
Poultry	0.14 (0.12)	0.21 (0.17)	0.28 (0.20)	0.34 (0.23)	0.42 (0.27)	<0.0001
Soup	0.12 (0.15)	0.18 (0.18)	0.22 (0.24)	0.29 (0.27)	0.40 (0.36)	<0.0001
Low-fat dairy products	0.25 (0.30)	0.38 (0.36)	0.46 (0.47)	0.58 (0.48)	0.82 (0.69)	<0.0001

Abbreviation: **BMI**, body mass index; **DHA**, docosahexaenoic acid; **EPA**, eicosapentaenoic acid.

¹ Value is not age adjusted.

² P values are for tests of linear trend, otherwise indicated. Linear regression models were constructed by using continuous characteristics variables as independent variables and continuous Oriental pattern score as the dependent variable.

³ Chi-square tests compare the characteristic distributions among Oriental pattern score quintile groups.

Table 4

Age-standardized characteristics and dietary consumptions by Western pattern score quintile groups (Q1-Q5 from low to high) in the Age-Related Eye Disease Study. Values are means (standard deviation) or proportions and are standardized to the age distribution of the study population.

	'Q1' (n=817)	'Q2' (n=818)	'Q3' (n=818)	'Q4' (n=818)	'Q5' (n=817)	P value ²
Age ¹	68.89 (4.85)	68.65 (5.11)	68.60 (5.07)	68.64 (5.20)	68.03 (5.16)	0.0006
Male gender	0.23	0.29	0.41	0.52	0.65	<0.0001 ³
College or higher	0.67	0.67	0.66	0.64	0.61	0.03 ³
White	0.94	0.97	0.96	0.97	0.97	0.02 ³
BMI (Kg/m ²)	26.36 (4.52)	26.81 (4.70)	27.33 (4.65)	27.54 (4.66)	28.27 (5.03)	<0.0001
Sunlight exposure (h/d)	0.92 (1.00)	1.03 (1.16)	1.02 (1.16)	1.05 (1.03)	1.15 (1.15)	<0.0001
Ever smoke	0.47	0.51	0.53	0.57	0.64	<0.0001 ³
Alcohol intake (g/d)	3.47 (7.13)	4.70 (11.57)	6.58 (11.70)	8.24 (13.00)	9.04 (14.74)	<0.0001
Hypertension history	0.38	0.37	0.39	0.39	0.35	0.30 ³
Daily energy-adjusted nutrient intake						
Vitamin C (mg)	122.58 (52.82)	108.52 (47.33)	106.29 (49.75)	101.46 (51.57)	86.77 (53.82)	<0.0001
Vitamin E (µg)	9.28 (4.46)	9.47 (4.57)	9.68 (4.91)	10.04 (4.50)	9.89 (5.36)	0.04
Beta-carotene (mg)	3090.33 (1995.89)	2647.77 (1495.08)	2565.71 (1475.25)	2491.95 (1755.12)	2111.81 (1531.48)	<0.0001
Zinc (mg)	9.80 (3.75)	9.45 (3.81)	9.78 (4.57)	9.83 (4.39)	9.76 (5.33)	0.91
Lutein plus zeaxanthin (µg)	1921.76 (1155.21)	1717.56 (1037.77)	1668.17 (1059.23)	1629.05 (1076.36)	1404.34 (1002.04)	<0.0001
DHA (mg)	0.05 (0.04)	0.05 (0.03)	0.05 (0.03)	0.05 (0.03)	0.05 (0.04)	0.01
EPA (mg)	0.04 (0.03)	0.03 (0.03)	0.03 (0.03)	0.03 (0.03)	0.03 (0.03)	<0.0001
Calorie intake (Kcal/d)	988.66 (354.72)	1192.50 (351.29)	1413.49 (349.78)	1686.49 (355.75)	2198.26 (461.74)	<0.0001
Daily intake of food or food group (medium servings/d)						
Red meats	0.11 (0.10)	0.22 (0.17)	0.30 (0.19)	0.42 (0.23)	0.62 (0.35)	<0.0001
Processed meats	0.05 (0.07)	0.11 (0.11)	0.19 (0.18)	0.29 (0.24)	0.54 (0.40)	<0.0001
Butter or margarine	0.29 (0.33)	0.59 (0.51)	0.82 (0.66)	1.11 (0.81)	1.76 (1.15)	<0.0001
High-fat dairy products	0.22 (0.27)	0.44 (0.40)	0.57 (0.50)	0.75 (0.59)	1.09 (0.73)	<0.0001
Gravies	0.01 (0.02)	0.03 (0.05)	0.04 (0.07)	0.08 (0.11)	0.17 (0.20)	<0.0001
French fries	0.01 (0.02)	0.02 (0.04)	0.04 (0.05)	0.06 (0.09)	0.13 (0.16)	<0.0001
Refined grains	0.44 (0.43)	0.61 (0.47)	0.78 (0.58)	0.93 (0.68)	1.26 (0.84)	<0.0001

	'Q1' (n=817)	'Q2' (n=818)	'Q3' (n=818)	'Q4' (n=818)	'Q5' (n=817)	P value ²
Eggs	0.06 (0.09)	0.08 (0.12)	0.12 (0.14)	0.17 (0.17)	0.27 (0.28)	<0.0001
Sweets and desserts	0.32 (0.39)	0.50 (0.52)	0.65 (0.62)	0.85 (0.78)	1.20 (1.01)	<0.0001
Potatoes	0.21 (0.21)	0.31 (0.26)	0.36 (0.27)	0.43 (0.30)	0.53 (0.35)	<0.0001
High energy drinks	0.16 (0.26)	0.21 (0.32)	0.27 (0.39)	0.36 (0.45)	0.52 (0.59)	<0.0001

Abbreviation: **BMI**, body mass index; **DHA**, docosahexaenoic acid; **EPA**, eicosapentaenoic acid.

¹ Value is not age adjusted.

² P values are for tests of linear trend, otherwise indicated. Linear regression models were constructed by using continuous characteristics variables as independent variables and continuous Western pattern score as the dependent variable.

³ Chi-square tests compare the characteristic distributions among Western pattern score quintile groups.