THE CORRELATION OF FRUIT AND VEGETABLE INTAKE WITH AGE-RELATED MACULAR DEGENERATION AND CATARACT FORMATION

A Thesis
by
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Abstract

THE CORRELATION OF FRUIT AND VEGETABLE INTAKE WITH AGE-RELATED MACULAR DEGENERATION AND CATARACT FORMATION

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Age-related macular degeneration and cataracts are common causes of blindness among older adults. Oxidation has been linked to the onset of age-related macular degeneration and cataracts. It is hypothesized that fruit and vegetable intake, due to their antioxidant content, may counteract this effect and lead to lower rates of age-related macular degeneration and cataracts. The Atherosclerosis Risk In Communities (ARIC) Study began in 1987, when approximately 4,000 individuals were randomly selected from four different urban communities for the epidemiological study. The second visit of the study took place in 1990-92, the third in 1993-95, and the fourth exam was in 1996-98. Dietary assessment via a 66-question food frequency questionnaire along with a retinal examination and cataract survey were used from the ARIC study at visit three. The food frequency questionnaire was converted into fruit and vegetable groups using the Food Patterns Equivalents Database Components 2009-10. The retinal examination was graded according to the Wisconsin age-related maculopathy grading system. Logistic regression was used via SPSS, controlling for gender, ethnicity, age, education level, BMI, smoking, diabetes, and total calorie intake. The

present study includes 5,690 male and 7,140 female participants who ranged in age from 51-70 at visit three. Six percent of the male study population and 5% of the female study population were found to have age-related macular degeneration. Nine percent of the male population and 10% of the female population reported that they had a cataract. Total fruit consumption was found to be 0.86 ± 0.71 servings per day. Total vegetable consumption among participants was 1.17 ± 0.84 servings per day. No significant correlation was found between any of the food groups and age-related macular degeneration or cataracts. In this cross-sectional study, there does not seem to be a relationship between fruit and vegetable consumption and age-related macular degeneration or cataract formation for this cohort with low fruit and vegetable intake.

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Foreword

Chapter Two of this thesis will be submitted to *The Journal of Nutrition, Health & Aging*, a peer-reviewed journal published by Springer; it has been formatted according to the style guide for that journal.

Chapter One

The fastest growing segment of the United States population is individuals aged 85 years and older, and about 10,000 citizens reach the age of 65 on a daily basis. [1] Furthermore, in 1900, only 40% of individuals lived beyond 65 years, where now 80% survive to age 65. The implications for the health needs of this escalating number of older individuals are vast. Therefore, age-related conditions are at the center of focus for the health of this population, with both age-related macular degeneration (AMD) and cataracts affecting an increasing number of individuals.

AMD is the most common cause of vision loss in the United States and other developed countries. [2] This particular condition affects 8.7% of individuals worldwide and is growing. [3] It is projected that by the year 2020, 3 million individuals across the world will suffer from AMD, with one study stating that this is a "global burden". [3] While there are means of treating AMD, these treatments are not always an option; and the cost may be too substantial for certain individuals. For this reason, preventative measures are desired for inhibiting or delaying the onset and progression of this condition.

By the age of 80, cataracts affect more than half of all Americans. [4] For individuals aged 55-80, the ten-year incidence rate of developing a cataract in either eye was found to be 43.6%. [5] Furthermore, cataracts account for about 49% of vision impairment in the world. Over the years, there appears to have been a decline in the study of this disease, as surgical techniques of removing the cataractous lenses and replacing them with synthetic implants have become more popular. Even so, the prevalence of suffering from a cataract remains relatively static due to new cases of cataracts replacing the old cases that have been treated

surgically. Therefore, surgery alone is unable to cope with the increasing incidence rate of this condition. Surgery may present complications, as removal of a cataract has also been thought to hasten the appearance of macular changes associated with aging and with diabetes. For these reasons, it would be beneficial to develop therapeutic measures to prevent or delay the process of cataract formation. [6]

Age-Related Macular Degeneration

In an effort to prevent the onset or progression of these age-related conditions, understanding their pathogeneses may be necessary. As research has found over the years, many aging processes have been associated with oxidative damage caused by reactive oxygen intermediates. The eye is not exempt from this aging process and may be particularly vulnerable due to light contacting the retina and causing an increased amount of oxidation. Studies have found that chronic photo-oxidative stress in the eye is related to the onset and progression of age-related macular degeneration. [4, 7, 8]

In one animal study conducted using mice, researchers used low-intensity, long-term light exposure to replicate typical light exposure. [7] Researchers found that in the mouse retina, light exposure appeared to cause phospholipid oxidation. These oxidized phospholipids that were created in the mouse retina led to an increased expression of monocyte chemoattractant protein-1, a chemokine that is involved in regulating movement of monocytes and macrophages across the endothelium. [7] This increase of the chemokine observed in the study produced macrophage accumulation and consequent inflammation. The researchers also found that older mice had significantly higher rates of these oxidized lipids than the younger mice in the study. Furthermore, the study demonstrated that oxidized

phospholipids at the subretinal level caused choroidal neovascularization, which is a characteristic of AMD. This choroidal neovascularization was inhibited by blocking monocyte chemoattractant protein-1, suggesting age-related macular degeneration pathogenesis is related to photic stress causing an inflammatory response as mediated by this chemokine. [8]

The effects of oxidation damage are apparent, and studies have been conducted in order to evaluate methods of reducing oxidative stress in the body. [9] A high-antioxidant formula was developed for the Age-Related Eye Disease Study (AREDS) and included 500 mg of vitamin C, 400 IU of vitamin E, 15 mg of β-carotene, 80 of mg zinc oxide, and 2 mg of cupric oxide per day. In one study, the formulation significantly reduced plasma oxidation as shown in cystine levels in the blood after five days of supplementation. [9] The AREDS study was a multicenter, randomized, controlled, clinical trial that explored the impact of the antioxidant supplementation on oxidative stress related to age-related macular degeneration and cataracts. The study supplemented participants with the AREDS formulation or a placebo. The progression of advanced AMD according to neovascular or central geographic atrophy and moderate acuity loss from baseline over five years was measured. For individuals with intermediate or advanced AMD in one eye, the AREDS formulation delayed the progression to advanced AMD. A follow up study was conducted and annual eye examinations were performed. The follow up study compared the participants who were originally assigned a placebo at baseline with those originally assigned to AREDS formulation and found that at 10 years there was a significant reduction in the risk of developing advanced AMD or the development of neovascular AMD. Additionally, a significant reduction for the development of moderate vision loss was observed. [10]

While the AREDS study showed prevention of macular degeneration with supplementation of antioxidants, other studies have explored the dietary sources of antioxidants. One such study set out to analyze which green leafy vegetables could be consumed as a dietary supplement for the carotenoids, as the authors noted that green leafy vegetables are often cited as having relatively high amounts of these carotenoids. Other fruits and vegetables were evaluated for these carotenoids in the study as well. The study found that most of the dark green leafy vegetables that have been noted as having higher amounts of lutein and zeaxanthin have 15-47% of lutein but very low content of zeaxanthin. Egg yolk and maize contained the highest mole percentage of lutein and zeaxanthin. Maize contained the highest quantity of lutein and orange pepper had the highest amount of zeaxanthin. Kiwi fruit, grapes, spinach, orange juice, zucchini and different kinds of squash also provided substantial amounts of lutein and zeaxanthin. The results show that fruits and vegetables of various colors can be consumed to increase dietary intake of lutein and zeaxanthin. [11] Further research has evaluated the association between lutein plus zeaxanthin on AMD. The Carotenoids in Age-Related Eye Disease Study (CAREDS) evaluated 1,787 participants from the Women's Health Initiative Study who were found to have lutein and zeaxanthin intake below the 28th percentile or above the 78th percentile. The CAREDS study evaluated AMD via a fundus photograph 4-7 years after participation in the Women's Health Initiative study. It was found that high levels of these carotenoids played a protective role against intermediate AMD in women younger than 75 years of age. [12]

Researchers carried out an epidemiologic prospective cohort study with 464 incident cases of early age-related maculopathy and 316 cases of neovascular age-related maculopathy among 77,562 women in the Nurses' Health Study and 40,866 men in the

Health Professionals Follow-up Study. The researchers evaluated the dietary intake of the subjects in the study with semi-quantitative food-frequency questionnaires. Researchers found that fruit intake was inversely associated with the risk of neovascular age-related maculopathy and participants who had consumed three or more servings of fruits per day had a significant reduction in incidence of age-related maculopathy as compared to those who had less than 1.5 servings per day. The researchers concluded that fruits play a protective role in the risk of neovascular age-related maculopathy. [13]

Cataracts

Not only has oxidative stress been associated with the pathogenesis of age-related macular degeneration, but it plays a role with the development of cataracts as well. With cataracts, light, UV radiation and oxidative stress affect the proteins, membranes and DNA of the lens in the eye. One particular study set out to evaluate the damage to a human cataractous lens of an eye by focusing on the DNA impacted. Following removal of the cataractous lens, 11 of the lenses were analyzed for DNA damage, and eleven others were incubated with 5% CO_2 for one week to mimic the endogenous oxidation that the human eye encounters, after which the lenses were analyzed by the same means. After one week of incubation, there was a significant increase in oxidative damage to purines in the DNA. This *in vitro* demonstration suggests that light damage and oxidative stress cause damage to the lens epithelium as noticed in the cataractous lens. [14] Epidemiologic studies have found that countries with higher UV indices also have higher incidence of cataracts. [6] The cataractous lenses extracted from individuals in these countries also appear to be more strongly pigmented with yellow and brown coloration than those of higher latitudes. This coloration

may be due to oxidation of proteins caused by light entering the eye. The higher incidence of cataracts found in countries with increased UV light exposure is thought to be due to greater amounts of reactive oxygen species generated from this light. Both *in vitro* and *in vivo* studies suggest that the development of a cataract is associated with oxidative stress from light entering the eye and causing oxidative damage. [6]

Studies have been conducted to explore whether antioxidants have an effect on cataract progression and development. A prospective study on the effect of carotenoid intake on risk of cataract extraction was carried out based on data from The Health Professionals Follow-up Study. This study included 51,529 US male dentists, optometrists, osteopaths, podiatrists, pharmacists and veterinarians. Participants were 40-75 years old at the start of the study in 1986 and filled out a mailed questionnaire at the onset of the study and every two years after that, including a semi-quantitative food frequency questionnaire. It was found that increased intake of lutein and zeaxanthin was associated with a modest decrease of cataract extractions, with men in the highest fifth of lutein and zeaxanthin intake at a 19% lower risk of cataract extraction, suggesting a protective effect of these antioxidants. [15] In one case-control epidemiologic study, researchers investigated intake of vitamins C and E. In the study, the researchers interviewed 250 cataract patients and a similar number of control subjects. The researchers found a statistical association between supplemented vitamin consumption and decreased rates of cataract conditions. The researchers noted that since this was a case-control study, further clinical trials would need to be executed in order to strengthen causation. [16] The AREDS study, which assessed the progression and incidence of age-related macular degeneration, also was utilized to evaluate the effects of those high-dose antioxidants on cataracts and related visual acuity loss. The AREDS formulation of

antioxidants or a placebo was given to 4757 subjects and baseline and annual lens photographs were taken as subjects were followed up for 6.3 years on average. Participants were evaluated for the severity of lens opacity using the AREDS cataract grading scale. Researchers evaluated change from baseline in nuclear, cortical or posterior subcapsular opacity grades or cataract surgery and moderate visual acuity loss. The study found that there was no statistically significant effect from the AREDS formulation on the development of age-related lens opacities. Furthermore, for those patients who did not suffer from age-related macular degeneration at baseline, there was no statistically significant impact of AREDS formulation on moderate visual acuity. [17]

Fruit and vegetable intake, in particular, has been explored in its relation to cataract formation in an analysis of the Women's Health Study, a prospective study aimed to explore cardiovascular disease and cancer incidence in women. The study was a randomized, double-blind trial which included 39,876 women who were health professionals over the age of 45. The study included a 131 item food frequency questionnaire from which fruit and vegetable intake was evaluated from average daily intakes of each item. Participants completed annual questionnaires that included occurrence of a cataract. The mean daily fruit and vegetable intake at baseline was 6.0 ± 3.3 total servings per day. Those women who had indicated higher intake of fruits and vegetables were less likely to be current smokers and were also found to be older. It was found that there were 2067 occurrences of a cataract and 1315 cases of a confirmed cataract extraction, after an average of a 10-year follow up period. Researchers found that consumption of over 3.4 servings of fruit and vegetables per day was associated with a 10-15% reduction in risk of both cataract and cataract extraction. The findings did not change significantly when accounting for smoking and other risk factors for

a cataract occurrence. [18] Another study using the Women's Healthy Study data was conducted to assess dietary intake of carotenoids, vitamin C and E and risk of cataract in women. The food frequency questionnaire, as well as information collected about vitamin supplement intake was used to assess consumption of these nutrients. The intakes of the carotenoids and vitamins were assessed for diet alone as well as with multivitamin supplements. Researchers found that higher dietary intakes of lutein and zeaxanthin and vitamin E from both dietary sources and supplements were associated with a significant decrease in the risk of a cataract. [19] An analysis of the Nurses' Health Study also explored the role of dietary choices on age-related cataract formation. The study consisted of 121,700 female registered nurses 30-55 years of age in 1976. The participants filled out questionnaires every two years for follow-up information. A 126-136 item semi-quantitative food frequency questionnaire was administered every two to four years starting in 1980, and the mean over an average of 10 years of consumption was used. Results of the food frequency questionnaire averages were then evaluated to indicate adherence to the 1990 Dietary Guidelines for Americans using the Healthy Eating Index. The 1990 Dietary Guidelines for Americans recommended intake of three or more servings of vegetables and two or more servings of fruits per day. [20] Participants were given an eye examination and color film slides of the lens were evaluated for opacity. Researchers found that adherence with the Dietary Guidelines for Americans was inversely associated with age-related nuclear lens opacity in women. [21]

Research suggests that components of fruits and vegetables can improve eye health. Studies have even found that high intakes of fruit and vegetable consumption can deter AMD and cataract formation. This study will investigate the association of different fruit and

vegetable groups, as defined by government standards according to MyPyramid, with age-related macular degeneration and cataract formation in a population that consumes low amounts of these foods.

Chapter Two

Abstract

Objectives: To determine the association of individual fruit and vegetable group consumption and total fruit and vegetable consumption with age-related macular degeneration and cataract formation. *Design*: Dietary assessment via a 66-question food frequency questionnaire, along with a retinal examination and cataract survey were used from the ARIC epidemiological study at visit three. The food frequency questionnaire was converted into fruit and vegetable groups using the Food Patterns Equivalents Database Components 2009-10. The retinal examination was graded according to the Wisconsin age-related maculopathy grading system. *Setting*: The Atherosclerosis Risk in Communities (ARIC) Study is an epidemiological prospective cohort study that began in 1987 and included approximately 4,000 individuals randomly selected and recruited from a defined population in four communities at visit one. Follow up studies took place in 1990-92, 1993-95 and 1996-98. *Participants*: The present study includes 11,532 of the biracial population evaluated at the third visit (1993-95). Subjects excluded were missing a food-frequency questionnaire (FFQ), covariate information or AMD or cataract information from visit three. *Measurements*: Logistic regression was used via SPSS version 22.0, 2013, controlling for gender, ethnicity, age, education level, BMI, smoking, diabetes and total calorie intake. *Results*: At visit three, participants ranged in age from 51-70 years old. Six percent of the male study population and 5% of the female study population were found to have age-related macular degeneration. Nine percent of the male population and 10% of the female population reported that they had a cataract. Total fruit consumption was found to be 0.86 ± 0.71 servings per day. Total

vegetable consumption among participants was 1.17 ± 0.84 servings per day. There was no significant association between AMD or cataracts and fruit and vegetable intake. *Conclusion:* In this cross-sectional study, there does not appear to be a relationship between fruit and vegetable consumption and age-related macular degeneration or cataract formation for this cohort with low fruit and vegetable intake. Further research needs to be done to explore this relationship.

Key words: Age-Related Macular Degeneration, Cataracts, Fruits, Vegetables

Introduction

Age-related macular degeneration (AMD) is the most common cause of blindness in developed countries. AMD affects 8.7% of individuals worldwide and it is projected that by the year 2020 that 196 million individuals across the world will suffer from AMD. [3] Treatments for AMD are not always an option and can be costly. For this reason, preventative measures are desired for inhibiting or delaying the onset and progression of this condition.

Cataracts affect more than half of all Americans by the age of 80. For individuals aged 55-80, the ten-year incidence rate of developing any cataract was found to be 43.6%, and cataracts accounts for about 49% of vision impairment in the world. [5] Over the years, there has been a decline in the study of this disease, as surgical techniques of removing and replacing the cataractous lenses have become popular, but the prevalence of cataracts remains static due to new cases arising. It would be beneficial to develop therapeutic measures to prevent or delay the process of cataract formation. [6]

Studies have found oxidative stress in the eye is related to the onset and progression of AMD. [7] When the AREDS formulation of antioxidants was given to a study population, researchers found significantly reduced plasma oxidation. [9] Further evidence suggested AREDS antioxidant supplementation improved AMD outcomes, even after a ten year follow up. [10] Researchers have also investigated AMD and the role of certain carotenoids, lutein and zeaxanthin, which are found in relatively high quantities in the eye. Results suggest higher intakes of these carotenoids may protect against intermediate AMD in certain populations. [12] Fruit has been found to play a protective role in the risk of neovascular age-related maculopathy as well. [13]

Oxidative damage has been associated with cataractous lenses. One study found the DNA in the lens suffers from oxidative damage, suggesting oxidative stress causes damage to the lens epithelium. [14] Epidemiologic studies have found that countries with higher UV indexes have high incidence of cataracts, possibly due to greater amounts of reactive oxygen species generated from this light. [6] Studies have found that intake of carotenoids was associated with a decrease in cataract extraction. [15] Furthermore, consumption of fruits and vegetables has been associated with a decreased risk of cataracts and cataract extraction in one cohort study. [18]

Previous research has suggested that components of fruits and vegetables can improve eye health. Studies have even found that high intakes of fruits and vegetables can deter AMD and cataract formation. The present study will investigate the association of different fruit and vegetable groups, as defined by USDA standards according to MyPlate, with AMD and cataract formation in a population that consumes low amounts of these foods.

Methods

Study Population

The Atherosclerosis Risk in Communities (ARIC) Study is an epidemiological prospective cohort study that began in 1987 and included approximately 4,000 individuals randomly selected and recruited from a defined population in four communities including Washington County, MD; Forsyth County, NC; Jackson, MS, and Minneapolis, MN. Of these communities, Jackson, MS, included black subjects only. At baseline, 15,792 subjects aged 45-64 years were examined from 1987 through 1989, [22] and 12,887 individuals were evaluated at a third clinical visit in 1993 through 1995. [23] The present study includes 11,532 of the biracial population evaluated at the third visit. [24] Subjects excluded were missing a food-frequency questionnaire (FFQ), covariate information or AMD or cataract information from visit three.

Dietary Intake

At visit three, an interviewer administered a semi-quantitative FFQ to study participants. [25] Subjects reported the frequency of consumption of 66 food items in nine different categories. Additional information was collected including the name brands of some items. [26]

Fruit and vegetable consumption collected from the FFQ and analyzed according to the Food Patterns Equivalents Database Components 2009-10 (FPED), which captured fruit and vegetable consumption in mixed dishes as well as solitary sources. The fruit and vegetable servings from the FFQ were categorized into the following groups using the FPED: 1) total fruit 2) citrus, melons, and berries 3) other fruits 4) fruit juice 5) total vegetables 6)

dark green vegetables 7) total red and orange vegetables 8) total starchy vegetables 9) other vegetables. [27] Total fruits and total vegetables were summed to create the category total fruits and vegetables.

Retinal Examination

At the third visit, a retinal examination light box was used to evaluate the condition of the participants' eyes. One eye of each participant was examined using a photograph of the participant's fundus at that time in a process that was detailed in a previous study. [28] In brief, the fundus photographs were assessed in a previous study using the Wisconsin age-related maculopathy grading system to evaluate early and late stage AMD.

Cataracts Survey

At visit three, participants completed a retinal examination form, which included questions about cataract prevalence. [29] The survey question used to evaluate cataract prevalence was, "Has a doctor ever told you that you have eye problems as a result of cataracts, or cloudiness of the lens, in one or both of your eyes?" Participants could answer with "Yes", "No", or "Unknown."

Statistical Analysis

SPSS version 19.0 was used to analyze the onset of AMD and incidence of cataracts associated with total fruit and vegetable consumption as well as FPED subgroups previously described. Logistic regression analysis for each of the eye pathologies was performed. Confounders were considered progressively from unadjusted results, results adjusted for

demographic factors, and finally results adjusted for several lifestyle and dietary factors. Covariates included in the final model were age, gender, ethnicity, education level, BMI at visit three, smoking status (current smoker or not at visit three), diabetes diagnosis at visit three, and total calorie consumption at visit three.

Results

Table 1
Description of Study Participants

Variable	Value	
	Male	Female
Gender	5690 (44%)	7140 (56%)
Age (years)	51-70	51-70
Black Ethnicity	1094 (19%)	1894 (27%)
BMI (kg/m^2)	28.2 ± 4.5	28.8 ± 6.3
Diabetes Diagnosis	555 (10%)	699 (10%)
Total AMD	295 (6%)	306 (5%)
Cataract	511 (9%)	708 (10%)
Food Group	Servings Per Day	
Citrus, Melon, Berry Fruits	0.19 ± 0.24	
Other Fruits	0.45 ± 0.44	
Fruit Juice	0.22 ± 0.28	
Total Fruits	0.86 ± 0.71	
Dark Green Vegetables	0.19 ± 0.29	
Total Red Orange Vegetables	0.22 ± 0.21	
Total Starchy Vegetables	0.56 ± 0.48	
Other Vegetables	0.20 ± 0.22	
Total Vegetables	1.17 ± 0.84	
Total Fruits and Vegetables	2.03 ± 1.28	

Servings per day are expressed as mean ± standard deviation

Table 1 gives a description of the study participants that were evaluated in this analysis at visit three. The majority of participants were female (56%), and the rates of cataracts and AMD did not differ greatly between the genders. The recommended fruit and

vegetable intake for a 2,000 kcal diet is five cups per day; the mean consumption of total fruit and vegetable servings were 2.03 servings per day in this study. Males consumed an average of 1.96 total fruit and vegetable servings per day, and females consumed an average of 2.08 total servings per day.

Table 2
Association of Food Group Servings per Day with Age-Related Macular Degeneration (AMD)and Cataract Prevalence

Variable	AMD		Cataracts	
	Odds Ratio	P Value	Odds Ratio	P Value
Citrus, Melon, Berry Fruits	0.914 0.874	0.626 0.477	1.177 1.001	0.173 0.991
Other Fruit	0.990 0.959	0.915 0.694	1.126 1.010	0.057 0.893
Fruit Juice	1.164 1.117	0.260 0.424	0.995 0.885	0.966 0.284
Total Fruit	1.013 0.991	0.822 0.884	1.067 0.984	0.102 0.730
Dark Green Vegetables	0.989 1.073	0.941 0.625	1.099 1.056	0.313 0.595
Total Red Orange Vegetables	1.240 1.173	0.238 0.405	1.392 1.180	0.009 0.237
Total Starchy Vegetables	1.020 1.107	0.817 0.855	0.882 0.951	0.085 0.488
Other Vegetables	0.934 0.957	0.733 0.825	1.091 1.029	0.493 0.828
Total Vegetables	1.014 1.020	0.775 0.694	1.007 1.006	0.852 0.879
Total Fruits and Vegetables	1.010 1.006	0.751 0.856	1.023 0.998	0.305 0.933

*Logistic regression model. Line one unadjusted results. Line two results controlled for age, gender and ethnicity

Table 2 shows the unadjusted associations between specific food groups and AMD and cataracts in the first line. The second line shows the associations after controlling for age, race and gender. The odds ratio is that associated with an increase of one fruit or vegetable serving per day.

Table 3
Association of Food Group Servings per Day with Age-Related Macular Degeneration (AMD) and Cataract Prevalence

Variable	AMD		Cataracts	
	Odds Ratio	P Value	Odds Ratio	P Value
Citrus, Melon, Berry Fruits	0.873	0.532	0.991	0.950
Other Fruit	1.031	0.805	0.952	0.603
Fruit Juice	1.130	0.419	0.878	0.303
Total Fruit	1.024	0.755	0.952	0.398
Dark Green Vegetables	1.025	0.897	0.870	0.345
Total Red Orange Vegetables	1.151	0.560	0.883	0.515
Total Starchy Vegetables	0.982	0.894	0.859	0.145
Other Vegetables	0.924	0.740	0.928	0.662
Total Vegetables	1.002	0.977	0.907	0.107
Total Fruits and Vegetables	1.013	0.815	0.933	0.091

*Logistic regression model controlled for gender, ethnicity, age, education, BMI, smoking, diabetes, and total calories

Table 3 depicts the associations of the specific food groups after being controlled for gender, ethnicity, age, education, BMI, smoking, diabetes, and total calories. Total red and orange vegetables were found to be significant in the unadjusted model, but when important cofactors were controlled for, the significance was not maintained. No significant associations between AMD or cataracts and fruit and vegetable groups were found.

Discussion

In this cross-sectional study, a link between intake of fruit and vegetable groups and AMD or cataracts in this population with relatively low fruit and vegetable consumption was not found. The low intake of fruits and vegetables in this specific study population may be an important factor in the generation of these non-significant results, while other studies with higher intakes showed more positive results. The low intake of fruits and vegetables in this study population could be a reflection of the limited FFQ, though fruit and vegetable consumption from mixed dishes in addition to solitary fruit and vegetable consumption was captured using the FPED to obtain a more accurate number of fruit and vegetable servings per day.

The relatively low intake of fruit and vegetables compared to higher intakes evaluated in other study populations is found to be less than the average intake in the United States during that time. In 1995, a telephone survey was performed evaluating intake over 16 states and found that mean intake was 3.3 servings per day for men and 3.7 servings per day for women, with only 20% of the population consuming the recommended 5 servings per day. [30] The Women's Health Study, conducted in 1993, found a higher consumption with an average of 2.2 servings of fruit and 3.9 servings of vegetables per day. [31] The discrepancy between the reported intakes of fruit and vegetables in the ARIC study and other study populations as well as with reported intakes in United States is indicative that the ARIC food frequency questionnaire may have limited the results of fruit and vegetable consumption. The Food Patterns Equivalents Database (FPED) was key to this study, as different food groups were examined individually in their relation to AMD and cataracts.

These unique fruit and vegetable groups were combined into a group of total fruits and vegetables to evaluate the overall correlation with AMD and cataracts.

Oxidative damage can contribute to certain eye conditions such as AMD and cataracts. [6, 7] Fruits and vegetables contain antioxidants that may prevent this oxidative damage from occurring. Evidence suggests that intake of antioxidant supplements can help to decrease progression and incidence of AMD. [9, 10] Fruit intake has also been shown to have a protective role in neovascular age-related maculopathy, an early stage of AMD. [13] Separate studies have found that intake of carotenoids from food as well as intake of vitamins C and E from foods has been shown to decrease the incidence of a cataract. [15, 16] Furthermore, fruit and vegetable consumption over 3.4 servings per day was found to decrease risk of both a cataract and cataract extraction. [18] Adherence to the Dietary Guidelines for Americans has also been shown to be inversely associated with lens opacity in one study. [21]

While other studies have found a link between antioxidant and fruit and vegetable consumption and AMD or cataracts, the current study did not find this link. It is speculated that higher intake of fruits or vegetables in other cohort studies could have led to a more positive result. The Women's Health Study reported an average of 6.0 ± 3.3 total servings per day of fruits and vegetables per day [18] compared to 2.03 ± 1.28 in this cohort.

Because the study was cross-sectional, it was limited by a single measure of food intake during visit three. The relatively low fruit and vegetable intake by the study population was also a limitation in this study, which may have been exacerbated by the limited FFQ that was used throughout the study. Although a fundus photograph was used to evaluate AMD,

cataract incidence was self-reported. The cohort was relatively large, including 11,532 participants of a biracial population, which strengthened the results of this study.

In conclusion, we did not find an association between intake of different fruit and vegetable groups or total fruit and vegetable intake and incidence of AMD or a cataract when accounting for confounding factors. Future research should focus on the amount of fruit and vegetable intake necessary to impact AMD and cataract prevalence.

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Appendix A

exp. 10/31/95

ARIC
Atherosclerosis Risk in Communities

DIETARY INTAKE FORM

ID NUMBER: [ ][ ][ ][ ][ ][ ][ ] CONTACT YEAR: [0][7] FORM CODE: [D][T][I] VERSION: C 09/09/92

LAST NAME: [ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ] INITIALS: [ ][ ]

Public reporting burden for this collection of information is estimated to average 15 minutes, including the time for reviewing instructions, gathering needed information and completing and reviewing the questionnaire. If you have comments regarding this burden, please send them to Attention: PRA Reports Clearance Officer, PHS, 721-B Hubert H. Humphrey Building, 200 Independence Avenue, SW, Washington, DC 20201, and to the Paperwork Reduction Project (0925-0281), Office of Information and Regulatory Affairs, Office of Management and Budget, Washington, DC 20503.

Instructions: This form is completed during the interview portion of the participant's visit. ID Number, Name and Contact Year are entered above. Whenever numerical responses are required, enter the number so that the last digit appears in the rightmost box. Enter leading zeroes where necessary to fill all boxes. If a number is entered incorrectly on the paper form, mark through the incorrect entry with an "X". Code the correct entry clearly above the incorrect entry. For "multiple choice" and "yes/no" type questions, circle or write in the letter corresponding to the most appropriate response. If a letter is circled incorrectly, mark through it with an "X" and circle the correct response.

"In this part of the clinic visit we want to obtain information on your usual eating habits. We will go over specific foods by groups. I'll name a food and a portion size and you tell me how often, on average, you ate that during the past year.

If your portion was <u>much</u> different from the amount I say, please tell me if it was at least twice as much, or half as much. We have a few sizes of cups and glasses here for reference. Here are the choices for "how often" (show RC 1). The choices are number of times a day or week or month. Please respond with the appropriate letter. For example, "once a day" would be "D". If you ate or drank something less than twelve times a year, that would be the same as "less than once a month," which is "I".

It is important that your answer be short in order to save time, but we want you to be as accurate as possible. If we miss food items that you usually eat, we will list those at the end. Feel free to ask questions or have me repeat instructions if I am not being clear."

Dietary Intake Form (DTIC screen 1 of 15)

Response Categories:	> 6 per day (A) 4-6 per day (B) 2-3 per day (C)	1 per day (D) 5-6 per week (E) 2-4 per week (F)	1 per week (G) 1-3 per month (H) Almost never (I)

A. DAIRY FOODS [RC 1]

"In the past year, how often on average did you consume..."

1. Skim or low fat milk; 8 oz. glass ..... ☐
2. Whole milk; 8 oz. glass ..... ☐
3. Yogurt; 1 c. ..... ☐
4. Ice cream; 1/2 c. ..... ☐
5. Cottage cheese or ricotta cheese; 1/2 c. ..... ☐
6. Other cheeses, plain or as part of a dish; 1 slice or serving ..... ☐
7. Margarine or a margarine/butter blend; pats added to food or bread ..... ☐
8. Butter; pats added to food or bread ..... ☐

Dietary Intake Form (DTIC screen 2 of 15)

Response Categories:	> 6 per day (A) 4-6 per day (B) 2-3 per day (C)	1 per day (D) 5-6 per week (E) 2-4 per week (F)	1 per week (G) 1-3 per month (H) Almost never (I)

B. FRUITS [RC 1]

"In the past year, how often on average did you consume..."

9. Fresh apples or pears; 1 ..... ☐
10. Oranges; 1 ..... ☐
11. Orange or grapefruit juice; small glass ..... ☐
12. Peaches, apricots or plums; 1 fresh or 1/2 c. canned or dried ..... ☐
13. Bananas; 1 ..... ☐
14. Other fruits; 1 fresh or 1/2 c. canned, including fruit cocktail ..... ☐

C. VEGETABLES [RC 1] -- Portion is 1/2 c.

"In the past year, how often on average did you consume..."

15. String beans or green beans; 1/2 c. ..... ☐
16. Broccoli; 1/2 c. ..... ☐

Dietary Intake Form (DTIC screen 3 of 15)

Response Categories:	> 6 per day (A) 4-6 per day (B) 2-3 per day (C)	1 per day (D) 5-6 per week (E) 2-4 per week (F)	1 per week (G) 1-3 per month (H) Almost never (I)

17. Cabbage, cauliflower, brussels sprouts; 1/2 c. ..... ☐
18. Carrots; 1 whole or 1/2 c. cooked ..... ☐
19. Corn; 1 ear or 1/2 c. ..... ☐
20. Spinach, collards or other greens, but do not include lettuce; 1/2 c. ..... ☐
21. Peas or lima beans; 1/2 c. fresh, frozen or canned ..... ☐
22. Dark yellow, winter squash such as acorn, butternut; 1/2 c. ..... ☐
23. Sweet potatoes; 1/2 c. ..... ☐
24. Beans or lentils, dried cooked, or canned, such as pinto, blackeye, baked beans; 1/2 c. ..... ☐
25. Tomatoes; 1, or tomato juice; 4 oz. ..... ☐

Dietary Intake Form (DTIC screen 4 of 15)

Response Categories:	> 6 per day (A) 4-6 per day (B) 2-3 per day (C)	1 per day (D) 5-6 per week (E) 2-4 per week (F)	1 per week (G) 1-3 per month (H) Almost never (I)

D. MEATS [RC 1]

"In the past year, how often on average did you consume..."

26. Chicken or turkey, without skin ..... ☐
27. Chicken or turkey, with skin ..... ☐
28. Hamburgers; 1 ..... ☐
29. Hot dogs; 1 ..... ☐
30. Processed meats: sausage, salami, bologna, etc.; piece or slice ..... ☐
31. Bacon; 2 slices ..... ☐
32. Beef, pork or lamb as a sandwich or mixed dish, stew, casserole, lasagne, or in spaghetti sauce, etc. ..... ☐
33. Beef, pork or lamb as a main dish, steak, roast, ham, etc. ..... ☐
34. Canned tuna fish; 3-4 oz. ..... ☐

Dietary Intake Form (DTIC screen 5 of 15)

Response Categories:	> 6 per day (A) 4-6 per day (B) 2-3 per day (C)	1 per day (D) 5-6 per week (E) 2-4 per week (F)	1 per week (G) 1-3 per month (H) Almost never (I)

35. Dark meat fish, such as salmon, mackerel, swordfish, sardines, bluefish; 3-5 oz. ..... ☐

36. Other fish, such as cod, perch, catfish, etc.; 3-5 oz ..... ☐

37. Shrimp, lobster, scallops as a main dish ..... ☐

38. Eggs; 1 ..... ☐

E. SWEETS, BAKED GOODS, CEREALS [RC 1]

"In the past year, how often on average did you consume..."

39. Chocolate bars or pieces, such as Hershey's, Plain M & M's, Snickers, Reeses; 1 oz. ..... ☐

40. Candy without chocolate; 1 oz ..... ☐

41. Pie, homemade from scratch; 1 slice ..... ☐

Dietary Intake Form (DTIC screen 6 of 15)

Response Categories:	> 6 per day (A) 4-6 per day (B) 2-3 per day (C)	1 per day (D) 5-6 per week (E) 2-4 per week (F)	1 per week (G) 1-3 per month (H) Almost never (I)

42. Pie, ready-made or from a mix; 1 slice ..... ☐

43. Donut; 1 ..... ☐

44. Biscuits or cornbread; 1 ..... ☐

45. Danish pastry, sweet roll, coffee cake, croissant; 1 ..... ☐

46. Cake or brownie; 1 piece ..... ☐

47. Cookies; 1 ..... ☐

48. Cold breakfast cereal; 1/2 c. ..... ☐

49. Cooked cereals such as oatmeal, grits, cream of wheat; 1/2 c. ..... ☐

50. White bread; 1 slice ..... ☐

51. Dark or whole grain bread; 1 slice ..... ☐

F. MISCELLANEOUS [RC 1]

"In the past year, how often on average did you consume..."

52. Peanut butter; 1 tbsp ..... ☐

Dietary Intake Form (DTIC screen 7 of 15)

Response Categories:	> 6 per day (A) 4-6 per day (B) 2-3 per day (C)	1 per day (D) 5-6 per week (E) 2-4 per week (F)	1 per week (G) 1-3 per month (H) Almost never (I)

53. Potato chips or corn chips; small bag or 1 oz. ..... ☐

54. French fried potatoes; 1 serving, 4 oz. ..... ☐

55. Nuts; 1 oz. ..... ☐

56. Potatoes, mashed; 1 c. or baked; 1 ..... ☐

57. Rice; 1/2 c. ..... ☐

58. Spaghetti, noodles or other pasta; 1/2 c. ..... ☐

59. Home-fried food, such as any meats, poultry, fish, shrimp, eggs, vegetables, etc.; 1 serving ..... ☐

60. Food fried away from home, such as any fish, chicken, chicken nuggets, etc. ..... ☐

Dietary Intake Form (DTIC screen 8 of 15)

Response Categories:	> 6 per day (A) 4-6 per day (B) 2-3 per day (C)	1 per day (D) 5-6 per week (E) 2-4 per week (F)	1 per week (G) 1-3 per month (H) Almost never (I)

G. BEVERAGES [RC 1]

"In the past year, how often on average did you consume..."

61. Coffee, not decaffeinated; 1 c. ..... ☐

62. Tea, iced or hot, not including decaf or herbal tea; 1 cup ..... ☐

63. Low calorie soft drinks, such as any diet Coke, diet Pepsi, diet 7-Up; 1 glass ..... ☐

64. Regular soft drinks, such as Coke, Pepsi, 7-Up, ginger ale; 1 glass ..... ☐

65. Fruit-flavored punch or non-carbonated beverages, such as lemonade, Kool-Aid or Hawaiian Punch; not diet; 1 glass ..... ☐

H. OTHER DIETARY ITEMS

66. How often do you eat liver; 3-4 oz. serving? ..... [rc 2]

1/week	A
2-3/month	B
1/month or less	C
Never	D

Dietary Intake Form (DTIC screen 9 of 15)

67. Are there any other foods that you usually eat at least twice per week such as tortillas, prunes, or avocado? Do not include dry spices nor something that has been listed previously. ..... Yes Y

No N

Go to Item 74, Screen 10

68. Food #1 eaten at least twice per week (enter code and specify food and usual portion size below): ..... [ ][ ][ ]

a. _____

69. Frequency for food #1: ..... [rc 3]

> 6/day	A
4-6/day	B
2-3/day	C
1/day	D
5-6/wk	E
2-4/wk	F

70. Food #2 eaten at least twice per week (enter code and specify food and usual portion size below): ..... [ ][ ][ ]

a. _____

71. Frequency for food #2: ..... [rc 3]

> 6/day	A
4-6/day	B
2-3/day	C
1/day	D
5-6/wk	E
2-4/wk	F

Dietary Intake Form (DTIC screen 10 of 15)

72. Food #3 eaten at least twice per week (enter code and specify food and usual portion size below): ..... [ ][ ][ ]

a. _____

73. Frequency for food #3: ..... [rc 3]

> 6/day	A
4-6/day	B
2-3/day	C
1/day	D
5-6/wk	E
2-4/wk	F

74. What do you do with the visible fat on your meat? [rc 4]

Eat most of the fat	A
Eat some of the fat	B
Eat as little as possible	C
Don't eat meat	D

75. What kind of fat do you usually use for frying and sauteing foods at home, excluding "Pam"-type spray? [rc 5]

Real Butter	A
Margarine	B
Vegetable Oil	C
Vegetable Shortening	D
Lard	E
Bacon Grease	F
Not Applicable	G
Unknown	H

Go to Item 77, Screen 11

76. Enter code and specify brand and form below: ..... [ ][ ][ ]

a. _____

Dietary Intake Form (DTIC screen 11 of 15)

77. What kind of fat do you usually use for baking? [rc 5]

Real Butter	A
Margarine	B
Vegetable Oil	C
Vegetable Shortening	D
Lard	E
Bacon Grease	F
Not Applicable	G
Unknown	H

Go to Item 79

78. Enter code and specify brand and form below: ..... [ ][ ][ ]

a. _____

79. What brand and form of margarine do you usually use at the table? [rc 6]

a. Form: ..... None A

Go to Item 80, Screen 12

Stick	B
Tub	C
Diet (low calorie)	D
Other	E

b. Code number: ..... [ ][ ][ ]

c. Brand: _____

Dietary Intake Form (DTIC screen 12 of 15)

80. What kind of cold breakfast cereal do you most often use? (Enter code and specify brand name below): ..... [ ][ ][ ]

a. Brand: _____

81. Are you currently on a special diet? ..... Yes Y

Go to Item 84, Screen 13 — No N

82. How many years have you been on it? .... [ ][ ]

83. People are often on more than one diet at a time. We are interested in learning what diet or diets you are currently on. Are you on any of these?

	Yes	No	Unknown
a. Weight Loss	Y	N	U
b. Low Salt	Y	N	U
c. Low Cholesterol	Y	N	U
d. Weight Gain	Y	N	U
e. Diabetic	Y	N	U
f. Other	Y	N	U

Dietary Intake Form (DTIC screen 13 of 15)

84. How many teaspoons of sugar do you add to your food daily? Include sugar added to coffee, tea, cereal, etc. ..... [ ][ ]

85. In cooking vegetables, how often do you add fat such as salt pork, butter, or margarine? ..... [rc 7]

2-3 times per day	A
1 time per day	B
5-6 times per week	C
2-4 times per week	D
1 time per week	E
1-3 times per month	F
Never	G
Unknown	H

86. How often is salt or salt-containing seasoning such as garlic salt, onion salt, soy sauce, or Accent added to your food in cooking? [rc 7]

2-3 times per day	A
1 time per day	B
5-6 times per week	C
2-4 times per week	D
1 time per week	E
1-3 times per month	F
Never	G
Unknown	H

87. How many shakes of salt do you add to your food at the table every day? ..... [ ][ ]

Dietary Intake Form (DTIC screen 14 of 15)

88. How often do you add catsup, hot sauce, soy or steak sauces to your food? ..... [rc 7]

2-3 times per day	A
1 time per day	B
5-6 times per week	C
2-4 times per week	D
1 time per week	E
1-3 times per month	F
Never	G
Unknown	H

89. How often do you eat special low salt foods such as low salt chips, nuts, cheese, or salad dressing? ..... [rc 7]

2-3 times per day	A
1 time per day	B
5-6 times per week	C
2-4 times per week	D
1 time per week	E
1-3 times per month	F
Never	G
Unknown	H

Dietary Intake Form (DTIC screen 15 of 15)

I. ADMINISTRATIVE INFORMATION

90. Interviewer's opinion of information:

Reliable	A
Questionable	B
Participant uncooperative	C
Participant unable to estimate frequencies	D

91. Date of data collection: [ ][ ] / [ ][ ] / [ ][ ]

Month Day Year

92. Method of data collection ..... Computer C

Paper form P

93. Code number of person completing this form: ..... [ ][ ][ ]

Appendix B

Cohort, Exam 3

Retinal Examination Light Box

Instructions: Retinal Image Processing Dataset

ID		*Aric Subject ID (Cir)*
N	*Value*	*Description*
12642	Present	Text suppressed

RLBA0		*St= Normal Reading, Q1=qc*
N	*Value*	*Description*
12642	ST	Normal Reading

RLBA1		*Eye (L,R)*
N	*Value*	*Description*
6323	L	Left
6319	R	Right

RLBA10		*Arterial: Focal Narrowing Within Disc Margin*
N	*Value*	*Description*
10611	0	No focal narrowing
431	1	Questionable focal narrowing
340	2	Definite focal narrowing in one or two substantial arterioles (definite).
15	3	Definite focal narrowing in three or more substantial arterioles (severe).
1245	8	Cannot grade.

RLBA11		*Arterial: Focal Narrowing In Zone A*
N	*Value*	*Description*
9975	0	No focal narrowing
720	1	Questionable focal narrowing
456	2	Definite focal narrowing in one or two substantial arterioles (definite).
30	3	Definite focal narrowing in three or more substantial arterioles (severe).
1461	8	Cannot grade.

RLBA12A		Arterial: Focal Narrowing, Quadrant Superior Temporal
N	Value	Description
10647	0	No focal narrowing
435	1	Questionable focal narrowing
358	2	Definite focal narrowing, combined length <1/2 DD (mild).
26	3	Definite focal narrowing, combined length >1/2 DD, but < 2 DD (moderate).
1	4	Definite focal narrowing, combined length = 2 DD (severe).
1175	8	Cannot grade.

RLBA12B		Arterial: Focal Narrowing, Quadrant Superior Nasal
N	Value	Description
10414	0	No focal narrowing
306	1	Questionable focal narrowing
212	2	Definite focal narrowing, combined length <1/2 DD (mild).
12	3	Definite focal narrowing, combined length >1/2 DD, but < 2 DD (moderate).
1698	8	Cannot grade.

RLBA12C		Arterial: Focal Narrowing, Quadrant Inferior Nasal
N	Value	Description
10470	0	No focal narrowing
205	1	Questionable focal narrowing
146	2	Definite focal narrowing, combined length <1/2 DD (mild).
9	3	Definite focal narrowing, combined length >1/2 DD, but < 2 DD (moderate).
1812	8	Cannot grade.

RLBA12D		Arterial: Focal Narrowing, Quadrant Inferior Temporal
N	Value	Description
10516	0	No focal narrowing
375	1	Questionable focal narrowing
303	2	Definite focal narrowing, combined length <1/2 DD (mild).
19	3	Definite focal narrowing, combined length >1/2 DD, but < 2 DD (moderate).
1429	8	Cannot grade.

Cohort, Exam 3

RLBA13A		Arterial: Sheathing, Quadrant Superior Temporal
N	Value	Description
12118	0	No arteriolar sheathing.
3	1	Questionable arteriolar sheathing.
8	2	Definite arteriolar sheathing, combined length <1/2 DD (mild).
5	3	Definite arteriolar sheathing, combined length = 1/2 DD, but < 2 DD (moderate).
508	8	Cannot grade.

RLBA13B		Arterial: Sheathing, Quadrant Superior Nasal
N	Value	Description
11877	0	No arteriolar sheathing.
7	1	Questionable arteriolar sheathing.
4	2	Definite arteriolar sheathing, combined length <1/2 DD (mild).
6	3	Definite arteriolar sheathing, combined length = 1/2 DD, but < 2 DD (moderate).
2	4	Definite arteriolar sheathing, combined length = 2 DD (severe).
746	8	Cannot grade.

RLBA13C		Arterial: Sheathing, Quadrant Inferior Nasal
N	Value	Description
11806	0	No arteriolar sheathing.
3	1	Questionable arteriolar sheathing.
5	2	Definite arteriolar sheathing, combined length <1/2 DD (mild).
4	3	Definite arteriolar sheathing, combined length = 1/2 DD, but < 2 DD (moderate).
2	4	Definite arteriolar sheathing, combined length = 2 DD (severe).
822	8	Cannot grade.

RLBA13D		Arterial: Sheathing, Quadrant Inferior Temporal
N	Value	Description
11975	0	No arteriolar sheathing.
4	1	Questionable arteriolar sheathing.
5	2	Definite arteriolar sheathing, combined length <1/2 DD (mild).
3	3	Definite arteriolar sheathing, combined length = 1/2 DD, but < 2 DD (moderate).
3	4	Definite arteriolar sheathing, combined length = 2 DD (severe).
652	8	Cannot grade.

RLBA14		Generalized Narrowing
N	Value	Description
11513	0	No generalized narrowing.
344	1	Questionable generalized narrowing.
53	2	Definite generalized narrowing.
7	3	Severe generalized narrowing, threads throughout.
725	8	Cannot grade.

RLBA15A		A/V Nicking, Quadrant Superior Temporal
N	Value	Description
10548	0	No A/V nicking.
661	1	Questionable A/V nicking.
446	2	Definite A/V nicking, < ETDRS Std. Photo. #9 (definite).
15	3	Definite A/V nicking, = ETDRS Std. Photo. #9 (severe).
972	8	Cannot grade.

RLBA15B		A/V Nicking, Quadrant Superior Nasal
N	Value	Description
11224	0	No A/V nicking.
129	1	Questionable A/V nicking.
43	2	Definite A/V nicking, < ETDRS Std. Photo. #9 (definite).
1246	8	Cannot grade.

RLBA15C		A/V Nicking, Quadrant Inferior Nasal
N	Value	Description
11242	0	No A/V nicking.
69	1	Questionable A/V nicking.
29	2	Definite A/V nicking, < ETDRS Std. Photo. #9 (definite).
1302	8	Cannot grade.

RLBA15D		A/V Nicking, Quadrant Inferior Temporal
N	Value	Description
10748	0	No A/V nicking.
461	1	Questionable A/V nicking.
239	2	Definite A/V nicking, < ETDRS Std. Photo. #9 (definite).
6	3	Definite A/V nicking, = ETDRS Std. Photo. #9 (severe).
1188	8	Cannot grade.

RLBA16		Number Of Microaneurysms
N	Value	Description
10453	0	No microaneurysms.
103	1	Questionable microaneurysm.
203	2	One microaneurysm.
67	3	Two microaneurysms.
37	4	Three microaneurysms.
17	5	Four microaneurysms.
164	6	Five or more microaneurysms.
1598	8	Cannot grade.

RLBA17		Number Of Retinal Hemorrhages
N	Value	Description
11229	0	No retinal hemorrhage.
67	1	Questionable retinal hemorrhage.
177	2	One retinal hemorrhage.
210	3	Two or more retinal hemorrhages.
959	8	Cannot grade.

RLBA18		Type Of Retinal Hemorrhage
N	Value	Description
11229	0	No retinal hemorrhage.
67	1	Questionable retinal hemorrhage (retinal hemorrhage questionably present).
64	2	Definite retinal hemorrhage (s), flame-shaped only.
238	3	Definite hemorrhage (s), blot only.
85	4	Definite hemorrhages, blot and flame-shaped.
959	8	Cannot grade.

RLBA19		Hemorrhages/Microaneurysms
N	Value	Description
10274	0	No hemorrhages or microaneurysms.
146	1	Questionable microaneurysm and/or retinal hemorrhage.
609	2	Definite microaneurysms and/or retinal hemorrhages, but the amount is < ETDRS Std. Photo. #1 or = ETDRS Std. Photo. #1 in only one to three quadrants.
23	3	Definite, = ETDRS Std. Photo. #1 in all four quadrants.
13	4	Definite, = ETDRS Std. Photo. #2A in an area approximating an ETDRS field.
1	6	Definite, = ETDRS Std. Photo. #2A in all four quadrants.
1576	8	Cannot grade.

RLBA2		Grader
N	Value	Description
12642	Present	Text suppressed

RLBA20		Hard Exudate
N	Value	Description
11520	0	No hard exudate.
39	1	Questionable hard exudate.
131	2	Definite hard exudate.
952	8	Cannot grade.

RLBA21		Macula Edema
N	Value	Description
11480	0	No macular edema.
27	1	Questionable macular edema.
3	2	Macular edema present but less than clinically significant, inferred from hard exudates and/or other appearances.
7	3	Clinically significant macular edema present, but center is not definitely involved, inferred from hard exudates and/or other appearances.
3	4	Clinically significant macular edema with center definitely involved, inferred from hard exudates and/or other appearances.
1122	8	Cannot grade.

RLBA22		Soft Exudate
N	Value	Description
11789	0	No soft exudate.
52	1	Questionable soft exudate.
159	2	Definite soft exudate.
642	8	Cannot grade.

RLBA23		Intraretinal microvascular abnormalities (IRMA)
N	Value	Description
11827	0	No IRMA.
20	1	Questionable IRMA.
47	2	Definite IRMA, < ETDRS Std. Photo. #8A, in one to three quadrants.
748	8	Cannot grade.

RLBA24		Venous Beading
N	Value	Description
12030	0	No venous beading.
4	1	Questionable venous beading.
2	2	Definite venous beading in one quadrant only.
606	8	Cannot grade.

RLBA25		New Vessels on the Disc (NVD)
N	Value	Description
12320	0	No NVD.
8	1	Questionable NVD.
5	2	Definite NVD, < ETDRS Std. Photo. #10A.
309	8	Cannot grade.

RLBA26		New Vessels Elsewhere (NVE)
N	Value	Description
12313	0	No new vessels elsewhere.
4	1	Questionable new vessels elsewhere.
4	2	Definite new vessels elsewhere, < 1/2 DA.
3	3	Definite new vessels elsewhere, = 1/2 DA.
318	8	Cannot grade.

RLBA27		Vitreous and/or Preretinal Hemorrhage (VH/PRH)
N	Value	Description
12393	0	No vitreous and/or preretinal hemorrhage.
2	1	Questionable vitreous and/or preretinal hemorrhage.
4	2	Definite vitreous and/or preretinal hemorrhage, totaling < 1 DA.
2	3	Definite vitreous and/or preretinal hemorrhage, totaling more than 1 DA.
241	8	Cannot grade.

RLBA28		Fibrous Proliferation (FP)
N	Value	Description
12350	0	No fibrous proliferation.
6	1	Questionable fibrous proliferation.
7	2	Definite fibrous proliferation.
279	8	Cannot grade.

RLBA29		Papillary Swelling
N	Value	Description
12287	0	No papillary swelling
46	1	Questionable papillary swelling.
16	2	Definite papillary swelling.
293	8	Cannot grade.

RLBA3		Date Graded
N	Value	Description
12642	Range	04/12/1993 - 03/22/1996

RLBA30		Laser Photocoagulation
N	Value	Description
12179	0	No photocoagulation treatment.
13	1	Questionable photocoagulation treatment.
15	2	Definite photocoagulation treatment, focal only.
34	3	Definite photocoagulation treatment, scatter and/or local only.
12	4	Definite photocoagulation treatment, focal and scatter and/or local.
389	8	Cannot grade.

RLBA31		Diabetic Retinal Level
N	Value	Description
12641	Range	10 - 90 (median=10 mean=21.2 std=26.9)
1		Missing

RLBA31A		Diabetic Retinopathy Level: Support Evidence: A
N	Value	Description
12641	Range	101 - 903 (median=101 mean=212.8 std=269.0)
1		Missing

RLBA31B		Diabetic Retinopathy Level: Support Evidence: B
N	Value	Description
1	101	Microaneurysms and other lesions absent.
11	352	Questionable soft exudate, IRMA or hard exudate.
38	353	Retinal hemorrhage.
37	354	Hard exudate.
1	612	NVE < 1/2 DA
2	652	NVE = 1/2 DA
1	901	Cannot grade for microaneurysms; no other background retinopathy is present.
12551		Missing

RLBA31C		Diabetic Retinopathy Level: Support Evidence: C
N	Value	Description
7	352	Questionable soft exudate, IRMA or hard exudate.
33	353	Retinal hemorrhage.
12602		Missing

RLBA31D		Diabetic Retinopathy Level: Support Evidence: D
N	Value	Description
2	352	Questionable soft exudate, IRMA or hard exudate.
12640		Missing

RLBA31E		Diabetic Retinopathy Level: Support Evidence: E
N	Value	Description
12642		Missing

RLBA32		Central Artery Occlusion
N	Value	Description
12642	0	Not seen.

RLBA33		Branch Artery Occlusion
N	Value	Description
12639	0	Not seen.
1	1	Questionably present.
2	2	Definitely present.

RLBA34		Central Vein Occlusion
N	Value	Description
12638	0	Not seen.
3	1	Questionably present.
1	2	Definitely present.

RLBA35		Branch Vein Occlusion
N	Value	Description
12623	0	Not seen.
12	1	Questionably present.
7	2	Definitely present.

RLBA36		Hollenhorst Plaque
N	Value	Description
12617	0	Not seen.
14	1	Questionably present.
11	2	Definitely present.

RLBA37		Asteroid Hyalosis
N	Value	Description
12582	0	Not seen.
15	1	Questionably present.
45	2	Definitely present.

RLBA38		Large Cup/Disc Ratio
N	Value	Description
12003	0	Not seen.
465	1	Questionably present.
174	2	Definitely present.

RLBA39		Retinal Hemorrhage On The Disc Or Crossing The Disc Margin
N	Value	Description
12624	0	Not seen.
2	1	Questionably present.
16	2	Definitely present.

RLBA4		Focus And Clarity
N	Value	Description
4770	1	Good
5271	2	Fair
1732	3	Borderline
747	4	Inadequate
122	8	Cannot grade

RLBA40		Peripalliary Atrophy
N	Value	Description
12429	0	Not seen.
54	1	Questionably present.
159	2	Definitely present.

RLBA41		Other Disc Abnormality
N	Value	Description
12541	0	Not seen.
46	1	Questionably present.
55	2	Definitely present.

RLBA42		Glial/Vitreous Thickening
N	Value	Description
12165	0	Not seen.
140	1	Questionably present.
337	2	Definitely present.

RLBA43		Medullated Nerve Fibers
N	Value	Description
12598	0	Not seen.
5	1	Questionably present.
39	2	Definitely present.

RLBA44		Cellophane Reflex
N	Value	Description
12194	0	Not seen.
87	1	Questionably present.
361	2	Definitely present.

RLBA45		Surface Wrinkling Retinopathy
N	Value	Description
12496	0	Not seen.
25	1	Questionably present.
121	2	Definitely present.

RLBA46		Soft Drusen Within 2 Dd Of Macular Center
N	Value	Description
11927	0	Not seen.
203	1	Questionably present.
512	2	Definitely present.

RLBA47		RPE Depigmentation
N	Value	Description
12412	0	Not seen.
96	1	Questionably present.
134	2	Definitely present.

Cohort, Exam 3

RLBA48		Hyperpigmentation
N	Value	Description
12299	0	Not seen.
77	1	Questionably present.
266	2	Definitely present.

RLBA49		SSR Detachment
N	Value	Description
12636	0	Not seen.
3	1	Questionably present.
3	2	Definitely present.

RLBA5		Field Definition
N	Value	Description
12165	1	Good
304	2	Fair
81	3	Borderline
92	8	Cannot grade.

RLBA50		Subretinal Hemorrhage
N	Value	Description
12639	0	Not seen.
2	1	Questionably present.
1	2	Definitely present.

RLBA51		Subretinal Fibrosis
N	Value	Description
12633	0	Not seen.
1	1	Questionably present.
8	2	Definitely present.

RLBA52		Geographic Atrophy
N	Value	Description
12630	0	Not seen.
4	1	Questionably present.
8	2	Definitely present.

RLBA57C		Date Of Notification
N	Value	Description
1	Range	11/22/1993 - 11/22/1993
12641		Missing

RLBA58		Date Of Data Entry
N	Value	Description
12642	Range	04/12/1993 - 03/22/1996

RLBA59		Method Of Data Collection
N	Value	Description
12642	C	Computer

RLBA60		Code Number Of Data Entry Person
N	Value	Description
12642	Present	Text suppressed

RLBA6A		Artifacts: Haze
N	Value	Description
7259	0	No - absent.
5383	2	Yes - present.

RLBA6B		Artifacts: Dust/Dirt
N	Value	Description
9258	0	No - absent.
3384	2	Yes - present.

RLBA6C		Artifacts: Lashes
N	Value	Description
11858	0	No - absent.
784	2	Yes - present.

RLBA6D		Artifacts: Arc
N	Value	Description
12259	0	No - absent.
383	2	Yes - present.

RLBA6E		Artifacts: Uneven Illum/Macula
N	Value	Description
9681	0	No - absent.
2961	2	Yes - present.

RLBA6F		Artifacts: Uneven Illum/Edge
N	Value	Description
12089	0	No - absent.
553	2	Yes - present.

RLBA6G		Artifacts: Uneven Illum/Disc Zone
N	Value	Description
12595	0	No - absent.
47	2	Yes - present.

RLBA6H		Artifacts: Total Blink
N	Value	Description
12570	0	No - absent.
72	2	Yes - present.

RLBA6I		Artifacts: Others
N	Value	Description
12129	0	No - absent.
513	2	Yes - present.

RLBA7		Gradeability
N	Value	Description
9170	1	Entire field gradable
2395	2	Disc zone gradable, macula ungradeable
1077	3	Macula gradable, disc zone ungradeable

RLBA8		Disc Obscured Or Missing
N	Value	Description
12433	0	No - disc is visible
209	2	Yes - disc is either obscured or missing

RLBA9		Macula Obscured Or Missing
N	Value	Description
11384	0	No - macular area is visible.
1258	2	Yes - macular area is either obscured or missing.

RLBACY		Contact Year
N	Value	Description
12642	7	

RLBAFLAG		Indicator For Presence Of Form
N	Value	Description
12642	1	

Appendix C

O.M.B. 0925-0821
exp. 10/31/95

ARIC
Atherosclerosis Risk in Communities

RETINAL EXAMINATION FORM

ID NUMBER: [ ][ ][ ][ ][ ][ ][ ] CONTACT YEAR: [ ][ ] FORM CODE: [R][E][X] VERSION: A 03-09-93

LAST NAME: [ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ][ ] INITIALS: [ ][ ]

Public reporting burden for this collection of information is estimated to average 7 minutes per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding the burden estimate or any other aspect of this collection of information including suggestions for reducing this burden to Reports Clearance Officer, PHS, 721-H Hubert H. Humphrey Bldg., 200 independence Ave. SW, Washington, D.C. 20201, Attn. PRA; and to the Office of Management and Budget, Paperwork Reduction Project (OMB 0925-0281), Washington, D.C. 20503.

INSTRUCTIONS: This form should be completed on paper during the participant's visit. ID Number, Contact Year, and Name must be entered above. Whenever numerical responses are required, enter the number so that the last digit appears in the rightmost box. Enter leading zeroes where necessary to fill all boxes. If a number is entered incorrectly, mark through the incorrect entry with an "X". Code the correct entry clearly above the incorrect entry. For "multiple choice" and "yes/no" type questions, circle the letter corresponding to the most appropriate response. If a letter is circled incorrectly, mark through it with an "X" and circle the correct response.

RETINAL EXAMINATION FORM (REXA screen 1 of 8)

1. When was the last time you saw a doctor, optometrist, or eye specialist concerning your vision?

Less than 1 year	A
At least 1 year but less than 2 years	B
At least 2 years but less than 3 years	C
3-10 years	D
Greater than 10 years	E
Never	F

2.a. Has a doctor ever told you that you had sugar diabetes? ..... Yes Y

No N

Go to Item 3a, Screen 2

2.b. Has a doctor ever told you that you have eye problems as a result of diabetes? ..... Yes Y

No N

Unknown U

Go to Item 3a, Screen 2

c. Which eye or eyes were affected? ..... Right R

Left L

Both B

Unknown U

d. Have you ever had laser treatments on your eyes for diabetes? ..... Yes Y

No N

Unknown U

Go to Item 3a, Screen 2

RETINAL EXAMINATION FORM (REXA screen 2 of 8)

2.e. On which eye or eyes? ..... Right R
Left L
Both B
Unknown U

3.a. Has a doctor ever told you that you have eye problems as a result of glaucoma, or increased pressure inside one or both of your eyes? ..... Yes Y
No N
Unknown U

Go to Item 4a, Screen 3

b. Which eye or eyes were affected? ..... Right R
Left L
Both B
Unknown U

RETINAL EXAMINATION FORM (REXA screen 3 of 8)

4.a. Has a doctor ever told you that you have eye problems as a result of age-related macular degeneration? ..... Yes Y
No N
Unknown U

Go to Item 5a, Screen 4

b. Which eye or eyes were affected? ..... Right R
Left L
Both B
Unknown U

4.c. Have you ever had laser treatments on your eyes for macular degeneration? ..... Yes Y
No N
Unknown U

Go to Item 5a, Screen 4

d. On which eye or eyes? ..... Right R
Left L
Both B
Unknown U

RETINAL EXAMINATION FORM (REXA screen 4 of 8)

5.a. Has a doctor ever told you that you have eye problems as a result of cataracts, or cloudiness of the lens, in one or both of your eyes? ..... Yes Y

No N

Unknown U

Go to Item 6a, Screen 5

b. Which eye or eyes were affected? ..... Right R

Left L

Both B

Unknown U

5.c. Have you ever had eye surgery because of cataracts? ..... Yes Y

No N

Unknown U

Go to Item 6a, Screen 5

d. On which eye or eyes? ..... Right R

Left L

Both B

Unknown U

RETINAL EXAMINATION FORM (REXA screen 5 of 8)

6.a. Has a doctor ever told you that you have eye problems as a result of blockage of an artery or vein in one or both of your eyes? ..... Yes Y

No N

Unknown U

Go to Item 7a, Screen 6

b. Which eye or eyes were affected? ..... Right R

Left L

Both B

Unknown U

6.c. Have you ever had laser treatments on your eyes for this blockage? ..... Yes Y

No N

Unknown U

Go to Item 7a, Screen 6

d. On which eye or eyes? ..... Right R

Left L

Both B

Unknown U

RETINAL EXAMINATION FORM (REXA screen 6 of 8)

7.a. Have you ever had eye surgery for another condition? ..... Yes Y

No N

Unknown U

Go to Item 8a.

b. What was the condition?

c. On which eye or eyes? ..... Right R

Left L

Both B

Unknown U

8.a. Have you ever had laser treatments on your eyes for another condition? ..... Yes Y

No N

Unknown U

Go to Item 9a, Screen 7

b. What was the condition?

c. On which eye or eyes? ..... Right R

Left L

Both B

Unknown U

RETINAL EXAMINATION FORM (REXA screen 7 of 8)

9.a. Are you completely blind in one or both eyes? ..... Yes Y

No N

Unknown U

Go to Item 10a.

b. In which eye? ..... Right R

Left L

Both B

10.a. Have you ever had an eye removed? ..... Yes Y

No N

Unknown U

Go to Item 11, Screen 8

b. Which eye was removed? ..... Right R

Left L

Both B

RETINAL EXAMINATION FORM (REXA screen 8 of 8)

11. Type of eye selection? ..... Assigned A
Selected S

If selected, explain:

_____

12. Which eye was photographed? .. Right R
Left L
Both B
None N

Go to Item 14.

13. Reason for not photographing?
Equipment failure A
Participant refusal B
Biologically not feasible C
Other D

14. Interviewer ID: [ ][ ][ ]

15. Photographer ID: [ ][ ][ ]

16. Date of data collection: [ ][ ] / [ ][ ] / [ ][ ]

Vita

Marci Elizabeth Rosenberg was born in Omaha, Nebraska, to Mark and Brenda Rosenberg. She graduated from Waverly High School in Waverly, Nebraska, in 2007, after which, she attended the University of Nebraska, Lincoln to study Nutrition Sciences and Dietetics, receiving a Bachelor of Science Degree in 2011. In August of 2013, she began her graduate career at Appalachian State University studying Nutrition. Ms. Rosenberg resides in Boone, North Carolina.