1.a. Full Title: Neighborhood Factors and The Prevalence of Age-Related Maculopathy, Diabetic Retinopathy And Retinal Arteriolar Disease

b. Abbreviated Title (Length 26 characters): Neighborhood And Retina Diseases

2. Writing Group (list individual with lead responsibility first):

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3. Timeline:

   The intent of this analysis is to investigate the cross-sectional association of neighborhood factor to prevalence of age-related maculopathy (ARM), diabetic retinopathy and hypertensive retinal arteriolar disease (generalized arteriolar narrowing, focal arteriolar narrowing, arterio-venous nicking and retinopathy in non-diabetics). Initial analyses and writing will take place between October and December 2003, final analysis between Jan 2004 and May 2004, and final writing and manuscript submission between June 2004 and October 2004.

4. Rationale:

   Age-related Maculopathy (ARM)

   ARM is a leading cause of visual impairment in the elderly. The pathogenesis of ARM is complex and remains poorly understood. Various markers of socio-economic status (SES) have been linked with risk of ARM. In the Beaver Dam Eye Study, while controlling for age and sex, lower educational levels, and being in a service-related occupation compared with a white collar professional occupation, was significantly associated with 5-year incidence of early ARM.\(^1\)

   Other characteristics that have been associated with risk of ARM include cigarette smoking, hypertension, cardiovascular disease and higher exposure to ultraviolet radiation. Biologically plausible hypotheses have been advanced for these associations but the mechanisms, particularly for ultraviolet radiation, appear complex. Additionally, other than cigarette smoking, the epidemiologic evidence for these risk factors is mixed. Dietary factors have also been investigated for risk of ARM. The Age-Related Eye Disease Study (AREDS), a randomized, multicenter, clinical trial reported a beneficial effect of high-dose supplements of antioxidants and zinc on, taken for approximately 6 years, in delaying the progression of intermediate ARM
to advanced ARM. Thus, the AREDS provided the strongest evidence to date of an association of antioxidant intake with lower risk of progression to late ARM.

Recent data suggest that neighborhood attributes themselves (i.e. where a person lives) may be important to health. Neighborhood characteristics are related to a variety of health-related behavior that are linked with ARM. These include the availability of resources and services to promote or maintain healthy lifestyles (including cigarette smoking and dietary habits) as well as the physical environment (including ultraviolet radiation). Neighborhood factors appear to be predict cardiovascular morbidity independent of these socioeconomic characteristics. The proposed study will investigate the relationship between neighborhood characteristics and ARM and whether this association is independent of cigarette smoking, SES and other factors.

**Diabetic Retinopathy**

It is known that lower SES is associated with a higher risk of developing diabetes. These socio-economic factors include being of African-American ethnicity, having lower household income, less education, no regular source of health care or health insurance, and being current cigarette smokers.

Evidence of an association between socio-economic attributes and risk of diabetic retinopathy, however, is sparse. In the Wisconsin Epidemiological Study of Diabetic Retinopathy, incident proliferative retinopathy was more likely to develop in younger-onset diabetic women with less education than in those with more education, but no relation was found in the group with older-onset diabetes. Additionally, less education was associated with incidence of visual loss in younger-onset women and older-onset men. In the Proyecto VER (Vision, Evaluation, and Research) study among a self-described Hispanic population, lower income was related to prevalence of proliferative retinopathy, adjusted for other factors (odds ratio of 3.93, 95%, confidence intervals, 1.31-11.80). Few other SES characteristics were related to diabetic retinopathy in that study. In the coronary artery risk development in young adults (CARDIA) study, neighborhood characteristics were associated with components of the insulin resistance syndrome, after controlling for personal income and education. In the current study, we will examine if neighborhood characteristics are associated with prevalence and severity of diabetic retinopathy, and if this association is independent of poorer SES, glycemic control, blood pressure and duration of diabetes.

**Retinal Arteriolar Disease**

Lower SES is associated with an increased risk of atherosclerosis, cardiovascular disease and mortality. In the ARIC study, neighborhood characteristics were related to risk of coronary heart disease and hypertension, independent of standard cardiovascular risk factors. Retinal arteriolar changes, such as generalized and focal arteriolar narrowing, and arterio-venous nicking, are markers of systemic small vessel disease and are related to persistently elevated blood pressure and a variety of cardiovascular diseases. We have previously shown that these retinal arteriolar changes are related to cigarette smoking, and alcohol consumption. However, the relationship between neighborhood traits and retinal arteriolar disease is unknown.

**Conclusion**

There are few population-based studies with data on large numbers of ARM and diabetic retinopathy cases, and retinal arteriolar changes assessed quantitatively. Recently developed methods in quantifying neighborhood traits in the ARIC study provide a unique opportunity to examine their associations with the occurrence of these retinal diseases.
5. Main Hypothesis/Study Questions:
(1) Lower neighborhood scores are associated with a higher prevalence of ARM, and this association is independent of age, gender, race, and cigarette smoking.
(2) Lower neighborhood scores are associated with a higher prevalence and severity of diabetic retinopathy, this association is independent of age, gender, race, duration of diabetes, fasting glucose levels, blood pressure, and lipid levels.
(3) Lower neighborhood scores are associated with a higher prevalence of retinal arteriolar changes, and this association is independent of age, gender, race, diabetes status, fasting glucose levels, blood pressure, body mass index, cigarette smoking and lipid levels.

6. Data (variables, time window, source, inclusions/exclusions):
(1) Neighborhood scores.
(2) ARM variables. Any ARM, early ARM, late ARM and specific ARM lesions (drusen, pigmentary changes)
(3) Diabetic retinopathy variables. Diabetic retinopathy presence and severity score. Macular edema and hard exudates.
(4) Retinal arteriolar variables. Focal retinal microvascular changes (arteriovenous nicking, focal arteriolar narrowing, retinopathy). Generalized arteriolar narrowing quantified as retinal AVR, central retinal arteriolar equivalent and central retinal venular equivalent.
(5) Covariates: age, sex, race, center, prevalent CHD and MI, diabetes and hypertension status, blood pressure, hemostatic and inflammatory markers (von Willebrand factor, factor VIIIc, fibrinogen, WBC), cigarette smoking, alcohol consumption, body mass index (variables from ARIC visit 1-3, except for von Willebrand factor, factor VIIIc, WBC, fibrinogen available ARIC visit 1 only)
(6) Exclusion criteria: From participants at ARIC visit 3 (n=12,887), exclude persons who whose race is not black/white, with no APOE information, ungradeable retinal photographs or missing retinal variables at visit 3.

7.a. Will the data be used for non-CVD analysis in this manuscript?  _____ Yes  X  No

    b. If Yes, is the author aware that the file ICTDER01 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used?  _____ Yes  _____ No

        (This file ICTDER01 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?  _____ Yes  X  No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER01 must be used to exclude those with value RES_DNA = “No use/storage DNA”?  _____ Yes  _____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://bios.unc.edu/units/csc/ARIC/study/studymem.html  X  _____ Yes  _____ No
10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)? See references below.

References