**ARIC Manuscript Proposal #** 3229

**PC Reviewed: 9/11/17** **Status: _____** **Priority: 2**
**SC Reviewed: _____** **Status: _____** **Priority: ____**

**1.a. Full Title**: Associations between of Visual Function and Cognition in an Older Adult Population

**b. Abbreviated Title (Length 26 characters)**: Vision and Cognition

**2.Writing Group**:

Writing group members:
Elizabeth Couser
Bonnie Swenor
Alison G. Abraham
Pradeep Y. Ramulu
Xinxing Guo
Xiangrong Kong
A.Richey Sharrett
(others TBD)

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __EC_ **[please confirm with your initials electronically or in writing]**


**First author**:
Address: 600 N. Wolfe Street, Wilmer Eye Institute, Room 116
Baltimore, MD 21287

Phone: (518) 391-9268 Fax: n/a
E-mail: ecouser1@jhmi.edu

**ARIC author** to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).
Name: Alison G. Abraham, PhD
Address: 600 N. Wolfe Stree, Wilmer Eye Institute, Woods 173
Baltimore, MD 21287

Phone: (410) 502-9763 Fax: (410) 955-7587
E-mail: Alison.abraham@jhu.edu

**3.Timeline**:
Analysis and draft will be completed in 12 months.

**4.Rationale**:

Previous work indicates associations between a decline in cognitive outcomes (i.e., Mini-Mental State Exam) and a decline in vision (i.e., visual acuity).[1] Additional research is necessary to further elucidate the relationship between cognition and vison, using a robust measure of cognition. Further, the association between contrast sensitivity, which has been shown to decline in AD and mild cognitive impairment,[2] and cognitive impairment has not been examined in a population-based study. Contrast sensitivity is a rapid method to assess visual function and could easily be used in combination with other cognitive measures to help form a complete picture of an individual's cognitive and health status.

EyeDOC, an ancillary study of the Atherosclerosis Risk in Communities (ARIC) Study, seeks to evaluate early markers of pathology and vascular changes using retinal imaging (i.e., OCT and optical coherence tomography-angiography [OCT-A]) in a population of community-dwelling older adults residing in Jackson, MS and Hagerstown, MD. All participants in the ARIC study undergo testing and questioning in several domains, including cognitive, functional, sensory, and behavioral tests. In addition, as part of the EyeDOC study, participants also undergo retinal imaging and visual function testing. Using the EyeDOC study data, we propose a project to determine the associations between cognitive performance (i.e., score on a factor of Ten Cognitive Tests – global score) and visual function (i.e., acuity and contrast sensitivity) over time (i.e., Visit 5 and 6) in a community dwelling older adult sample.


**1.** Zheng DD, Swenor BK, Christ SL, West SK, Lam BL, Lee DJ. Longitudinal Associations Between Visual Impairment and Cognitive Functioning: The Salisbury Eye Evaluation Study. *JAMA Ophthalmology.* 2018.

**2.** Risacher SL, Wudunn D, Pepin SM, et al. Visual contrast sensitivity in Alzheimer's disease, mild cognitive impairment, and older adults with cognitive complaints. *Neurobiology Of Aging.* 2013;34:1133-1144.


**5. Main Hypothesis/Study Questions**: Using data from the EyeDOC study, this project seeks to determine the associations between decline in cognitive performance (i.e., score on a factor of Ten Cognitive Tests – global score) and visual function in an older adult population residing in Jackson, MS and Hagerstown, MD. We aim to:

1. Determine whether impaired visual function is associated with a lower global cognitive function score at visit 6 to understand cross sectional associations; and
2. Determine whether impaired visual function is associated with a greater decline in the global cognitive function score between visits 5 and 6 in this community dwelling older adult sample,

where "visual function" is measured by acuity and contrast sensitivity.

We hypothesize that lower visual function will be associated with a lower Visit 6 global cognitive function score and a greater decline from visit 5 to visit 6.

**6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).**

## Study Design

We will analyze cross sectional (Hypothesis 1) and semi-longitudinal data (Hypothesis 2) collected during the EyeDOC study visit and during ARIC visits 5 and 6.

## Inclusion/Exclusion Criteria

ARIC participants recruited for the EyeDOC ancillary study will be included in this analysis. Participants have Mini-Mental State Examination (MMSE) scores of no less than 22 (Jackson study site) or 24 (Hagerstown study site).

## Primary Outcome

1. Cognitive Measures
    a. Ten Test Factor Score
    b. Change in the Ten Test Factor Score
2. Measures of Visual Function
    a. Acuity
    b. Contrast Sensitivity
    c. Near acuity/Reading speed

## Other Variables of Interest

Demographic variables:

a. Age
b. Race
c. Gender
d. Education level (< high school, high school or equivalent, > high school)
e. Diabetes

## Summary of Data Analysis

### Study Population

ARIC participants recruited for the EyeDOC ancillary study will be included in this analysis. Participants have Mini-Mental State Examination (MMSE) scores of no less than 22 (Jackson study site) or 24 (Hagerstown study site).

### Proposed Analysis

EyeDOC participants will be compared with invited non-participants with respect to education and demographic characteristics to understand generalizability of results.

For the primary analysis, we will divide participant data into four groups using standard ophthalmic cutpoints: (1) no visual impairment (2) impaired acuity; (3) impaired contrast sensitivity; (4) impaired acuity *and* contrast sensitivity. We will run descriptive statistics for each group and compared means (of demographic variables and cognitive measures) between groups 1 and 2; groups 1 and 3; and groups 1 and 4.

To determine whether impaired visual function is associated with a lower Factor Score (Aim 1), we will run linear regressions to estimate associations of the 4 visual function groups with the global Factor Score (at visit 6), using no impairment as the reference group. We will also look at visual acuity and contrast sensitivity continuously in regression models. Lowess smoothers will be used to understand functional relationships between visual function and cognition; smooth functions will be approximated using spline terms in the regression to get optimal combination of model fit and interpretability. Interactions terms between contrast sensitivity and acuity will also be explored based upon graphical analysis.

Additional analyses will examine differences in measures of acuity (i.e., near, presenting, best corrected). Additionally, with data from the near vision test to calculate reading speed, we will examine whether slower reading speed is associated with a lower Factor Score. We will run linear regressions to estimate associations between reading speed and global Factor Score at visit 6.

To determine whether impaired visual function is associated with a greater decline in the Factor Score between visits 5 and 6 (Aim 2), we will repeat the analyses above for the new outcome of a change in global cognitive function score over time. In order to simplify the interpretation, we will use a repeated measures analysis, regressing cognitive function score on visual function and using generalized estimating equations to account for the repeated assessments within a person.

We will control for age, race, gender, education level and diabetes in both aims.

**Limitations**

Since education may be a confounding factor in both vision (visual impairment/measurement) and cognitive testing, years of education will be entered as a covariate in all models. We acknowledge that this variable may not control confounding completely.

The EyeDOC study includes only participants with normal cognition or mild cognitive impairment. Greater levels of cognitive impairment may be associated with greater impaired visual function, but this will remain unknown given the MMSE exclusion criteria. However, large changes in cognition from V5 to V6 are still included in the sample and can be examined in relation to visual function.

**7.a.Will the data be used for non-CVD analysis in this manuscript? __X_ Yes ____ No**

**b.If Yes, is the author aware that the file ICTDER03 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? _X__ Yes ____ No**
(This file ICTDER 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 ICTDER03 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://www.cscc.unc.edu/ARIC/search.php

__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)**
#738 Retinal microvascular abnormalities and cognition: The Atherosclerosis Risk in Communities Study

**11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _X__ Yes ____ No**

**11.b. If yes, is the proposal**
**_X_ A. primarily the result of an ancillary study (list number* EyeDOC)**
**___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)**

*ancillary studies are listed by number at http://www.cscc.unc.edu/aric/forms/

**12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.**

**12b. The NIH instituted a Public Access Policy in April, 2008** which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted

in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.