1.a. Full Title: Traffic exposure and retinal abnormalities in the Atherosclerosis Risk in Communities (ARIC) study

b. Abbreviated Title (Length 26 characters):

2. Writing Group:
   Writing group members: Haidong Kan, Kathryn M. Rose, Ronald Klein, Eric Whitsel, Fred Lurmann, Stephanie London

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

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3. Timeline: A first manuscript should be available for circulation to the ARIC investigators before June 1, 2006.

4. Rationale:
   Some epidemiologic evidence suggests associations between traffic-related air pollution and cardiovascular mortality & morbidity. However, the underlying mechanisms remain poorly understood. Microvascular disease has long been suggested as a possible pathogenic factor in the development of different cardiac diseases. We hypothesize that long-term exposure to traffic-related air pollution may lead to systemic microvascular disease, manifest as smaller retinal arteriolar caliber and larger retinal venular caliber and other manifestation of microvascular changes, including A/V nicking, focal retinal arteriolar narrowing and retinopathy.
   Traffic emissions result in small-scale spatial variations and higher concentrations within short distances from major roads. Thus typical use of air pollution data from fixed monitoring...
stations may be inadequate to study traffic-related air pollution and health outcomes, especially for those living close to busy roads. Traffic-related assessment can enhance the health studies of ambient air pollution because local sources are important, because most people do not live close to the monitoring stations, and because monitoring stations are purposefully located away from local sources such as busy roads. For people living close to busy roads, air pollution from traffic sources may be more important than the area background levels of air pollution measured by fixed monitors.

The retinal examination at visit 3 of the ARIC study provides us an opportunity to non-invasively study the association between retinal microvascular circulation and traffic-related air pollution. To our knowledge, there have been no previous data investigating air pollution in relation to retinal microvasculcular caliber and other manifestations of microvascular disease.

5. Main Hypothesis/Study Questions:
Subjects with higher exposure to traffic-related air pollution have higher rate of retinal microvascular disease and fundus abnormalities.

5a. Data analysis:
The main measurement of retinal abnormalities for this analysis is derived AV nicking, generalized arteriolar narrowing and retinopathy. We will quantify small-scale spatial variations of traffic exposure by two measurements: geographical information system (GIS)-mapped traffic density assignments at residences, and the distance of residences to nearest roadways of various types. Generally, traffic density values give a relative indication of which residence locations are likely to be most exposed to traffic activity.

The relations between measures of traffic density/distance and retinal abnormalities will be explored using logistic regression. In the regression models, we will examine a number of confounding factors, including personal demographic characteristic, cigarette smoking, background air pollution, neighborhood socioeconomic variables and other cardiovascular risk factors. Taking lowest quartiles of traffic density and unexposed in distance as the reference group, we will compare the ORs with various traffic exposure levels after adjustment for the covariates above.

6. Data (variables, time window, source, inclusions/exclusions):
Visit 3: retinal AV measurements, retinal abnormalities, anthropometric measures, blood pressure at the time of the retinal exam, demographic characteristic, smoking, exposure to environmental tobacco smoke, diabetes, other cardiovascular risk factors; traffic exposure and background air pollution concentration at visit 3. We will also examine neighborhood level socioeconomic variables as potential confounders.

7a. 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 ICTDER02 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 ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8a. 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 ICTDER02 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)?

# 450, 760, 782, 860, 861, 907

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* AS#2003.03)
   _____ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* __________ __________ )

Note – original ancillary study proposal expansion to include cardiovascular endpoints was approved by the Steering Committee at the meeting on April 14, 2004.

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

12. 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.

Reference:


