1.a. Full Title:
Cigarette Smoking, Coffee and Alcohol Consumption in relation to Parkinson’s Disease in Atherosclerosis Risk in Community Cohort

b. Abbreviated Title (Length 26 characters): Smoking and Parkinson

2. Writing Group:
(Currently in alphabetical order): Chen, Honglei; Huang, Xuemei; Mailman, Richard; Mosley, Thomas H; Rosamond, Wayne

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

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3. Timeline:
From approval to finish data analysis: 3-6 months.
From approval to submission of manuscript (6-9 months).

4. Rationale:
Parkinson’s disease (PD) is a common age-related neurodegenerative disorder. In rare cases, PD could be caused by genetic mutations; but for most of the typical PD, the causes are not known. Many epidemiological studies have reported that PD risk was lower among smokers and coffee drinkers(1), which are the most established epidemiological findings on PD. The nature of these associations, however, is still debatable. Some believe a causal relationship that smoking and caffeine reduce the risk of PD; others hypothesize that PD patients have a “risk-avert” personality and are thus more likely to avoid addictive behaviors such as smoking and coffee drinking. Analysis of
environmental tobacco smoke among never smokers would be able to help tease out these possibilities. Lower risk of PD among alcohol drinkers has also been reported but with much less consistency across studies. Further, most of the previous studies conducted among Caucasian populations in the US or European countries and a few among Asian populations. We have not yet found any data on these associations among African Americans or Blacks.

The ARIC study, with its bi-racial composition, may offer us a good opportunity to examine this association among whites as well as among African Americans. The data collected good information on smoking, environmental tobacco smoke, coffee and alcohol consumption. Previously, we have obtained some data from ARIC with the permission to examine potential associations between apolipoprotein E and plasma cholesterol levels and PD risk (Manuscript #1176). We controlled for smoking status and caffeine and alcohol intake as potential confounders in these analyses. We found that PD patients smoked less and had lower intakes of caffeine, which is consistent with prior reports. Further, we found that alcohol drinkers had lower PD risk.

We therefore plan to expand the analysis on smoking, coffee and alcohol consumption and PD in the ARIC cohort and prepare a manuscript on this topic. The purposes of this analysis are 1) to investigate further the relationship between alcohol consumption and risk of PD; 2) to investigate whether environmental tobacco smoke is related to lower risk of PD; 3) to examine whether smoking, coffee consumption, and alcohol intake is related to lower PD risk in African Americans as well as in Caucasians.

5. Main Hypothesis/Study Questions:

Cigarette smoking, environmental tobacco smoke, coffee consumption and alcohol intake are associated with lower risk of PD in both African Americans and Caucasians.

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:

Study participants will be selected from ARIC study, a prospective investigation of ARIC involving 15,792 persons aged 45-64 years at recruitment of 1987-1989 from four US communities: Forsyth County, NC; Jackson, MI, the northwestern suburb of Minneapolis, MN; and Washington County, MD. Approximately 27% (4,000) of the participants are African Americans. At baseline survey in 1987-1989, participants were asked to provide dietary and lifestyle information, including cigarette smoking, environmental tobacco smoke, coffee and alcohol consumption. The cohort has since been followed by similar comprehensive surveys approximately every three years and a brief annual phone interview to update health status. Medication data was collected during home visits and hospitalization data are available from routine ARIC data collection. Suspected PD patients will be identified from multiple sources (see below). We will primarily examine the relationship between baseline smoking, coffee and alcohol consumption and risk of PD.
**Inclusion criteria:**
1) All ARIC participants.

**Exclusion criteria:**
1) None

**Outcome measures.**
1) Potential PD cases will be identified from multiple sources: hospital discharge record, medication data from follow-up surveys, death certificates, as well as self-reports at visit 4 (1996 -1998) when a question “Have you ever been told by an MD that you have PD?” was asked. In the current analysis on cholesterol and PD (manuscript #1176), 172 suspected PD cases were identified and 111 of them were confirmed to be PD cases by review all these information by Dr. Xuemei Huang, blinded to the exposure status.

4) **Potential confounders:** age, sex, race will be adjusted throughout the analysis. Other potential confounders (education, study site, BMI and other obesity measures, physical activity, milk intake, NSAIDs use and cholesterol) will be considered individually and adjusted as appropriate. We have obtained information on most of these covariates as part of the data request for cholesterol and PD analysis. Variables not yet available will be requested as part of this analysis.

**Summary of Data analysis**
Logistic regressions will be conducted, adjusting for age, sex and race throughout the analysis and for other potential confounders as appropriate. Exposure variables will be first defined as never, past and current in reference to the time of baseline survey, and then exposures will be defined according to duration and amount of consumptions. Subgroup analysis will then be conducted according to race and gender. Analysis on environmental tobacco smoke will be conducted among the entire population as well as among never smokers only.

**Limitations/Challenges:**
A major limitation of this study is the ascertainment of incident PD cases, which primarily relies on hospital discharge records and other indirect sources. This case-finding procedure may not be as sensitive and specific as conducting clinical PD diagnostic examinations on all participants. We hope this study, along with study as outlined in manuscript application #1176 will eventually lead to a study with systematic approach of case identification. Nevertheless, PD cases have been identified by hospital discharge records and self-report of clinical diagnosis in other studies (3, 4) In addition, our preliminary analysis showed that all known risk factors of PD seemed to be related to the risk of PD in the expected direction: risk increases with age, higher in men and lower among smokers and coffee drinkers.

Another limitation is that we were unable to differentiate incident from prevalent cases. However, as the PD rarely occurred before age 60, most of the cases should be incident. Further, the number of cases is small and we may not have sufficient power in subgroup analysis. We will explicitly acknowledge these limitations in our publications.
7.a. Will the data be used for non-CVD analysis in this manuscript?  

Yes  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

8.a. Will the DNA data be used in this manuscript?  

Yes  No

Will base on existing data (apo E), no new genotyping.

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

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)?

We are aware of no other manuscripts on this topic in ARIC. Drs Mosley and Rosamond had prior experiences in studying cognitive endpoint and alcohol related exposures in ARIC, respectively. We are currently working on Cholesterol, Apo E and PD (manuscript #1176).

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  

Yes  No

11.b. If yes, is the proposal

__X__ A. primarily the result of an ancillary study (list number* )

__X__ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* MS# 1176 _____) *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.

Understand

References:

