

## ARIC Manuscript Proposal # 1121

PC Reviewed: 01/24/06

Status: \_\_\_\_\_

Priority: \_\_\_\_\_

SC Reviewed: \_\_\_\_\_

Status: \_\_\_\_\_

Priority: \_\_\_\_\_

**1.a. Full Title:** Cognitive change over 12 years and its relationship to cardiovascular risk factors  
ARIC MR Study

**b. Abbreviated Title (Length 26 characters):** Cognitive change

### 2. Writing Group:

Writing group members: **Knopman, Mosley, Catellier, Coker**

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

**First author:** David Knopman MD

Address: Department of Neurology,  
Mayo Clinic, 200 First Street SW, Rochester MN 55905

Phone: 5075381038

Fax: 5075386012

E-mail: knopman@mayo.edu

Corresponding/senior author (if different from first author correspondence will be sent to both the first author & the corresponding author):

Address:

Phone:

Fax:

E-mail:

**3. Timeline:** Begin analyses when approved by Pubs committee

**4. Rationale:** The purpose of this analysis is to replicate and extend prior findings based on a 6 year change in cognition. In addition to having a longer window for cognitive change, we will also use analysis of slope to analyze the longitudinal cognitive data. Although the number of subjects will be smaller than the prior analysis (Knopman, 2001), the doubling of the time interval and the availability of at least 3 observation points should act as a “magnifier” of effect if a risk factor truly has a causal role in degrading cognition.

Cardiovascular risk factors are increasingly recognized as relevant to cognitive changes in the elderly. Our own work with ARIC, as well as findings from other large population-based studies such as CHS (eg Kuller, Haan), Rotterdam study (Breteler), and others show that cardiovascular disease impacts cognition. This association is important because some of these risk factors are modifiable. These associations are also important because they have a direct bearing on the role of vascular disease in late life dementing illnesses.

With the unique opportunity to study cognitive change over a 12 year period in over 1100 ARIC participants in the ARIC-MRI study, we can address whether some of the associations we had seen previously (over a 6 year time period) became more or less important. Not only will it be helpful and informative to verify that diabetes and hypertension are associated with cognitive decline over 12 years, but also it will be important to determine whether other risk factors such as lipid levels, for example, did not.

We also have a more complete neuropsychological battery that was completed in 2004-2006 (“CY16”), and we propose to analyze that data in this project. Because there is no earlier data on the elements in this cognitive battery, the type of analysis will be different from that described above, and instead will assess relationships between visit 2 cardiovascular risk factor data and CY16 cognitive performance. The more complete neuropsychological battery given at visit 5 will allow us to assess the impact of earlier cardiovascular risk factor states on a broader view of cognition rather than simply the 3 tests from the longitudinal battery.

**5. Main Hypothesis/Study Questions:** Do baseline cardiovascular risk factors predict cognitive decline? Do different cardiovascular risk factors exert effects on different aspects of cognition?

**6. Data (variables, time window, source, inclusions/exclusions):** visit 2 cardiovascular risk factor data; visit 2, visit 4 and visit CY16 cognitive data. Specifically:

**Inclusions:**

- 1 = Center not J, or F
- 2 = Race not Black or White

**Exclusions:**

Missing data for cnfa01, cnfa02, cnfa04, dwr16, dss16, wf16

**Visit 1 variables:**

History of stroke/TIA (hom10d tiab01), occupational status at baseline (hom55 hom57), FEV-1 (fev\_101), education level (elevel01, elevel02), gender (gender),

**Visit 2 variables:**

Age, (v2age22), fasting blood sugar (glusiu21), history of diabetes (diabts22), smoking status (cursmk21, forsmk21, evrsmk21, cigt21), hypertension status incl. antihypertensive meds (hypert25), IMT (mnb45\_1s), BMI (bmi21), drinking status and alcohol intake (drnkr21 ethanl24), lipid variables (total chol, HDL, LDL, triglycerides), blood pressure (sbpb21 sbpb22)

Medications with CNS effects

Cognitive function: (cnfa01, cnfa02, cnfa04)

**Visit 3 datasets (variables):**

Cognitive function: (cnfb1, cnfb2, cnfb4)

**Visit 4 variables:**

Cognitive function (cnfc1, cnfc2, cnfc4)

**Visit CY16 variables:**

Cognitive variables: dmri0510 (keep=id curage16 dwr16 dss16 wf16) + others

**Incident event datasets (variables):**

incident stroke: istrby02 (keep=id ed02dp in02dp)

A series of linear models will be fit. Initially, we will simply examine the effect of a single risk factor on mean V2-CY16 change in cognitive function controlling for age, race/center, sex, and education level. Alternatively, we will fit a mixed model to estimate the effect of the risk factor on the rate of change (slope) in cognitive function over the V2-CY16 period. Finally, we will build a model with the most predictive set of risk factors for cognitive decline.

**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

(This file ICTDER02 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 ☐ 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.csc.c.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)?**

ARIC # 672 Knopman Neurology 2001  
ARIC # 953 Knopman Neurology 2005  
ARIC # 314 Mosley Neurology 2005

**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**

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

**\_XX B. primarily based on ARIC data with ancillary data playing a minor role  
(usually control variables; list number(s)\* 1991.01)**

\*ancillary studies are listed by number at <http://www.csc.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.