ARIC Manuscript Proposal #2120

1.a. Full Title: Prevalence of Mild Cognitive Impairment and Dementia and Their Relationship to Diabetes and Hypertension in ARIC

b. Abbreviated Title (Length 26 characters): Dementia Prevalence

2. Writing Group: Knopman, Mosley, Sharrett, Coresh, Albert, Schneider, Selnes, Coker, Gottesman, McKhann, Windham

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal.

First author: David Knopman
Address: Dept. of Neurology, Mayo Clinic, Rochester MN 55905
Phone: 507 538 1038 Fax: 507 538 6012
E-mail: knopman@mayo.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: David Knopman

3. Timeline: within 6 months of completion of the dementia adjudications in ARIC NCS

4. Rationale: Mild cognitive impairment (MCI) and Dementia prevalence are one of the main aims of the ARIC NCS. The role of the two major cardiovascular risk factors – diabetes and hypertension – that were ascertained >20 years ago in modulating the prevalence of dementia, is also one of the major foci of the ARIC NCS. ARIC is in a unique position to use the combination of cardiovascular risk factors and cognitive assessments obtained two decades ago to understand better how dementia prevalence is modified. This paper will describe ARIC NCS methods for ascertaining and diagnosing MCI and dementia, their prevalence, and associations with mid-life diabetes and hypertension.

5. Main Hypothesis/Study Questions:

A. The prevalence of MCI and dementia in general and dementia due to Alzheimer disease (AD) and cerebrovascular disease (CVD), rises with advancing age, is equivalent in men and women.
B. Midlife (ARIC V1 or V2) diabetes and hypertension are related to MCI and dementia prevalence. Both are also related to dementia due to AD and to CVD.  
(Note: while V1 is the true baseline visit, cognition was assessed beginning at V2).  

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).  
The basis for the ascertainment and diagnoses of MCI and dementia, laid out in ARIC MOP 17, and developed by the co-authors of this proposal, will be described in this publication. The description will include  
- selection for expert clinical review, which is based on  
  - Performance on tests of several cognitive domains comprised of pairs of cognitive tests both from the ARIC Brain MRI study (described in ARIC ms#? [Schneider, Mosley], and other sources (described in this paper),  
  - The race-specific, age and education-adjustment employed to avoid bias in the application of standards for the cognitive tests,  
  - Decline from previous exams in performance on DWRT, DSSST and WFT, and  
- The diagnostic criteria, review procedures, and reliability of the expert review.  

Two estimates of the prevalence of dementia will be derived. The first will be based on information obtained from all the participants we examine (those examined in clinic and those examined at home or in long-term care facility). We will also use inverse probability weighting to adjust for any selection bias introduced by estimation of the dementia rates from the examined sample and allow extrapolation to the population of all living ARIC participants. The second estimate will combine the dementia cases ascertained in the examined sample with probable dementia cases identified only by telephone interview, informant interview, or diagnoses from the Medicare billing claims database. We will estimate the accuracy of dementia diagnoses in CMS claims data by estimating the sensitivity and specificity of the CMS diagnosis in the sample which we examine. The expected number of dementia cases identified by CMS will then be adjusted for misclassification using the stratum-specific (age, sex, race, education) sensitivity and specificity rates.  

In addition, we will estimate the incidence of dementia among all (approximately 14,000) ARIC participants who attained the age of 65 before ARIC exam 4 and were not covered by an HMO (since CMS does not provide data on HMO participants) by adding to cases identified in the estimated 7,229 participants examined or otherwise evaluated as part of the NCS all those who were identified in the CMS database between 1987 and 2010.  

Similarly, the MCI prevalence estimate will be based on MCI diagnoses among participants we examine with inverse probability weighting to account for expected cases among those we cannot examine (as described above).  

We will examine associations between vascular factors – in particular ARIC visit 1 and visit 2 diabetes and hypertension (defined as we have in the past using a combination
of clinical diagnoses, laboratory measurements or usage of medication) – and dementia (or MCI + dementia) with logistic regression and Poisson regression with robust variance and the incidence of dementia using survival analyses. For incident dementia, person-years of follow-up will be computed as the amount of time since age 65 to (1) the first date of diagnosis in the CMS database, (2) the point at which the event was predicted to have occurred based on cognitive data available at the ascertaining and previous exams (for cases identified at the current exam; sensitivity analyses will use date of ascertaining exam), or (3) date of last contact (for non-cases). The proportional hazards assumption will be examined using log-log plots and by testing risk factor × time interactions; if the assumption is violated the interactions term(s) will be kept in the model and the time-dependent nature of the risk will be interpreted accordingly.

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? _X_ 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 ICTDER03 must be used to exclude those with value RES_DNA = “No use/storage DNA”? _X_ 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)?

ARIC has never performed dementia diagnoses up until now. We have looked at cognitive change, eg Knopman 2009, and Gottesman in preparation.

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
___   A. primarily the result of an ancillary study
___   B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)*) 2008.06

*ancillary studies are listed by number at http://www.cscce.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.