1.a. **Full Title**: Impact of coronary artery bypass surgery on cognitive function

b. **Abbreviated Title (Length 26 characters)**: CABG and cognition

2. **Writing Group (list individual with lead responsibility first):**

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3. **Timeline:**

   - Manuscript proposal to Publication's Committee: December / 2003
   - Data analysis completed: January / 2003
   - Completed manuscript to Publication's Committee: April / 2004

4. **Rationale:** Cognitive dysfunction is a frequent complication of CABG surgery occurring in 20% to 50% of patients 6 weeks after CABG surgery, and in 10% to 30% patients 6 months after surgery (Dijk et al., 2002; Selnes et al., 2001). The most provocative claim was that of Newman and colleagues (2001), who asserted that long-term cognitive decline was substantial in survivors of CABG. Considerable controversy exists, because most studies of CABG lack a suitable control group and lack measures of pre-operative cognitive status. The claims of cognitive impairment, therefore, do not take into account the possibility that subjects who had poor cognitive outcomes might have been cognitively impaired pre-operatively, nor do they take into account the reality that CABG patients are elderly people with major cardiovascular disease, many of whom would be expected to decline cognitively regardless of surgery. Other studies have found no change (e.g., Selnes et al., 2003) at least after 1 year post surgery compared to a nonsurgical control group. The ARIC cohort contains a modest number of subjects (~ 169) who underwent CABG between visits 2 and 4. These subjects will have had a preoperative cognitive assessment (visit 2).

5. **Main Hypothesis/Study Questions:** The main question to be addressed is: do subjects undergoing CABG between ARIC visits 2 & 4, who had cognitive testing at both visits 2 and 4 and survived until visit 4, have greater cognitive decline than subjects not undergoing CABG. We will limit the analysis to subjects who have had only one CABG. Using multivariate
techniques, we will control for the presence of various risk factors present at visit 2. We anticipate that subjects who underwent CABG will have more cardiovascular risk factors preoperatively.

We acknowledge that we will not be able to control for different operative issues such as number of vessels bypassed, pump time, or perioperative complications as this data is not contained in the ARIC dataset. These limitations will be acknowledge in the manuscript. We also acknowledge that we can evaluate only those who survive from the time of the CABG to visit 4. Thus, we will be commenting only on those who survived and returned for visit 4.

6. Data (variables, time window, source, inclusions/exclusions):

Exclusions:
1. Missing cognitive function at Visit 2 (cnfa01, cnfa02, cnfa04)
2. Hx of stroke/TIA at baseline (tiab01 = Y or hom10d ne N)
3. Incident stroke prior to Visit 4 (in00dp=1 and ed00dp < v4date41)
4. Missing cognitive function at Visit 4 (cnfc01, cnfc02, cnfc04)
5. Race not black or white, or blacks from Minn. or Washington

Demographic data: age (at Visit 2, v2age22), gender, education (elevel01 and elevel02), BMI (bmi21)
Visit 2: CV risk factor data: fasting blood sugar (glusiu21), history of diabetes(diabts22, diabts23), history of CHD (prvchd05 or (in_00sp=1 and .Z < dateisp < v2date21), cholesterol (from Visit 1 Apo-A1=lipa06, Lp(a)=lipa08; from Visit 2 LDL=ldl22, total cholesterol=lipb01a, HDL=lipb03a), smoking status (cursmk21, forsmk21, evrsmk21, cigt21), hypertension status including antihypertensive medication use (hypert24-26).
Medications with CNS effects
Cognitive test data from Visits 2 and 4: cnfa01, cnfa02, cnfa04, cnfc01, cnfc02, cnfc04
APOE genotype

Datasets needed to define the CABG exposure variable:
1) latest version of CELB dataset (e.g., celb0309), keep all ICD9 codes (celb10*),
2) latest incidence file (e.g., inc_by00), keep indicator variable for cardiac procedures (cardproc dateproc)

Define: CABG procedure between Visit 2 and Visit 4 as follows:
1 if cardproc=1 & ICD9 code is 36.1 - 36.2 & (v2date21 < dateproc <= v4date41)
0 otherwise

Analysis: The primary outcome will be “change” in cognition from V2 to V4 (for 3 semi-continuous cognitive variables) and the primary exposure variable will be an indicator of having had a CABG procedure between V2 and V4 (~ n = 169). A series of linear models will be fit. Model 1 will control for age, race/center, and education level. Subsequent models will adjust for potential confounders measures at Visit 2 (see above list).

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://bios.unc.edu/units/csc/ARIC/stdy/studymem.html ___ 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)? - Knopman paper on Cardiovascular risk factors and cognitive decline (Neurology, 2001) Blair, MS # 924, APOE and cognitive change (in preparation)

11. 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.

References

