1. **Title:** Cross-sectional association of alcohol and cognition

**Abbreviated Title:** Cross-sectional alcohol & cognition

**Writing Group:** Eigenbrodt M, Mosely T, Hutchinson R, Szklo M, Andrew M, Watson R, Vitelli L, Knopman D

Correspondence: Preventive, Cardiology/ARIC, UMC, 2500 N. State St., Jackson, MS 39216
Phone: (601) 984-5644, Fax: (601) 9865693, E-mail: mie@fiona.umsmed.edu

**Timeline:** immediate

**Rationale:** Cognitive impairment has been linked to consumption of large quantities of alcohol with severe impairment in patients with Wernicke-Korsakoff syndrome (Parsons 1993). Cognitive defects in sober alcoholics with a subclinical syndrome are less severe and more variable (Parsons 1993). Anatomic studies have also identified abnormal neurons in alcoholic patients compared to controls (Harper 1987). While cognitive deficits are clearly associated with alcoholism, there have been conflicting results on the effect of alcohol on cognition in non-alcoholics. Several studies have found that certain aspects of cognitive function were negatively associated with the amount of alcohol consumed by social drinkers (Parker 1977 and 1983, MacVane 1982). In contrast, other studies of light to moderate alcohol use found no cognitive decline or even some improvement in cognition (Christian 1995, Hebert 1983, Launer 1996, Geroldi 1994, Mangione 1993). Christian et.al. (1995) found that the highest quintile of alcohol intake in identical twins was associated with poorer cognitive function, but found no evidence of significant effect of moderate alcohol intake compared to light intake. They did find that past alcohol intake was predictive of significantly poorer cognitive function. The ARIC manuscript by Cerhan et.al. (ARIC MS #148) on multiple correlates of cognition is currently under review.

There are several reasons possible for the conflicting results from the various studies. One is the accuracy of the reported alcohol intake. Carpenter et.al. are currently evaluating the reliability of the reported alcohol intake in the ARIC cohort (ARIC MS 164). Other potential reasons include the measure of alcohol consumption used, the cognitive test that was used, the populations studied, and lack of information on covariates. ARIC has data that will allow determination of the measure of alcohol consumption that is most closely associated with cognitive function and extensive data on covariates that may impact on cognition so that adjustment can be made, and a cohort from four sites that is population based. The measures of cognitive function used by ARIC are Delayed Word Recall (a test of short term memory), Digit-Symbol Substitution (a test of response speed, sustained attention, and visual-spatial skills), and Word Fluency (a measure of verbal function that requires speed, sustained attention and visual-spatial skills. While these exact tests were used only in a few other studies of alcohol and cognition, the functions tested overlap the cognitive functions tested in other studies.

We would therefore, like to do a comparative evaluation of the cross sectional association of alcohol and cognitive function. There are plausible explanations for either a negative or positive association. If alcohol contributes to cell death or injury via direct neurotoxicity or indirectly through diet, then a negative association could be anticipated. However, studies suggest that
alcohol at moderate levels provides a protective effect on the cardiovascular system and may therefore improve cognition through better cerebral circulation (Christian 1995). Therefore, a positive correlation could be anticipated in moderate drinkers when cardiovascular disease is not used as a covariate. Alternatively, the effect may vary with level of consumption, i.e. protection at light to moderate intake, but a negative association at the highest levels of consumption.

Main Study Question:

The following questions will be addressed controlling for age, gender, race, history of cardiovascular disease, prior stroke or TIA. Education, depression, diabetes, hypertension, and possibly for income, medication (especially diuretics, antidepressive, or other CNS drugs), and a measure of obesity. Participants on CNS drugs may be excluded from the study.

1. At visit 2, compared to never drinkers
   a. Is the quartile of current alcohol consumption among current drinkers associated with cognitive scores controlling for known covariates such as age, gender, race, education, diabetes, and cardiovascular disease (Potential measures of alcohol intake include current alcohol intake in grams per week, alcohol intake in past 24 hours, or % kcal from alcohol).
   If alcohol intake in past 24 hours is significantly associated with cognition, we may need to evaluate after stratifying for risk factor or exclude those who reported drinking within 24 hours of the clinic visit.
   b. Is the quartile of past alcohol intake among past drinkers (i.e., gms/week) associated with cognitive scores controlling for known covariates?
   c. Is the quartile of lifetime alcohol intake associated with cognitive scores among ever drinkers, past drinkers, or current drinkers controlling for known covariates?
2. At Visit 3, compared to never drinkers, is the quartile of current alcohol consumption associated with cognitive score controlling for known covariates such as age, gender, race, education, diabetes, and cardiovascular disease? (Again potential measures of current alcohol intake include grams of alcohol per week, alcohol intake in past 24 hours, or % kcal from alcohol. Additionally, at visit 3, questions were asked which will allow correlation of cognitive function with two other measures of alcohol intake. These include whether a participant has ever consumed more than 5 drinks almost every day for some period of time and the amount of alcohol consumed per drinking occasion which can be calculated from data collected.
   However, only a subset of the cohort had cognitive function evaluated at visit 3.)
3. For participants with similar levels of alcohol intake (i.e., quartile), is the type of alcohol (i.e., beer, wine, or hard liquor) consumed associated with level of cognition?
4. For participants with similar levels of alcohol intake (i.e., quartile) is the association of alcohol intake and cognitive function affected by level of thiamin intake?

Data (variables, sources, inclusion/exclusion):

The following variables will be needed for the analysis:
Visit 2 and 3: Age, gender, race, history of prior stroke or 15A, education level, income level, depression,
diabetes, hypertension, medication (especially antihypertensives, antidepressives, or other CNS drugs), cardiovascular disease, weight, BMI, subscapular fat measurement, MCV and the measures of alcohol intake.

**References for cross-sectional study:**
Harper CG, Kril IJ, Daly J. Does a "moderate" alcohol intake damage the brain? J Neurol Neurosurg Psychiatr 1988;S1:909-913.