1. Full Title: A study of MRI-diagnosed white matter lesions and infarcts among migrainers participating in a population-based study of cardiovascular disease: the ARIC study, 1993-94
   Abbreviated Title: Migraines, WML & Infarcts

2. Writing Group (list individual with lead responsibility first):
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3. Timeline:
   Analysis can start immediately after approval, the MRI data set is available; migraine and CHD/CVD
descriptive data are available in the Visit 3 data set; data sets for Visit 1 and 2 are also here.

4. Rationale:
   The clinical diagnosis of migraine headaches is traditionally based on clinical impressions of patient reported
descriptions of pain (onset, location, type) and prodromal, concomitant and residual symptoms. The introduction in 1988 of diagnostic criteria by the International Headache Society (IHS) have greatly enhanced the standardization in the diagnosis of migraines in both clinical practice and epidemiologic studies. The advent of MR technology has allowed the imaging of the brain before, during and after the onset of clinically defined migraines. However, to date, only a small number of MRI studies of migraine headaches among clinical populations (and none from population-based samples) have been reported, resulting in inconsistent findings of white matter lesions and cerebral infarcts among patients with and without migraines and little insight into the etiology and neurologic consequences of migraines.

   Although the cause of migraine headaches is unknown, there is clear evidence that migraines are associated
with cerebral ischemia and stroke, both of which have been shown to be associated with increased prevalence of white matter lesions and infarcts. We have, therefore, hypothesized a higher prevalence of MRI detectable white matter lesions and infarcts among individuals reporting a history of migraine headaches, in contrast to those without migraines, and higher proportions in migrainers with aura than those without. As encountered in many of the studies on migraines and MRI findings published to date, the very small sample sizes will severely restrict the testing of any hypotheses. Unless odds ratios are very high, it is unlikely that anything besides descriptive analyses can be presented.

   The cross-sectional data of African and European Americans who volunteered to have a cerebral MRI during the third visit of the ARIC study provide an opportunity to compare white matter lesions and infarcts identified by MRI scans among 110 ARIC participants with a history of IHS classified migraine headaches (available in Visit 3) with the cerebral MRI scan of the 1585 participants who did not report a history of
headaches lasting at least 4 hours (the entry criteria for migraine headaches). Although the sample size of migraineurs is small, to our knowledge, ARIC has the opportunity to contribute the first studies on MRI findings in migraineurs from a non-clinical population. To the extent that sample sizes permit, we will explore the following hypotheses.

5. Main Hypothesis:
(1) Migraine headaches are associated with white matter lesions and infarcts identified by cerebral MRI scans.
(2) The associations between migraines and WML and migraines and infarcts are independent of "traditional" CHD and CVD risk factors determined at Visit 3 (self-reported history of MD-diagnosed stroke/TIA, hypertension, diabetes, current smoking and total cholesterol).
(3) These associations vary by age, ethnicity, sex, and type of migraine (aura vs no aura).
(4) These associations may vary by lifetime history of migraines, medications (aspirin, beta blockers), and in women, the use of oral contraceptives and/or hormone replacement therapy. Because of the very small sample sizes and limited statistical power, there will be limited ability to test any of these effect modifiers. This will be attempted when odds ratios are high, i.e., at least 3.0.

6. Data (variables, time window, source, inclusions/exclusions):
DERIVED VARIABLES: age, center, racegrp, sex
VISIT 1: medications-Medication Survey, Reproductive History, Oral contraceptive use-Reproductive History, prevalent stroke, CHD, diabetes, hypertension, hyperlipidemia, smoking
VISIT 2: medications-Medication Survey, Reproductive History, AFU oral contraceptive use-Medication Survey, prevalent stroke, CHD, diabetes, hypertension, hyperlipidemia, smoking
VISIT 3: medications-Medication Survey, Reproductive History, AFU oral contraceptive use-Medication Survey, prevalent stroke, CHD, diabetes, hypertension, hyperlipidemia, smoking

history of migraine headaches-Personal History form
White matter lesions - MRI scans
Infarcts - MRI scans

As it is unlikely that the descriptive paper on migraines will be complete prior to this, official analysis will be requested because the migraine variable is new. All MRI and CVD risk factor variables used will have been included in previous manuscripts.

INCLUSIONS/EXCLUSIONS: The data set is limited to persons from Forsyth County, NC and Jackson, MS who volunteered to have a cerebral MRI during Visit 3, excluding those who reported headaches lasting at least 4 hours which did not qualify as an IHS migraine (Table 1).

**To request Table 1, please contact the ARIC Student Assistant at (919) 962-3268.**