1.a. Full Title: Dietary fat and white matter disease, and infarction on magnetic resonance imaging: The Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): Dietary fat and MRI stroke

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

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3. Timeline: By December 2000

4. Rationale: Saturated fat has been shown to increase low-density lipoprotein (LDL) cholesterol levels (Grundy 1982). The major randomized clinical trials have shown that substantial reduction in the risk of stroke, especially ischemic, resulted from the reduction of blood cholesterol (Crouse JR, 3rd 1997). However, the Framingham heart Study suggested that saturated fat was associated with reduced risk of ischemic stroke in men (Gillman 1997). Another cohort study of Japanese men living in Hawaii also showed an inverse association between saturated fat and cerebrovascular mortality (McGee 1985).

   Facing the conflicting results from above, it is necessary to further explore the mechanisms of the effect of diet fat on stroke. With magnetic resonance imaging (MRI), it has possible to detect subclinical markers of cerebrovascular disease, such as silent infarct and white matter disease (Bryan 1997). While silent infarct has been well known as a subclinical cerebrovascular disease, the clinical significance of white matter disease is still uncertain. However, arteriosclerosis has been suggested as the primary factor in the pathogenesis of diffuse white matter lesions, which may be followed by demyelination and loss of axons (van Swieten 1991). White matter disease has also been found to be positively associated with age, history of stroke, and hypertension (Manolio 1994).
No epidemiological study, to our best knowledge, has dealt with the relationship between dietary fat and white matter disease or infarction. The proposed study, with a large, diversified, community-dwelling population, will provide essential information about mechanism of dietary fat and stroke, and further understanding of clinical significance of white matter disease. The possible associations will warrant further studies to explore the causal relationship, which may offer bases for prevention of stroke.

5. Main Hypothesis/Study Questions: We hypothesize that a low saturated fat and high unsaturated fat diet is a protective factor in white matter disease and infarction.

6. Data (variables, time window, source, inclusions/exclusions): The ARIC study is a prospective study conducted in four U.S. communities, Forsyth County, North Carolina; Jackson Mississippi; Suburban Minneapolis, Minnesota; and Washington County, Maryland. A total of 16,000 persons, aged 45-64 years at initial recruitment (1987-1989), were randomly selected from each community. Since 1987, annual follow-up interviews and clinical examinations per three years were performed. During 1993 and 1994, among cohort members aged 55 years and older at two sites (Forsyth County, North Carolina and Jackson, Mississippi) who are eligible of a cerebral MRI examination, 1,920 subjects were randomly selected to participate in the MRI study. The proposed study population will consist of these 1,920 subjects.

The ARIC dietary questionnaire was a 66-item modified version of the 61-item questionnaire used by Willett et al. Nutrient values of foods were computed by Willett et al. primarily on the basis of data from the US Department of Agriculture (Tell 1994). Participants with 10 or more missing items on the dietary questionnaire, or with extremely low or high energy intake (<600 and >4,000 kcal/day for men and <500 and 3,600 kcal/day for women), or with previously diagnosed myocardial infarction, stroke, or diabetes will be excluded. Animal fat, vegetable fat, saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, cholesterol, and Keys’ score from both baseline and third clinical examination (during 1993 and 1994) will be examined.

White matter disease, identified as hyperintensity signal on T2 weighted and spin density weighted images and isointensity signal on T1 weighted image, was scaled from 0 to 9 based on the visual ‘pattern matching’ of the participant’s scans to reference standards. Infarction, identified as hyperintensity signal on T2 weighted and spin density weight images and hypointensity signal on T1 weighted image, was coded as ‘Yes’ or ‘No’ (8). Other baseline information, such as age, sex, race, BMI, years of cigarette smoking, drinking status, HDL, LDL, hypertension, diabetes, and sports index, has been collected.

Baseline characteristics distributions according to presence of white matter disease and infarction, respectively, will be presented. Each measurement of dietary fat will be utilized as categorical (quartiles). The univariate associations between dietary fat
and white matter disease, and infarction will be explored with logistic regression. Finally, the associations between dietary fat and white matter disease, and infarction will be assessed with logistic regression, after adjusting for other risk factors of stroke. Because of repeated measurements of dietary fat in the proposed study, both effects of accumulation and changing of dietary fat will be assessed, respectively.

7.a. Will the data be used for non-CVD analysis in this manuscript? ____
   Yes __X__ No

b. If Yes, is the author aware that the file ICTDER01 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 ICTDER01 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 __X__ No

b. If yes, if the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER01 must be used to exclude those with value RES_DNA = “No use/storage DNA”? ____ Yes _____ No