ARIC Manuscript Proposal # 902

1.a. **Full Title:** USE OF NON-ASPIRIN NONSTEROIDAL ANTI-INFLAMMATORY DRUGS AND RISK OF CARDIOVASCULAR DISEASE

b. **Abbreviated Title (Length 26 characters):** Non-aspirin NSAIDs and Incident CVD

2. **Writing Group**
   
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3. **Timeline:**
   

4. **Rationale:**

   The protective effects of aspirin use for coronary heart disease (CHD) are well known, but whether the use of non-aspirin non-steroidal anti-inflammatory (NANSAID) drugs affects risk of CHD or stroke has not been studied extensively. The complex properties of NANSAIDS can support hypotheses of both their prevention and promotion of atherosclerotic processes. In addition to anti-inflammatory effects, NANSAIDS inhibit thromboxane production and platelet aggregation, and thus theoretically might minimize atherosclerosis. Conversely, NANSAIDS interfere with the production of the platelet inhibitor prostacyclin, which could result in an increased risk of platelet aggregation and thrombosis. Apart from a recent study by Ray, et al. (1), which showed no protective effect of NANSAIDS for risk of CHD, data on the risk of CHD and stroke associated with regular use of NANSAIDS are scarce.

   The ARIC Study provides an opportunity to examine this important question in a large population-based cohort. Data from the 1993-1995 follow-up phone survey will be used to establish the NANSAID use status of participants at their baseline clinic examination. The association between NANSAID usage and risk of incident CVD events through 1999 will then be examined.
5. Main Hypothesis/Study Questions:

(1) Regular use of NANSADS at the baseline ARIC clinic exam will be associated negatively with risk of incident MI and stroke during nearly 10 years of follow-up. (Since we don’t have NANSAD use information that completely overlaps follow-up data through 1999, we will also test this hypothesis for a follow-up time period more proximal to usage, i.e. maybe from the time of the phone survey through 1999.)

(2) Duration of use will be negatively associated with risk of CVD events in a dose-response pattern.

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

Dependent Variables: (1) Incident MI/Fatal CHD through 1999 (INC_BY99) (2) Incident MI/Fatal CHD/SMI/Proc through 1999 (IN_99SP) (3) Incident ischemic stroke through 1999 (IN99ISC)

Independent Variables: Non-aspirin NSAID and aspirin use as assessed by 1993-1995 follow-up phone survey – will examine (1) any regular use vs. no regular use, and (2) duration of use (no regular use, 1-2 yrs, 3+ yrs). Covariates to be considered: age, gender, race-center, smoking, diabetes, hypertension (SBP and meds), LDL and HDL cholesterol, BMI, WHR, alcohol intake, education, physical activity, and aspirin use. Inflammatory markers might also be considered.

Exclusions: Subjects not black or white, subjects with prevalent CHD or stroke at baseline, subjects with incomplete NANSAD use data (i.e. did not complete the 1993-1995 phone survey).

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 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  _ X_ No

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/cscs/ARIC/stdy/studymem.html](http://bios.unc.edu/units/cscs/ARIC/stdy/studymem.html)

___X___ Yes _______ No