ARIC Manuscript Proposal # 974

1.a. Full Title: Change in carotid IMT is associated with Incident CHD and Incident Stroke

b. Abbreviated Title (Length 26 characters): IMT Change and CVD

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

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4. Rationale: ARIC and other studies have shown an association between baseline carotid IMT and incident coronary heart disease (CHD) and ischemic stroke. This baseline IMT can be considered to include both “normal” anatomic thickness and thickness due to atherosclerosis. Fewer studies have considered whether recent IMT change (as an index of the current rate of atherogenic progression) is associated with incident CVD following that baseline IMT level. ARIC has now accumulated enough post-second examination follow-up to examine this issue. As in analysis of baseline IMT data, change in carotid IMT may be considered as a marker for recent general atherosclerosis.

5. Main Hypothesis/Study Questions:
   a. For each sex and race group (black or white) average annual change in common carotid IMT between the first ARIC examinations is associated with later incident CHD or incident ischemic stroke, adjusted for baseline (Visit 2) age. We will consider the same hypothesis adjusting in addition for traditional risk factor smoking (cursmk21,forsmk21), sbp+antihypertension meds (or hypertension), total cholesterol (lipb01, continuous or categorical), HDL cholesterol (lipb03, continuous or categorical), and diabetes (diabts23). We will also consider additional adjusting for baseline IMT (possibly categorical, “thick” and “non-thick”), and consider additional adjusting for prior changes in the risk factors..
   b. For each sex and race group (black or white) average annual change in common carotid IMT between the most recent ARIC examinations is associated with later incident CHD or incident ischemic stroke, adjusted for baseline (Visit 2) age. We will consider the same hypothesis adjusting in addition for traditional risk factor smoking (cursmk21,forsmk21), sbp+antihypertension meds (or hypertension), total cholesterol (lipb01, continuous or categorical), HDL cholesterol (lipb03, continuous or categorical), and diabetes (diabts23). We will also consider additional adjusting for baseline IMT (possibly categorical, “thick” and “non-thick”), and consider additional adjusting for prior changes in the risk factors.
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**c.** We will also consider estimating the effect of change in IMT in the presence or absence of lesions.

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

   Incident events through 2001. Incident CHD is defined by hospitalized MI, fatal CHD, silent MI by ECG, or coronary revascularization. Incident hospitalized ischemic stroke is defined by the ARIC stroke review.

   Change in IMT will be from the common carotid only, because of known measurement drift problems. “Average annual change in common carotid IMT between the first ARIC examinations” will be interpreted as computed from the first two examinations for which there are data at both exams on IMT for the left side or at both visits from the right side or from both sides. Common carotid (optimal angle) IMT change between those exams will then be computed as the left side change if it is the only side with measurements at both visits, or the right side if similar conditions prevail for the right, or the mean of the two changes if both are available. From this the average annual change is calculated by dividing by the time between examinations.

   We will exclude those with event (CHD for the CHD analysis, CHD or stroke for the stroke analysis) prior to the second visit used in the IMT change calculation, using prvchd05 plus incident CHD before the visit for the CHD exclusion and HOM10d and incident ischemic stroke for the stroke exclusion. We will also exclude races other than whites or blacks and blacks at Minneapolis and Washington County. We will further exclude persons with no IMT change definable.

   Baseline covariables will be defined from second visit used in the IMT change calculation, but for brevity here we list only the Visit 2 versions, the ones that will most often be used. V2age21, cursmk21, forsmk21, sbpb21, hyptmd21, total cholesterol (lipb01), HDL cholesterol (lipb03), and diabetes (diabts23). We will also consider as possible covariates change in risk factors from the first ultrasound visit available to the second. Adjusting for any non-demographic covariates that may affect risk through IMT change will be a secondary analysis.

   The important data that will NOT be used is ancillary study data on measurement error in measuring IMT change, since it does not exist. We will discuss the issue of measurement error and assume a range of reliability coefficients for measurement of IMT change to show the effect of correction for measurement error.
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

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  ____X__ 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)?

I think this is the first proposal to consider IMT change as an exposure.

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.