ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #090A

1. Title (length 26):
Lp[a] & Case/Control Status
Full Title: Lp[a] as a risk factor for prevalent atherosclerotic case/control status

2. Writing Group:
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3. Timeline:
Short-term analysis to augment case/control data included in the abstract entitled "Lipoprotein[a] as a Risk Factor for Preclinical Atherosclerosis", accepted for presentation at the AHA Conference on Cardiovascular Disease Epidemiology (March 1991).

4. Rationale:
This manuscript is an extension of MS#O90.and is.based on the same scientific rationale, namely, that traditional cardiovascular risk factors have proven insufficient to explain the development of atherosclerosis. While many of these risk factors increase with age or behavior and affect the progression of disease, lipoprotein Lp[a] remains constant in adults regardless of age, diet, exercise, or lifestyle. Elevated Lp[a] levels have previously been associated with incidence of myocardial infarction, vein graft restenosis, coronary artery disease and cerebrovascular disease, as well as family history of MI among asymptomatic individuals. Lp[a] has also been isolated antigenically from existing atherosclerotic plaque.

B-mode ultrasonography provides information as to the thickness of the carotid wall, but does not indicate composition. By using the ARIC definition of case status, we are attempting to distinguish thickening due to plaque from thickening due to hyperplasia, for example. Lp[a] is believed to be more strongly associated with actual atherosclerosis than with wall thickening as a continuous distribution.

5. Main Hypothesis:
1) Lp[a] levels are positively correlated with carotid atherosclerosis, measured as wall thickness by B-mode ultrasound.

6. Data
Visit 1 (extant) data set of cases and controls pair-matched by race, gender, study center, 10-year age group, and time of examination. Additional matched pairs are obtained from the 5th sampling cycle and will be added to the 386 matched pairs derived from cycles 1-4, bringing the total number of pairs to 492. Data analysis is to be performed by the lead author. Independent variables: lipoproteins and apolipoproteins, home interview data, hemostatic factors, medical history, antihypercholesterolemic medication, diabetes, waist-to-hip ratio, blood pressure, smoking status, alcohol consumption, physical activity, gender, race, and center. Dependent variables: case or control status defined as a dichotomous variable. Cases are defined as exceeding 2.5 mm wall thickness, or having a bilateral wall thickening above the 90th percentile value of wall

thickness at the carotid artery (common, internal, or its bifurcation). Controls are chosen from below the 75th percentile of wall thickness distribution.