FHS-ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #364

1. Title: Family history of coronary heart disease predicts incident coronary heart disease through its association both pre-clinical atherosclerosis and risk factors: the ARIC and FHS Studies

2. Writing Group:

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3. Timeline:

Submit Proposal to Publications Committee	1/1/96
Complete Analysis	6/1/96
Submit First Draft to Publications Committee	9/1/96
Submit to Journal	12/1/96

4. Rationale:

The family aggregation of clinically manifest coronary heart disease (CHD) and its major risk factors have been well documented. We have recently completed the first report of the association of family history with pre-clinical atherosclerosis as assessed by carotid artery intima-media thickness (ARIC Manuscript #273, FHS Manuscript #02, "Family History of Coronary Heart Disease and Pre-clinical Carotid Artery Atherosclerosis in African Americans and Whites: The ARIC and FHS Studies"). A quantitative measure of family history of CHD (Family Risk Score-FRS) was related to carotid artery intima-media wall thickness (MIT) in white and black women and white men free of clinical evidence of coronary heart disease. The association persisted in white men and women after adjusting for the major risk factors. Thus, there is the possibility that the relation of family history to incident CHD may be explained by the intervening development of silent atherosclerosis, observations missing from earlier studies of family history in which the familial aggregation of risk factors failed to explain fully the predictiveness of the family history.

5. Main Study Questions:

The present proposal tests the following hypotheses:

(1) Pre-clinical atherosclerosis, as assessed by carotid artery intima-media wall thickness (IMT), is an intervening and possibly an effect modifying variable of the relationship of FRS and risk factors to incident

coronary heart disease; and (2) that the associations are the same among the four race-gender groups of white and black, males and females.

6. Data:

The following variables are needed for this proposal: ARIC Visit 1 age, race, sex, field center, date of examination, Prev CHD, FRS, IMT, systolic and diastolic blood pressure, anti-hypertensive medication, smoking history, total cholesterol, LDL-C, HDL-C, TG, Lp(a), weight, height, waist-hip ratio, insulin, diabetes, fibrinogen, education, income, occupation; incident CHD occurring after ARIC visits one.

7. Analytic approach:

Cox proportional hazards analysis will be used to determine the coefficient of Family Risk Score as a predictor of time to event of incident CHD, in race-gender specific, age adjusted models. Test for interaction effect of IMT and FRS on CHD will be performed. If there is no evidence of interaction, change in the coefficient by adding IMT to the models containing age and FRS will be assessed. Finally the effect of adding the risk factors will be determined.