ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #293

1. Title (length 26 letters):
The Association of the Dyslipidemic Hypertension and the FRS (The ARIC Study)

2. Writing Group (list individual with lead responsibility first):
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3. Timeline:
Analysis could begin immediately. Draft distributed to writing group by April.

4. Rationale:
The presence of hypertension with mixed lipid abnormalities (low HDL cholesterol, high LDL cholesterol, and high triglycerides) is considered a manifestation of a common familial syndrome, “familial dyslipidemic hypertension” (FDH). FDH is present in 48-63% of persons with hypertension diagnosed before the age of 60 years and who have at least one sibling with hypertension diagnosed before the age of 60 (JAMA 259:3579). FDH is also linked with a number of other metabolic and/or anthropomorphic abnormalities: central obesity, elevated fasting insulin and glucose, diabetes, and elevated uric acid. FDH may derive from shared genes and/or shared environmental factors. The identification of probands with FDH may target families at high risk of atherosclerotic heart disease.

5. Main Hypothesis:
Within the ARIC cohort, participants with dyslipidemic hypertension have a higher family CHD risk score (FRS) compared to normotensive, normolipidemic participants. The presence of other metabolic abnormalities (hyperinsulinemia, high fasting glucose, elevated WHR, elevated BMI, hyperuricemia) clustering with FDH will be associated with higher mean FRS in a graded fashion with greater cluster size.

6. Data (variables, time window, source, inclusions/exclusions):
All data will be obtained from existing ARIC Visit 1 tapes, currently available at the University of Minnesota. Variables include: FRS, systolic and diastolic blood pressure, antihypertensive medication use (specific antihypertensive agents used), triglycerides, HDL and LDL cholesterol, insulin, glucose, uric acid, diabetes, body mass index, waist-to-hip ratio, gender, race group, and age.
Inclusions/exclusions: Although the unvalidated FRS will be used, special attention will be given to misclassification of the FRS (as evaluated in the Minneapolis, Forsyth Field Centers). Ethnic groups other than white and African American will be excluded.
Analysis: The analysis is not intended to evaluate the association between lipids, apolipoproteins, insulin, and/or body fat distribution and their interrelationship with the FRS. Rather, it will test the hypothesis that dyslipidemic hypertension is associated with a higher CHD FRS, and that the addition of other metabolic abnormalities are associated with a greater FRS. Secondary hypotheses will test the association between dyslipidemic hypertension and parental history of hypertension and stroke.

All analyses will be gender specific, with adjustment for ethnicity. Analyses will be done separately using the validated CHD FRS, and the FRS for the combined ARIC cohort.

The approach will be categorical, with the following definitions:
**Hypertension**: DBP greater than or equal to 90 mmHg or SBP greater than or equal to 140 and/or current use
of antihypertensive medications.

**Dyslipidemia**: The presence of at least one of the following abnormalities:

- HDL less than or equal to 35 mg/dl
- Triglyceride greater than or equal to 190 mg/dl
- LDL greater than or equal to 160 mg/dl

Note: Lipids will be adjusted for diuretic and beta blocker use according to previous reports (Williams, Selby). For diuretic users, triglycerides, HDL, and LDL will be multiplied by 0.978, 0.982, and 0.978, respectively. For beta blocker users, similar adjustments will be 0.797, 1.106, and 0.964, respectively.

**Other characteristics:**

- **Diabetes/elevated glucose**: fasting serum glucose greater than or equal to 140 mg/dl or reporting hypoglycemic medication use.
- **Hyperuricemia**: uric acid greater than or equal to 8 mg/dl
- **Hyperinsulinemia**: insulin greater than or equal to 20 µU/ml
- **Obesity**: Women, BMI greater than or equal to 36.3 kg/m², Men BMI greater than or equal to 32.5 kg/m² (based on ARIC 90th percentile cutpoint, gender specific distributions)
- **Central adiposity**: WHR greater than or equal to 1.03, men; greater than or equal to 1.0 for women (based on ARIC 90th percentile cutpoint, gender specific distributions)