ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #382

1. Title:
Trends in subclinical atherosclerosis (intima-media wall thickness) by social class in the ARIC Study

2. Working Group:
(lead) AV Diez-Roux, FJ Nieto, M Massing, HA Tyroler, M Szklo, P Sorlie, CC representative

3. Rationale:
A previous ARIC Study manuscript based on the cross-sectional analysis of visit 1 data (Diez-Roux et al 1995) has documented increased intimal-medial wall thickness in the lower social classes, suggesting that the process of atherosclerosis itself, and not only its clinical expression is patterned by social class. The proposed analyses would attempt to confirm these findings in a longitudinal setting, investigating whethere the progression of subclinical atherosclerosis (as assessed by intimal-medial thickness) over the first three visits also varies by social class. Documenting the mechanisms responsible for social class differences in CHD is particularly relevant in view of increasing disparities in death rates by social class (of which atherosclerotic disease is an important component). In addition, since social class is such an important predictor of atherosclerotic disease, studying the mechanisms responsible for social class differences may help contribute to our understanding of the etiology of the disease.

Carotid intimal medial thickness (IMT) will be used as an indicator of atherosclerosis in participants without clinical signs of atherosclerotic disease. Both individual-level and neighborhood-level social class indicators will be investigated, and their associations with changes in wall thickness compared. Associations of social class with changes in wall thickness will be investigated before and after adjustment for established cardiovascular risk factors.

4. Hypotheses:
Carotid atherosclerosis, as assessed by IMT, progresses more rapidly in the lower than in the higher social classes.

Differences by social class are only partly accounted for by differences in established risk factors.

5. Study Population:
Analyses will be restricted to participants without clinical signs of atherosclerotic disease at baseline (CHD, stroke, intermittent claudication, Rose angina) and to participants with IMT measurements for the first three visits.

6. Variables:
Average wall thickness over the six sites (sum45_1 for the first visit and analogues for visits 2 and 3) will be the outcome of interest. Reader and trend adjusted wall thickness will be used in the analyses. Income and education at the individual-level and the neighborhood-level (block-group level) wil be the main exposures investigated. The additional risk factors included in the analyses will be LDL-cholesterol, HDL-cholesterol, smoking, hypertension (standard ARIC definition), exercise indices, waist-hip ratio, diabetes (standard ARIC definition), and Keys score.

7. Analyses:
Analyses will be stratified by race and gender. Initially, simple exploratory analyses will be used to describe

the distributions and changes in IMT over the first three visits (means at each visit, plots of IMT for individuals at each visit). These descriptive analyses will be repeated for each social class. Regression techniques will then be used to investigate associations between social class and IMT. In order to account for the correlation between IMT measures within individuals over time, random effects models with IMT as the dependent variable and a random intercept will be used. A time indicator and the social class indicators will be included as independent variables. The need to model the time effect as random (a random slope associated with time) will be evaluated. The interactions betwen time and social class will be investigated in order to determine whether the progression of IMT differs by social class. AFter estimating unadjusted associations with social class, additional risk factors (both time-dependent as well as time-independent) will be included in the models to test whether any effects observed disappear after adjustment for risk factors.

In order to minimize the potential effect of measurement error, alternative strategies will also be explored. Some of these strategies may include, for example, focusing only participants with either no change or extreme increase in IMT across visits, and comparing the proportions in these groups across social classes. Other strategies may be developed as the work progresses in collaboration with the coordinating center.

8. Timeline:
Analyses could begin as soon as IMT measurements for the first three visits are available. All other data is already available. Procedures for fitting linear random effects models are available in SAS software (Proc Mixed).