ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #546

1. Full Title: Subclinical markers and incident CHD in diabetes mellitus
   Abbreviated Title (length 26): CHD in diabetes

2. Writing Group (list individual with lead responsibility first):
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3. Timeline:
   11/97-5/98

4. Rationale:
   CHD is the most common cause of death in diabetes mellitus, and risk of CHD death is 2 to 3 times higher in diabetes (1). Though diabetes associates with many CHD risk factors, CHD risk of those with diabetes remains elevated even after control for these factors (1, 2). Though much speculation exists about the causes of this excess, the subject has been relatively little investigated in large population studies.

   The availability of several markers of subclinical disease in ARIC permit investigation of this question with a different focus. The degree to which these markers indicate risk of incident CHD in diabetes is an important question in itself. Additionally, however, these markers indirectly permit an evaluation of the potential importance of different disease processes to CHD in diabetes.

   One of these markers, carotid artery intima-media thickness, if associated with increased risk among those with diabetes, would suggest that excess risk in diabetes occurs, at least in part, due to factors acting through the atherosclerotic process.

   Others, if associated with excess risk, would suggest the importance of other pathways. Other such pathways include arterial stiffness, which is increased in diabetes, and
diabetic autonomic dysfunction. This dysfunction could impact on the heart both directly, through processes associated with diminished heart rate variability, and indirectly, through processes associated with abnormal blood pressure responses to postural change.

Knowledge of the relative importance of these indicators of different pathophysiologic processes of subclinical disease can help guide efforts toward prevention of CHD in diabetes.


5. Main Hypotheses:
A. Among individuals with diabetes mellitus:
   1. IMT associates with incident CHD/angina.
   2. Arterial stiffness associates with incident CHD/angina.
   3. Heart rate variability associates with incident CHD/angina.
   [Note: Incident angina will only be combined with the standard ARIC incident CHD events if the associations studied are found to be consistent across these outcomes.]
B. The presence of diabetes mellitus does not modify the association between these subclinical markers and incident CHD.
C. After adjustment for the above markers of subclinical disease, no increased risk for incident CHD exists for individuals with diabetes mellitus.

6. Data (variables, time window, source, inclusions/exclusions):
All ARIC subjects, Visit 1 and 2 baseline data and incident CHD/angina data. Baseline data to define diabetes at Visit 1 (fast0802, medication use, physician history, glucos0l) and at Visit 2 (equivalent variables). Exposure variables: IMT, arterial stiffness variables, postural blood pressure change variables, heart rate variability. Covariates: Gender, age, center, ethnicity, BMI, WHR, physical activity, blood pressure, lipids, smoking, alcohol, aspirin use, hormone replacement therapy, menopause status, medication use, glucose, age at onset of diabetes. Outcomes: Incident CHD, angina