1. Title:
Association of Serum Albumin with Lower Extremity Arterial Disease and Carotid Artery Plaque in Participants Without Symptomatic Cardiovascular Disease at Baseline

2. Working Group:
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3. Timeline:
April - May: Initiation and completion of statistical analyses
June - July: Preparation of manuscript

4. Rationale:
Several investigators have published reports on the inverse association of serum albumin with morbidity and mortality from cardiovascular disease\(^1\text{-}^5\), though mechanisms have not been established. In a recent analysis under ARIC Manuscript Proposal #172, there was a statistically significant inverse association of serum albumin and incident CHD in current smokers, but not in former and never smokers, suggesting a possible role of serum albumin as an agent limiting the effect of free-radicals from tobacco smoking or as a factor tied to inflammation. Folsom\(^6\) and colleagues examined the cross-sectional association of albumin and atherosclerosis and concluded there was no association between age-adjusted carotid intima-media thickness in persons without clinical CVD. There was an association with prevalent cardiovascular disease, but this association was not statistically significant when adjustment was made for traditional CHD risk factors.

To further explore possible etiologic roles of low serum albumin, the proposed analysis will examine the cross-sectional association of serum albumin with two additional indicators of atherosclerosis, pre-clinical lower extremity arterial disease and carotid artery plaque.

5. Purpose:
The purposes of this study are: (1) to determine whethere there is an association between serum albumin and two types of pre-clinical atherosclerosis, lower extremity arterial disease and presence of plaque in the carotid artery; and (2) given an association, to explore whether smoking or factors related to inflammation are effect modifiers.

6. Data:
a) Exposure variable: Serum albumin
b) Outcome variables: lower extremity arterial disease, defined by low ankle-brachial index (ABI), and carotid artery plaque in participants without prevalent CHD, Rose Questionnaire intermittent claudication, and self-report physician-told TIA or stroke at baseline
c) Co-variables as possible effect modifiers or confounders: smoking as an acute phase reactor; WBC as a factor related to chronic inflammation; variables considered to be markers of endothelial dysfunction, such as von Willebrand factors; traditional CVD risk factors, such as diabetes and hypertension.

7. Analysis Strategy:
Participants with prevalent symptomatic cardiovascular disease will be excluded. Multivariable logistic regression and analysis of co-variabne will be used to determine the independent association of serum
albumin and prevalent LEAD and plaque, respectively.