ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #599

1. Full Title: Hemochromatosis gene polymorphism and incident CHD
Abbreviated Title (length 26): Hemochromatosis gene & CHD

2. Writing Group (list individual with lead responsibility first):

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3. Timeline:
Analysis and draft completed summer 1998. (Preliminary analysis MN, final analysis at CSCC).

4. Rationale:
It has been theorized that excess iron in the human body catalyzes reactions, which produce tissue damaging free radicals. In the cardiovascular system, these free radicals cause LDL oxidation, which enhance atherosclerotic plaque formation. Initial studies found an association between excess serum ferritin levels and heart attacks, however, the majority of epidemiological research has failed to support the hypothesis of an iron/CHD association.

The association between hemochromatosis, a common autosomal recessive disease characterized by disordered iron metabolism, and CHD has not been well studied. Recently, data on the hemochromatosis genotype identifying heterozygous (one hemochromatosis gene allele) and homozygous (two hemochromatosis gene alleles) individuals have become available for a subset (n=815) of ARIC participants: incident CHD cases through 1991 and a random sample of the cohort This nested case-cohort design offers an opportunity to examine the relation of individuals with one or two hemochromatosis gene alleles and incident CHD.

5. Main Hypothesis:
After adjusting for age, gender, race, ARIC community, smoking status, LDL-C, HDL-C, and hypertension there will be no association between one or two hemochromatosis gene alleles verses none and incident CHD.

6. Data (variables, time window, source, inclusions/exclusions):
Inclusion: incident CHD cases and a subset of the cohort random sample Exclusion: prevalent CHD, stroke, or TLS at baseline
Independent variable: hemochromatosis genotype of baseline blood samples
Dependent variable: incident CHD through 1991
Covariates: Visit 1 - age, gender, race, ARIC community, smoking status, LDL-C, HDL-C, hypertension