

## ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #389

1. a. Title: Associations of homocystein with incident CHD and MRI stroke
- b. HCN-Incident CHD/MRI Stroke

### 2. Writing Group:

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### 3. Timeline:

Analysis to begin 6/96

### 4. Rationale:

Although there is mounting evidence that serum total homocysteine (tHcy) is a CHD risk factor, there still have been few prospective tHcy studies that also examined vitamin levels and several related genotypes. We have measured tHcy on MRI and CHD cases, and in addition have measured vitamins (B<sub>12</sub>, B<sub>6</sub>, folate) and genotype (MTHFR<sub>C677T</sub>, cystathionine  $\beta$ -synthetase mutations<sub>T833C, G919A</sub>) on CHD cases and random cohort participants.

### 5. Main Hypothesis:

1. CHD incidence and MRI stroke are
  - a. associated positively with serum tHcy concentration,
  - b. inversely associated with plasma B<sub>12</sub>, B<sub>6</sub>, folate, and
  - c. increased in people with MTHFR<sub>C677T</sub>
2. There is an interaction of B vitamins with tHcy or MTHFR genotype to increase CHD risk.

### 6. Data (variables, time window, source, inclusions/exclusions):

Endpoints - CHD incidence, MRI stroke (could be one combined or two separate papers).

Independent variables - tHcy, B vitamins, genotypes

Covariates - Other CHD risk factors, vitamin supplement use