1. **Title:** Does vital exhaustion increase CHD risk?

2. **Writing group:**
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4. **Timeline:**
   Complete data analysis - January 1999
   Draft of manuscript to the Publications Committee - March 1999
   Journal submission - May 1999

5. **Hypotheses:**
   1. Vital exhaustion will be a significant predictor of incident CHD, independent of the established CVD risk factors.
   2. Vital exhaustion will more strongly predict shorter-term CHD events than longer-term events.

6. **Rationale:**
   There is convincing evidence that depression precedes CHD events (1, 2). Depression is also common among patients who have suffered a coronary event (3). Recently, vital exhaustion (VE), a condition that is related to depression, has been investigated for its influence on CHD. VE is defined as a state of excess fatigue, hopelessness, and demoralization and may be the final common pathway for the inability to cope with a host of psychosocial stressors. This construct is compatible with Selye's general adaptation model in which exhaustion is the final stage in a protracted experience with psychosocial stress (4). There is considerable convergence in symptomatology between VE and depression as they share up to 70% of common variance (5, 6). Though there is overlap, the work of van Diest and Appels (7) suggests that VE is conceptually distinct from depression since VE does not include feelings of sadness, guilt and low self esteem. Still, in their study, symptoms of depression were more common among the exhausted than the non-exhausted.

   The deleterious impact of VE on CHD has been confirmed in a number of reports employing retrospective (8), prospective (9), and case-control study designs (10). Each has demonstrated a significant role of VE in the onset of myocardial infarction, independent of the established CVD risk factors. There is also evidence that VE is a more powerful short-term than long-term predictor of CHD. In ARIC, VE has been investigated for its association with carotid atherosclerosis (11). Independent of the CVD risk factors, no association was found in women and only a modest association with men.

   The physiological mechanism linking VE to CHD is not well understood. The work of Van Doornen and
Blokland (5) suggests a role of lipid metabolism in the VE-CHD link, while the work of Kop, Hamulyak, Appels (11) implicates reduced fibrinolytic activity.

So far, the available evidence of the association between VE and clinical events has been derived from European populations, exclusively. The proposed study would provide not only a test of these hypotheses in a US sample, but also in a bi-ethnic sample of white and black men and women. The results have implications for our increased understanding of the role of acute psychological distress syndromes on cardiac risk.

7. Variables:
Visit 1 variables: educational level, prevalent CHD; Visit 2 variables, age, race/ethnicity, occupational level, gender, smoking status, serum total cholesterol level, drinking status, BMI, hypertensive status, SBP, DBP, HDL cholesterol, LDL cholesterol, the Maastricht questionnaire, medications; CHD events through 1995.

8. Statistical analysis:
The association between VE and CHD risk will be determined using Cox proportional hazards regression, separately for events occurring within one year and more than one year after the assessment of VE. Models will be run with and without adjustment for the relevant covariables.

References