1.a. Full Title: Vital Exhaustion and incident coronary heart disease

b. Abbreviated Title (Length 26 characters): VE & CHD

2. Writing Group: Tom Mosley, Woody Chambless, Sue Everson-Rose, Ken Butler, Maria Bryant, Kimberly Truesdale, June Stevens, others welcome

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __THM__ [please confirm with your initials electronically or in writing]

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3. Timeline:
Manuscript proposal to Publication's Committee: August / 2006
Data analysis completed: November / 2006
Completed manuscript to Publication's Committee: January / 2007

4. Rationale:
Depression has been linked to CHD risk factors, morbidity, and mortality. Following myocardial infarction (MI), depression has been associated with risk of recurrence and mortality (Frasure-Smith, Lesperance, & Talajic, 1993; Frasure-Smith, Lesperance, & Talajic, 1995). Associations between depression and excess CHD morbidity and mortality have also been found in several prospective studies (Kubzansky & Kawachi, 2000). A related construct, hopelessness, has been associated with incident MI, progression of carotid atherosclerosis, and CHD mortality (Everson et al., 1996; Everson, Kaplan, Goldberg, Salonen, & Salonen, 1997; Stern, Dhanda & Hazuda, 2001). Vital exhaustion is a closely related construct and overlaps considerably with measures of depression (e.g., the Zung and Beck Depression Inventory). Vital exhaustion has been related to incident MI (Appels & Mulder, 1989), recurrence of cardiac events (Kop et al., 1994), and severity of coronary artery disease (Kop, Appels, Mendes de Leon, de Swart, & Bar, 1993). Findings from ARIC also revealed significant associations between vital exhaustion and metabolic syndrome (Mosley, Andrew, Dubbert, Wyatt, & McGovern, 1998).

Mechanisms linking depression and CHD are not fully understood. Individuals with higher levels of negative emotions tend to have poorer behavioral risk profiles (e.g., greater smoking, higher alcohol use, less physical activity). However, this association does not adequately explain excess risk, which persists in most studies after controlling for these risk factors. Negative emotions may interact with other psychosocial risk factors. For example, individuals high in hostility may engender stressful interpersonal environments and ultimately reduced social support. The most direct pathway whereby negative emotions may influence CHD risk is through sympathetic activation involving elevated cardiovascular and neuroendocrine responses, with alterations in the hypothalamic-pituitary-adrenal axis and sympathetic-adreno-medullary axis (Musselman, Evans, & Nemeroff, 1998).

In the current study, we propose to examine the association between vital exhaustion and incident CHD in the ARIC cohort.

5. Main Hypothesis/Study Questions:

We hypothesize that vital exhaustion will be associated with a significantly increased risk of CHD independent of traditional risk factors.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

The primary dependent variable will be incident CHD (defined as acute MI/fatal CHD, silent MI, or cardiac revascularization procedure) occurring in the follow up period between V2 and 2004. The association between vital exhaustion (assessed by the
Maastricht Questionnaire, MQ) and CHD will be examined using Cox proportional hazards regression, with the MQ entered into the model as an indicator variable. Models will adjust for age, race/center, sex, education level, total cholesterol, LDL cholesterol, fibrinogen, systolic BP, hypertension, diabetes, smoking, alcohol use, and BMI. In secondary analyses, separate models will be fit for combined CHD and "hard" events.

The MQ is composed primarily of items assessing fatigue and demoralization. A significant subset of MQ items appears to measure more traditional symptoms of depression (e.g., problems with sleep, irritability, decreased libido, crying, difficulty concentrating, etc.). In secondary analyses, we will employ (principal components) factor analysis to examine the potential contribution of factor derived MQ subscales to CHD risk.

Exclusions:
1. CHD at V2 or prior
2. Missing the MQ

7.a. Will the data be used for non-CVD analysis in this manuscript? _Yes _XX No

b. If Yes, is the author aware that the file ICTDER02 must be used to exclude persons with a value RES_OTH = “CVD Research” for non-DNA analysis, and for DNA analysis RES_DNA = “CVD Research” would be used? _Yes _No
(This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes _XX__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 must be used to exclude those with value RES_DNA = “No use/storage DNA”?

_____ Yes _____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/ARIC/search.php

_____XX__ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

MS # 692 (Mosley): Dimensions of Social support and risk of CHD
MS # 1004 (Chambless): ARIC CHD Risk Prediction from Behavioral, Psychosocial, and Socioeconomic Factors
MS # 1136 (Bryant): Obesity, Vital Exhaustion and Cardiovascular Disease

These authors are collaborators on the proposed manuscript.

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  ____ Yes  _XX_ No

11.b. If yes, is the proposal
___  A. primarily the result of an ancillary study (list number* _________)
___  B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _________ _________  _________)

*ancillary studies are listed by number at http://www.cscc.unc.edu/arin/forms/

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

Understood.

References


