ARIC Manuscript Proposal # 1226

1.a. Full Title: Psychosocial distress and risk for recurrent adverse cardiac events: The Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): anger/exhaustion and recurrent CHD

2. Writing Group (list individual with lead responsibility first): Janice E. Williams, David J. Couper, F. Javier Nieto, Willem J. Kop, Wayne D. Rosamond

   Lead: Janice E. Williams
   Address: Post Office Box 3168
            LaGrange, Georgia 30241

   Phone: 706-884-2321
   E-mail: jwill22@bellsouth.net

3. Timeline: Start analyses: January 2007
   First draft of manuscript to ARIC Publications Committee: July 2007
   Submit to journal: September 2007

4. Rationale:
   The role of psychological factors (e.g., such as depression, anger/hostility, and social support) in coronary heart disease (CHD) onset has been demonstrated in a large number of epidemiologic studies (1-3), but less population-based evidence is available on the extent to which these factors influence the clinical course among people with established disease. There are data showing that psychosocial distress among patients hospitalized for CHD is positively associated with an increased likelihood of rehospitalization (4), increased risk for recurrent events (4), and increased health care costs (5). Among the psychological factors being investigated for their prognostic value, depression has received the greatest amount of research attention. In large-scale studies, depression in people with CHD is positively associated with short-term (6) and long-term CHD mortality (7), all-cause mortality (7), and recurrent events (8). Anger and exhaustion have received much less attention for their role in the clinical course among people with established CHD.

   In one study, anger alone and anger and exhaustion jointly predicted recurrent CHD events in men who had received percutaneous transluminal angioplasty, although the results were marginally statistically significant after controlling for the established CHD risk factors (9). In a separate analysis from that study, vital exhaustion independently predicted new cardiac events after angioplasty (10). Compared with their non-exhausted counterparts, exhausted patients had a four-fold greater risk for a subsequent cardiac event within 18 months. These studies have contributed to our understanding of the role of anger and exhaustion in the clinical course among people with established disease, but their generalizability may be limited since the investigations
were not population-based and the participants comprised predominantly men. The joint effect of anger and exhaustion on recurrent events has not been established in large, epidemiologic studies.

The purpose of the proposed analysis is to examine the separate and joint effects of trait anger and exhaustion on recurrent CHD in participants with established disease. This investigation will complement a previous ARIC analysis in which it was demonstrated that participants with high trait anger and high exhaustion were at increased risk for incident CHD(11). The ARIC cohort provides a unique opportunity to examine these relationships in a large, population-based cohort of both men and women and black and white participants.

5. **Main Hypothesis/Study Questions:**

1) Participants with established CHD and high trait anger have significantly greater risk for recurrent CHD (e.g., acute MI/fatal CHD) compared to their counterparts with low trait anger. 1a. There is heterogeneity of association by level of predicted CHD risk such that the strength of the association will be weaker in participants who have high predicted CHD risk, based on the ARIC risk prediction model (12).

2) Participants with established CHD and high exhaustion have significantly greater risk for recurrent CHD compared to their counterparts who have low exhaustion. 2a. There is heterogeneity of association by level of predicted CHD risk such that the strength of the association will be weaker in participants who have high predicted CHD risk.

3) Participants with established CHD and a combination of high trait anger and high exhaustion have significantly greater risk for recurrent CHD compared to their counterparts who have low trait anger and low exhaustion. 3a. There is heterogeneity of association by level of predicted CHD risk such that the association will be weaker in participants who have high predicted risk.

**Statistical analyses:**

At visit 2 (baseline for the current analysis), after exclusions (e.g., participants with a racial/ethnic identity other than black or white, black participants from the Minnesota and Washington County field centers, and participants with incomplete responses on the anger and exhaustion questionnaires), there are 628 participants with prevalent CHD, among whom 240 subsequent events (acute MI or fatal CHD) occurred through 2003.

Descriptive: A one-way analysis of variance or chi-square test of association will be used to assess differences in means (for continuous variables) and percentages (for categorical variables), respectively, for the baseline CHD risk factors.

Inferential: Cox proportional hazards regression analysis will be used to assess the separate and joint effects of trait anger and exhaustion on risk for recurrent CHD. Each measure of psychosocial distress (ie, trait anger [high vs low], exhaustion [high vs low], and the combination of trait anger and exhaustion [high-high vs low-low]) will be entered into the models as dummy variables. Separate models will be conducted to assess interactions of trait anger and predicted CHD risk; exhaustion and predicted CHD risk; and trait anger and exhaustion combined and predicted CHD risk for recurrent CHD. If the test of interaction by predicted CHD risk is significant, then the remaining analyses will be stratified by high and low predicted risk. The Kaplan-Meier product limit method will be used to estimate cumulative probabilities of recurrent CHD over time.
6. **Data (variables, time window, source, inclusions/exclusions):**
Variables: Spielberger Trait Anger scores at Visit 2, exhaustion scores at Visit 2, age, center, race/ethnicity, educational level, factors in the ARIC predicted CHD risk equation (total cholesterol, HDL cholesterol, systolic blood pressure, use of antihypertensive medication, current smoking, and prevalent diabetes mellitus), prevalent CHD, CHD events through 2003. Participants without prevalent CHD will be excluded.

7.a. **Will the data be used for non-CVD analysis in this manuscript?**  ____ Yes  ____ No  

7.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  ____ 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.csecc.unc.edu/ARIC/search.php  

  ____ X ____ 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)?**

    #640 (Convergence of trait anger and exhaustion and incident CHD risk)  

11. **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.**

**References**


