**ARIC Manuscript Proposal # 1770**

PC Reviewed: 3/8/11  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title: Clinical outcomes in depression and heart failure

b. Abbreviated Title (Length 26 characters): Depression, HF, and outcomes

2. Writing Group:
   Writing group members: Janice Williams, Anna Kucharska-Newton, Laura Loehr, Sharon Wyatt, Thomas Mosley, David Couper

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

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3. **Timeline:** Abstract will be submitted for presentation consideration at the 2012 scientific session of the AHA Council on Cardiovascular Disease Epidemiology and Prevention; Manuscript will be completed December 2012

4. **Rationale:**
Heart failure is a rapidly growing public health problem. According to the most recent statistics provided by the American Heart Association (AHA), approximately 5 million Americans are living with heart failure, and 550,000 new cases are diagnosed each year (1). Among the psychosocial factors associated with heart failure, depression has received the greatest amount of research attention. Depression is an established prognostic factor in patients with coronary artery disease. Evidence is beginning to mount for a similar impact in HF patients. The prevalence of depression in people with heart failure (22 – 77%) (2) is substantially higher than in the general population (9.5%) (3). Depression associated with cardiovascular disease is so common and deleterious that the AHA now recommends that all cardiac patients be screened for this disorder.

Among HF patients, depression has been associated with an adverse clinical trajectory. In a recent meta-analysis of outcome studies, the authors reported that HF patients with depression were more than twice as likely to visit the hospital emergency department compared to their nondepressed counterparts (4). HF rehospitalization rates among HF patients with depression were also significantly elevated, ranging from 25 – 54.8% among the depressed compared to 16.1 – 35.7% among the nondepressed. Strong inverse associations were reported between severity of depressive symptoms and the prognosis of HF. In addition, from the meta-analysis, the authors reported an overall risk of death as 2.1 in depressed versus nondepressed HF patients. In an examination of functional decline in HF patients with depressive symptoms, the authors reported a two-fold increase in the risk for reduced activities of daily living and increased limitations due to dyspnea (5). Depression may be linked to poor clinical outcomes through biological (ie, neurohormonal dysregulation and inflammation) and behavioral (ie, maladaptive health behaviors, including poor compliance with recommended medical regimens) mechanisms (6).

In a recent ARIC analysis, we found that cohort participants with high depressive symptoms, compared to their non-depressed peers, had a 94% increased risk for incident hospitalized heart failure (7). We propose to extend the depression-HF hypothesis by examining the clinical trajectory (defined as rehospitalization, length of stay, frequency of outpatient visits, and all-cause mortality) of participants from the aforementioned analysis who had depressive symptoms and who experienced incident hospitalized HF.

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

1. Participants with depressive symptoms who experienced incident hospitalized HF will have a different pattern of health care services utilization (i.e., a greater risk for rehospitalization, a greater frequency of rehospitalization, a greater frequency
of outpatient visits (linking to CMS data), and longer lengths of stay) compared to their non-depressed counterparts.

2. Participants with depressive symptoms who experienced incident hospitalized HF will have an increased risk for all-cause mortality compared to their non-depressed counterparts.

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).

Hypothesis 1: Cox proportional hazards regression will be used to determine the risk for rehospitalization among participants with depressive symptoms who experienced incident hospitalized HF compared to their non-depressed peers. Analysis of variance will be used to determine differences in frequency of rehospitalization, frequency of outpatient visits, and length of stay.

Hypothesis 2: Cox proportional hazards regression will be used to determine the risk for all-cause mortality and the probability of survival among participants with depressive symptoms who experienced incident hospitalized HF compared to their non-depressed counterparts.

**Please note that we will also examine all-cause mortality rates and length of stay for those heart failure patients with depression compared to those without depression from the community surveillance data. These data will be analyzed separately.

Variables: Depressive symptom subscale scores from the Maastricht Questionnaire at Visit 2; age, center, race/ethnicity, educational level, prevalent heart failure, incident heart failure, rehospitalization for HF, length of stay, frequency of outpatient visits (from CMS data), alcohol intake, cigarette smoking, systolic BP, diastolic BP, diabetes mellitus, all-cause mortality.

As in our prior ARIC analysis of depressive symptoms and incident HF, Visit 2 participants with diabetes mellitus, hypertension, and a history of MI or HF will be excluded from the proposed analysis.

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

b. If Yes, is the author aware that the file ICTDER03 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
8.a. Will the DNA data be used in this manuscript?  ____ Yes  ___x__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 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
   ___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)?

ARIC MS# 1276. Williams JE, Rose KM, Loehr L, Mosley T, Couper DJ. Depressive symptoms increase the risk for incident hospitalized heart failure among healthy men and women: Prospective evidence from the Atherosclerosis Risk (ARIC) in Communities Study. Poster presentation at the scientific session of the American Heart Association Council on CVD Epidemiology and Prevention, March 2011.


11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  ____ Yes  ___x_ 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/aric/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.

References