ARIC Manuscript Proposal #2528

PC Reviewed: 4/14/15  Status: A  Priority: 2
SC Reviewed: _______  Status: _____  Priority: ____

1.a. Full Title: Prognostic Value of Heart Failure Self-Report in the Community: The ARIC study

b. Abbreviated Title (Length 26 characters):
HF Self-Report in ARIC

2. Writing Group:
Writing group members: Amil M Shah, Brian Claggett, Scott D. Solomon, Lisa Wruck, Dalane Kitzman, Kunihiro Matsushita, Patty Chang, Laura Loehr, Anna Kucharska-Newton, Sally Stearns, Christie Ballantyne, Gerardo Heiss; Others welcome.

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

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ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).

Name:
Address:

Phone:  Fax:
E-mail:

3. Timeline:
Analysis will begin once this manuscript proposal is approved. Anticipate manuscript completion in approximately 3 months following proposal approval, as the majority of the analysis has been completed and previously presented to the ARIC Heart Failure Committee and Steering Committee in the course of work on MP#1921 (“Frequency and Correlates of Heart Failure Stages in the Community”).

4. Rationale:
Heart failure (HF) is a major public health problem, affecting 5.7 million Americans with >550,000 new cases per year.\textsuperscript{1} The identification of heart failure can be challenging in epidemiological studies, despite the presence of several validated criteria,\textsuperscript{2,3} and recent guidelines have advocated the use of the serum biomarker NT-proBNP to help assess the likelihood of HF when the diagnosis is in uncertain.\textsuperscript{4} HF diagnosis is particularly difficult among persons without a previous hospitalization for HF decompensation, an understudied and poorly characterized group that is increasingly recognized as an important component of the HF population. Several epidemiologic studies collect information regarding self-report of HF diagnosis from participants, which may provide useful information regarding the burden of non-hospitalized HF. However, limited data exists regarding (1) the frequency and consistency of such self-report, and more importantly, (2) the relevance of such self-report for subsequent incident hospitalized heart failure or mortality. A better understanding of the prognostic relevance of HF self-report for relevant cardiovascular outcomes may provide insight into ways to utilize this information to characterize outpatient HF in epidemiologic studies. This, in turn, may form an important foundation and reference for further studies in ARIC characterizing HF generally, and outpatient HF in particular.

5. Main Hypothesis/Study Questions:

We hypothesize that, among persons without a prior HF hospitalization or known physician diagnosis, HF self-report will be associated with a heightened risk of HF hospitalization or death, and that participants who consistently report HF on serial questioning will be at further heightened risk compared to those who are inconsistent. Furthermore, we hypothesize that, among participants self-reporting HF, data on consistency of self-report and ambulatory NT-proBNP level will allow for identification of a sub-set of participants at very low risk of incident HF hospitalization or death, who are unlikely to have the clinical syndrome of HF.

Specifically, we aim to use data on HF self report and self report of HF treatment collected on ARIC participants through the end of 2004 to:

2. Characterize the consistency of HF self-report on serial assessments between 1987 through 2004 and determine the prognostic importance of consistency of HF self-report.
3. Determine whether a greater number of HF indicators (HF self report, HF treatment self-report, consistency of HF self-report, and an ambulatory measure of NT-proBNP) is associated with a higher risk of subsequent adjudicated HF or mortality.

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).

Study design:
This will be a time to event analysis based on data collected in ARIC through 2004 and subsequent follow-up for mortality and adjudicated HF hospitalization.

**Inclusion/exclusion criteria:**
The sample population will consistent of ARIC participants alive at the end of 2004.

**Key variables of interest:**
1. HF self-report assessed at Visits 3 and 4 and on AFU forms G-K and L-M
2. HF treatment self-report assessed at Visits 1-4 and on AFU forms L-M
3. ARIC adjudicated HF hospitalizations from 2005 onward
4. All-cause mortality from 2005 onward
5. NT-proBNP at Visit 4
6. Clinical covariates (assessed at visit 4 and updated by AFU through 2004 where applicable): age, gender, race/ethnicity, height, weight, blood pressure, heart rate, history of hypertension, diabetes, dyslipidemia, coronary artery disease, prior MI or revascularization procedure, prior stroke or TIA, atrial fibrillation, chronic kidney disease, use of loop diuretics, high sensitivity troponin T, creatinine, eGFR

**Data analysis:**
The sample population will consistent of ARIC participants alive at the end of 2004. The study population will be divided into the following categories: (1) prior HF self-report without a hospitalization with ICD code 428 in any position prior to January 1, 2005 or a physician confirmation of HF diagnosis by Physician Survey Form prior to January 1, 2005; (2) ICD code 428 in any position prior to January 1, 2005 or a physician confirmation of HF diagnosis by Physician Survey Form prior to January 1, 2005; and (3) no prior HF self-report, ICD code 428, or physician confirmation by Physician Survey Form prior to January 1, 2005. Demographics and clinical covariates will be compared between groups. Key outcomes for this analysis will be: (1) incident adjudicated HF post-2004; (2) all-cause mortality post-2004; and (3) the composite of adjudicated HF or all-cause mortality post-2004. To address the first aim, the presence of any prior self report of HF will be associated with the risk of these outcomes using Cox proportional hazards models. Univariate analysis will be performed, in addition to multivariable analysis adjusting for demographic and clinical characteristics differing between groups. Similar analysis will be performed with HF treatment self-report.

To address the second aim, we will employ data from serial responses regarding HF at Visits 3 and 4 and on AFU forms through 2004. We will quantify the number of times participants were asked about HF and, among those who self reported HF, the number of times they responded yes. Consistency will be characterized as the number of ‘yes’ responses after the first ‘yes’ response divided by the total number of times the participant was asked after the first ‘yes’ response. Consistency will have values ranging from 0 to 1. Participants self-reporting HF will be divided into 3 groups based on consistency value: consistency=0 versus consistency >0 and <1, versus consistency =1. Demographics and clinical covariates will be compared between groups and the association of this consistency classification with the composite of adjudicated HF and all cause mortality, and the components individually, will be assessed relative to those not self-reporting HF and those with prior ICD 428 hospitalization. Univariate and multivariable Cox proportional hazards models will be used as described above.
For the third aim, participants will be classified based on the number of heart failure indicators (HF self report, HF treatment self-report, consistent HF self-report, and Visit 4 NT-proBNP>125 pg/ml) present, with categories ranging from 0-4. The prevalence of each category will be described, along with incidence rates by category of each of the outcomes of interest. Univariate and multivariable Cox proportional hazards models will be used to assess the association of category (with category 0 as referent) for the composite of adjudicated HF and all cause mortality, and the components individually.

**Anticipated methodologic limitations:**
Clinical covariates are not available coincident with the beginning of follow-up (Jan 1, 2005), which may introduce variability in adjusted models. Gold-standard measures for HF diagnosis, and physician assessment of HF diagnosis, are not available in the large majority of participants – a limitation in the ARIC data that partially motivates this analysis. Although we may be able to identify subgroups among the participants self-reporting HF who demonstrate either low event rates similar to those without HF self-report, or high event rates similar to those with a prior ICD 428 hospitalization, we cannot exclude and definitively establish the presence of HF based on the available data.

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
(This file ICTDER03 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 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](http://www.cscc.unc.edu/ARIC/search.php)

_____ 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)?

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.csc.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


