ARIC Manuscript Proposal #1282

PC Reviewed: _8_/21_/07   Status: __A__   Priority: _2___
SC Reviewed: _____   Status: _____   Priority: ____

1. a. **Full Title:** Outpatient Surveillance of Heart Failure

    b. **Abbreviated Title (Length 26 characters): Outpatient Surveillance of HF**

2. **Writing Group:** Heiss G, Anthony J, Rosamond W, Irving S, ARIC Executive Committee

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

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3. **Timeline**:

Analysis to begin on August 2007 data retrieval as well as on AFU versions G through K (through latest contact year of version K).

4. **Rationale**:

Most of the extant information on the frequency of occurrence of heart failure (HF) and its temporal trends is based on HF associated with hospitalization or death attributed to HF. Although it has been reported that between 50 and 74% of HF cases are eventually hospitalized (Roger, 2004), estimation of the population burden of HF and of its temporal trends is constrained by an incomplete assessment of the pool of HF in the community, i.e., one that is asymptomatic/ undiagnosed, or is managed in the outpatient setting.

Although criteria of known validity are available to classify HF in the outpatient setting (Fonseca, 2004), little empirical information is available on the feasibility of quantifying HF in an outpatient surveillance setting, on the repeatability of simple questionnaire instruments and on the validity of event classification in that context. In fact, very little information has been published on the degree to which outpatient medical records contain diagnostic information that permits a standardized classification of HF. Published reports based on outpatient databases have relied on physician diagnoses and codes containing HF-related items. (Maru, 2005). Because individuals with HF identified in general practice frequently manifest several morbid conditions such as hypertension,

diabetes, obesity and a history of coronary heart disease, some added complexity in the classification of HF in the outpatient setting can be expected.

It is the goal of this proposal to examine the operational feasibility, reproducibility, validity and predictive value of the simple and inexpensive approaches currently used in the ARIC study to quantify the prevalence of HF managed in the outpatient setting. This proposal combines quality analyses of the data collected during ARIC cohort follow-up, the development of derived variables for study wide use, and the estimation of instrument performance characteristics and of associations and that are generalizable and thus of wider scientific interest.

5.   Main Study Questions:

Estimate the reproducibility of self reported HF and the validity and predictive value of individual phone interview questionnaire items that assess self reported HF symptoms, signs and treatment for HF vs. (a) reports by a medical provider and (b) hospitalization discharge codes that include HF.

Address the feasibility of a simple, validated HF classification criterion based on self reported HF signs and symptoms, supplemented by a physician questionnaire.

Estimate the association of self-reported symptoms and signs attributable to HF and of physician-diagnosed HF over the course of the ARIC cohort follow-up with (a) hospitalization that lists HF ICD-9-CM screening codes, (b) with physician reported HF diagnosis / treatment for HF and (c) with (outpatient) HF that meets the Gothenburg criteria.

Describe the frequency of occurrence of reproducible and valid indicators of HF and their population correlates.

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).

Data base

Questionnaire Items from various versions of the AFU interview

The ARIC Annual Follow-Up (AFU) phone interviews are one source of case identification of HF in the cohort. Self reported physician diagnoses of HF have been recorded staring in 1998 with version G of the AFU. The question asked of the cohort members reads: "Has a doctor ever said you had heart failure or congestive heart failure ?"

Version L of the AFU questionnaire (09/14/06) was expanded to identify the medical practitioners who during the previous 3 years reportedly told the ARIC cohort member that she/he had heart failure or congestive heart failure, and asked for the participant's authorization to request corroborating information from the practitioners. Participants were also asked whether they had been hospitalized for heart failure (identifying the hospital and the date). Other questions incorporated into version L of the AFU assessed symptoms and signs attributable to HF, inquiries about physician diagnosed HF using different medical terms, and questions based on the cardiac and pulmonary criteria of the Gothenburg classification schema of HF.

Use of version L of the ARIC annual follow-up (AFU) form began in the fall of 2006. We propose to begin the descriptive analyses for this proposal based on the forms in the central database at the Coordinating Center as of May, 2007 retrieval. The Physician Heart Failure (PHF) form is used

when triggered by responses to AFUL items 8.f, 9.f, or 10.f. Because some field centers delayed mailing the PHF the database for the proposed analyses will be updated based on the August retrieval of forms in the central database at the Coordinating Center.

Variables for Quality Analyses

AFU version L Qx items 6 through 20.a, and 46 through 48.t. Define variable names based on item numbers, response categories and missing values based on skip patterns.

Completeness of the AFU interview items and skip pattern-adjusted frequencies of response by questionnaire item, field center and interviewer, as well as centers combined, to be defined for:
- AFU Qx items 6 through 20.a
- AFU Qx items 46 through 48.t

Variables from Cohort Surveillance

Retrieve hospital discharge codes and medication recorded on the HRA for all cohort participants.

ICD-9-CM code	Heart failure screening codes used in ARIC Surveillance
398.91*	Rheumatic heart disease
402.01	Hypertensive heart disease-malignant with congestive heart failure
402.11	Hypertensive heart disease-benign with congestive heart failure
402.91	Unspecified hypertensive heart disease with congestive heart failure
404.00*	Hypertensive heart disease and renal failure –malignant
404.01*	Hypertensive heart disease and renal failure –malignant with congestive HF
404.03*	Hypertensive heart disease and renal failure – malignant with CHF and renal failure
404.10*	Hypertensive heart disease and renal failure –benign
404.11*	Hypertensive heart disease and renal failure –benign with congestive heart failure
404.13*	Hypertensive heart disease and renal failure – benign with CHF and renal failure
404.90*	Hypertensive heart disease and renal failure – unspecified
404.91*	Hypertensive heart disease and renal failure –unspecified with congestive heart failure
404.93*	Hypertensive heart disease and renal failure – unspecified with CHF and renal failure
415.0*	Acute cor pulmonale
416.9*	Chronic pulmonary heart disease, unspecified
425.4*	Other primary cardiomyopathies
428.x	Congestive heart failure
518.4	Acute edema of lung, unspecified
786.0*	Dyspnea and respiratory abnormalities

Derivation of the Gothenburg Criteria for use on AFU version L   (Draft)

The Gothenburg Score can take a value of 3, 2, 1, 0, or missing. Three factors; cardio, pulmonary, and heart failure therapy make up the Gothenburg score (see descriptions below). AFUGOTH__ takes a non-zero value only if CARDIAC has a value of 1. AFUGOTH__ can then take a value of 2 or 3 based on PULMONARY and (HF)THERAY.

Gothenburg Score	CARDIAC	PULMONARY	THERAPY
3	1	1	1
2	1	1	0 or Miss
	1	0 or Miss	1
1	1	0 or Miss	0 or Miss
0	0	N/A	N/A
Miss	Miss	N/A	N/A

Gothenburg Criteria based on data elements from AFU and PHF

Classification	Criteria	Points	AFU (L) or PHF (A) Data Elements	Data element
Gothenburg Criteria Algorithm (pts): **Grade 0** (absent) if all 3 scores are 0. **Grade 1** (latent) if cardiac score > 0 and pulmonary and therapy score = 0. **Grade 2** (manifest heart failure) if cardiac score > and either pulmonary or therapy score > 0. **Grade 3** if cardiac score > 0 and both pulmonary and therapy score > 0. **Grade 4** if the person died in heart failure.	Cardiac score **:			
	Coronary heart disease present in past	1	PHF question 3 and AFU(L) 11.a	(PHF): Has pt ever had previous MI? Has pt ever had other CHD? (AFU): Has a doctor ever said that you had a heart attack?
	Coronary heart disease present within last year	2	--	--
	angina pectoris present in the past	1	PHF question 3 or AFU(L) Question 11.b	(PHF): Has pt ever had angina pectoris? (AFU): Has a doctor ever said that you had angina, angina pectoris or chest pain due to heart disease?
	angina pectoris present within last year	2	--	--
	swollen legs at end of day	1	AFU(L) question 13.a	Do you often have swelling in your feet or ankles at the end of the day?
	Dyspnoea at night	1	AFU(L) 19.a	Are there times when you wake up at night because of difficulty breathing?
	pulmonary rales	1	PHF question 3	Has pt ever had pulmonary rales on a PE?
	atrial fibrillation on ECG	1	PHF question 3 or AFU(L) question 12	(PHF): Has pt ever had atrial fibrillation on ECG? (AFU): Has a doctor ever said that you had an irregular heart beat called atrial fibrillation, or atrial fibrillation on a heart scan or ECG tracing?
	Pulmonary score:			
	History of chronic bronchitis	1	AFU(L) question 18.a	Has a doctor ever told you that you had chronic lung disease, such as bronchitis, or emphysema?
	history of chronic bronchitis within last year	2	AFU(L) question 18.b	Were you told by the physician that you had chronic lung disease since we last contacted you on mm/dd/yyyy?
	history of asthma	1	AFU(L) 20	Has a doctor ever said you had asthma?
	history of asthma within last year	2	AFU(L) 20.a	Did the doctor say that you have asthma since we last contacted you on mm/dd/yyyy?
	history of coughing, phlegm or wheezing	1	AFU(L) 19.g	Do you usually have some cough or wheezing?
	presence of rhonchi at PE	1	PHF question 3	Has pt ever had rhonchi on a PE?
	Therapy score§			
	History of digitalis administration	1	PHF question 5	Was this pt prescribed digitalis in the past year?
	history of diuretic administration	1	PHF question 5	Was this pt prescribed diuretics in the past year?

§ Therapy score to be expanded to include medications currently used for HF in outpatient setting

Heart Failure Medications

Heart failure medications (HFMEDS) is a combination of (HF) THERAPY defined based on digoxin and diuretics per the original definition of the Gothenburg criteria and a derived variable that takes on a value of 1 if any of the medications listed below are reported on the PHF.

Look-up table for medications used to treat heart failure	
Drug	Code
Angiotensin converting enzyme (ACE) inhibitors	
Captopril	
Enalapril	
Fosinopril	
Lisinopril	
Quinapril	
Ramipril	
Trandolapril	
Beta-blockers	
Bisoprolol	
Carvedilol	
Metoprolol succinate	
Digoxin	
Digoxin	
Angiotensin receptor blockers	
Candesartan	
Valsartan	
Aldosterone blockers	
Eplerenone	
Spironolactone	

Plan of Analysis

I. Systematic Quality Analysis of AFUL Question Items
    A. Code question items 6 through 20A and 46 through 48t of AFUL form to reflect responses and skip pattern.
        1. Variable names will reflect the AFU form and the question number.
        2. Labels will reflect AFUL Question Item.

    B. Identify extreme, unusual observations, by center and interviewer.

    C. Categorize and identify trends in missing and misplaced data
        1. Categories include: missing (.) , missing skipped (.s), missing unknown (.u), missing should skip (.k)
        2. Assess the distribution of missing data by center and interviewer

    D. Compute simple descriptive statistics
        1. Report results stratified by field center and combined

II. Quality Analysis of PHF Question Items
    A. As above, address data completeness (forms expected according to AFUL responses vs. PHF forms received; completion of the data items on the form, by center (but not by interviewer).

III. Repeatability and Validity of self-reported HF
    A. Reproducibility of self-reported HF
        1. Having ever been told by a physician to have HF (AFU versions G through L) AFUL item 8 ("In a previous ARIC phone call in **[< year >]**, you indicated that you had been diagnosed with heart failure or congestive heart failure. Do you recall that you had such a diagnosis of heart failure?")

    B. Self-reported HF vs. Hospitalization for HF
        1. Determine the concordance of self-reported HF vs. hospital discharge codes for HF
            a. Link previous AFU forms with HF items (Versions G – K)
                i. Create a derived variable that indicates self-reported HF and the dates of such reports
            b. Compare self-reported HF variable to indications from all available HRA forms
                i. Create a derived variable to indicate HF-related hospitalization by scanning HRA form for ICD-9 codes that indicate HF in ARIC surveillance
                ii. Create a derived variable to indicate the number of hospitalizations with a 428 discharge code
            c. Assess the concordance between self-reported HF and HF hospitalized events (Cohen's Kappa)
                i. Present the raw number of concordance and discordance (2 x 2 table)
                ii. Examine agreement (e.g. Cohen's Kappa)

    C. Self-reported vs Physician-diagnosed HF
        1. Determine the validity of self-reported HF by comparing it to MD-Diagnosed HF
            a. Assess the relationship (agreement/disagreement) between AFUL Question Items 8, 9, or 10 with PHF Question 1.
            b. Estimate agreement, sensitivity and specificity of self-report vs. PHF question 1 as gold standard

    D. Quality analysis of other variables
        1. Assess the relationship between specific PHF question items and their corresponding AFUL question items to estimate concordance between self reported Gothenburg criteria items on AFUL vs. the corresponding items reported by the provider of medical care on the PHF form. E.g., AFUL11A vs. PHF3, AFUL11B vs. PHF3, AFUL12 vs. PHF3
        2. Estimate the concordance of HF medication use reported during the AFU interview vs. that reported by the provider of medical care on the PHF
            a. Compare responses to AFUL question items 46 through 48t (medication) with responses from PHF question item 5.
                i. Analysis will be restricted to those that have both an AFUL and PHF questionnaire on file.
                ii. Medications will be included from the categories identified in the PHF. (Listed in Medications Table)
                iii. Statistically examine agreement

    IV. Estimation of out-patient HF via Gothenburg criteria

A. Construct an out-patient "Gothenburg" derived variable using PHF and AFUL question items
   1. Reflect on data quality analysis of AFUL and PHF.
      a. Examine benefits/limitations of Gothenburg criteria constructed in this manner.
      b. Availability of participant and physician-reported data to to fulfill Gothenburg criteria.
      c. Analysis will be restricted to observations that have both an AFUL and PHF questionnaire on file.
   2. Components of the derived variable based on the 3 criteria elements for the Gothenburg Score:
      a. Cardiac score
      b. Pulmonary score
      c. Therapy score
         i. Extended to include medications that are typically prescribed in HF treatment (taken from PHF categories)

B. Burden of out-patient (OP) HF via derived variable
   1. Estimation of OP HF prevalence
      a. Comparison of derived OP HF vs self-reported HF
      b. Comparison of derived OP HF vs MD-diagnosed HF
      c. Comparison of derived OP HF vs hospitalized events

I) References

Fonseca C, Oliveira AG, Mota T, Matias F, Morais H, Costa C, Ceia F. Evaluation of the performance and concordance of clinical questionnaires for the diagnosis of heart failure in primary care. *Eur J Heart Fail.* 2004;6(6):813-820, 821-812.

Maru S, Koch GG, Stender M, Clark D, Gibowski L, Petri H, White AD, Simpson RJ Jr. Antidiabetic drugs and heart failure risk in patients with type 2 diabetes in the U.K. primary care setting. *Diabetes Care* 2005;28:20-6.

Roger VI, Weston S, Redfield MM, et al. Trends in heart failure incidence and survival in a community-based population. *JAMA* 2004;292:344-50.

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

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
___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)?**

   a. **None based on annual follow-up interview data**

   b. **Ms. Proposals that consider hospitalized HF and/or its case fatality:**

   Ms #1160 Life Course Socioeconomic Exposures and Heart Failure in the Atherosclerosis Risk in Communities (ARIC) Study (Roberts)

   Ms# 617 Evaluation of international classification of diseases codes to identify hospitalized heart attack patients with acute congestive heart failure: the Atherosclerosis Risk in Communities Study (Goff)

   Ms# 927 Heart failure incidence and survival: 13 year follow up of the ARIC cohort (Rosamond)

   Ms# 855 Retinal microvascular abnormalities and congestive heart failure (Wong)

   Ms# 922 Alcohol consumption and risk of congestive heart failure (Henderson, Rosamond)

   Ms# 1118 Kidney function as a risk factor for heart failure hospitalization: the ARIC Study (Kottgen)

   Ms# 1182 Diet and the risk of congestive heart failure in the Atherosclerosis Risk in Communities Study (Nettleton)

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 . . . N.A.**

   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.**
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