1.a. Full Title: Patterns of healthcare utilization preceding an initial heart failure hospitalization. The Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): HF signs and symptoms

2. Writing Group:
   Writing group members: Lloyd Chambless, Gerardo Heiss, Patricia Chang, Darren DeWalt, Sunil Agarwal, Miguel Quibrera, Jackie Wright, Norrina Allen, Eyal Shahar, Alain Bertoni, Ricky Camplain, others welcome

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

First author: Anna Kucharska-Newton
Address: University of North Carolina at Chapel Hill
         Bank of America Center
         137 E. Franklin St., Suite 306
         Chapel Hill, NC, USA 27514

Phone: 919-966-4596       Fax: 919-966-9800
E-mail: anna_newton@unc.edu

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: Gerardo Heiss
Address: University of North Carolina at Chapel Hill
         Bank of America Center
         137 E. Franklin St., Suite 306
         Chapel Hill, NC, USA 27514

Phone: 919-962-3253       Fax: 919-966-9800
E-mail: gerardo_heiss@unc.edu
3. **Timeline:** Analysis to begin upon approval. Complete the manuscript within eight months of approval by ARIC. This proposal is submitted in conjunction with the following manuscript proposals: Kucharska-Newton et al. “Patterns of healthcare utilization following an initial diagnosis of heart failure. The Atherosclerosis Risk in Communities (ARIC) Study” and Heiss G. et al., “Linked Measures of Outpatient and Inpatient Heart Failure Burden – The ARIC Study “

4. **Rationale:**
Although heart failure is a common clinical condition, its diagnosis is not straightforward. For majority of heart failure (HF) patients, the first heart failure-related hospitalization represents a significant exacerbation of signs and symptoms. That first hospitalization can follow extended care in the outpatient setting, which may, but does not have to, include an overt diagnosis of HF, it may be corollary to multiple Emergency Department visits or observation stays, or it may be the very first clinical manifestation of HF. Patients seen in the outpatient setting may present with signs and symptoms of HF inconsistently over an extended period of time before a frank diagnosis of HF is made. Furthermore, physicians are reluctant to provide a diagnosis of heart failure without confirmatory tests and procedures. Information on how frequently and for how long HF-related signs and symptoms, such as dyspnea, fatigue, and edema [1] occur prior to a frank inpatient or outpatient diagnosis of heart failure, is very sparse[2].

A comprehensive awareness of the longitudinal patterns of healthcare utilization leading to the first HF hospitalization can have significant implications for improvements in quality of care for HF and prevention of adverse outcomes and is critical to the evaluation of the burden of heart failure, most significantly the outpatient burden of HF.

We propose to describe patterns of health care utilization preceding the initial heart failure hospitalization using CMS Medicare data available for all fee-for-service Medicare-eligible residents of the four ARIC Study geographic areas for the years 2003-2012.

Estimates of the frequency of healthcare encounters preceding the first HF hospitalization will be informative for the estimation of the burden of outpatient HF in the ARIC Study communities and in relation to the estimates of HF hospitalizations derived from the National Inpatient Sample (NIS) survey which are included in the accompanying manuscript proposal: Heiss G. et al., “Linked Measures of Outpatient and Inpatient Heart Failure Burden – The ARIC Study “

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

In describing patterns of healthcare utilization prior to the first HF diagnosis we specifically aim to:

1) Estimate monthly rates and temporal sequence for the use of ICD-9 codes denoting signs and symptoms of heart failure in outpatient health care encounters occurring within 3 years prior to the first HF hospitalization.
2) Describe monthly rates and temporal sequence of outpatient HF encounters occurring within 3 years prior to the first heart failure hospitalization.

3) Describe frequency and temporal sequence of heart failure-related Emergency Department visits and observation stays occurring within three years prior to the first heart failure hospitalization.

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 population:

Analyses will be conducted using CMS Medicare data available for the ARIC Study geographic areas and limited to fee-for-service encounters by selecting Medicare beneficiaries with continuous fee-for-service enrollment during the entire observation period (2003-2012). Medicare enrollment information will be obtained from the Medicare Denominator file. We will use the Medicare Provider Analysis and Review (MedPAR) file to identify hospitalized events and Emergency Department visits which resulted in a hospitalization. Ambulatory care encounters, observation stays, and Emergency Department visits which did not result in a hospitalization will be identified using the Carrier and Outpatient files as described below.

Outpatient claims representing outpatient healthcare encounters will be identified from the Carrier (Part B) files using the following Evaluation and Management (E&M) codes:

<table>
<thead>
<tr>
<th>E&amp;M code</th>
<th>Code explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>99201 - 99205</td>
<td>New office visit</td>
</tr>
<tr>
<td>99211 - 99215</td>
<td>Established office visit</td>
</tr>
<tr>
<td>99241 - 99245</td>
<td>Consultation</td>
</tr>
<tr>
<td>99385 - 99387</td>
<td>New preventive medicine visit</td>
</tr>
<tr>
<td>99395 - 99397</td>
<td>Established preventive medicine visit</td>
</tr>
<tr>
<td>99441 - 99444</td>
<td>Telephone and online physician services</td>
</tr>
</tbody>
</table>

Additionally, outpatient events occurring in Federally Qualified Health Centers will be identified from annual Outpatient files using Revenue Center codes 521 and 522.

Observation stays will be identified from the Outpatient file using Healthcare Common Procedure Coding System (HCPCS) codes. Observation HCPCS codes differ by year, we will therefore create annual algorithms for the retrieval of claims for observation stays.

Event identification:

Heart failure-related events occurring during the years 2003-2012 will be identified using ICD-9 code 428.xx. For hospitalized HF events, we will differentiate between ICD-9 code 428.xx in first position versus ICD-9 code 428.xx in an effort to identify primary heart failure diagnoses. The position of the ICD-9 code in the outpatient setting is not associated with diagnostic priorities.
In an effort to identify HF-related events which are coded according to signs and symptoms at presentation rather than as frank HF events, we will examine patterns of ICD-9 codes for outpatient services provided during three years prior to the first HF hospitalization. Our focus will be on ICD-9 codes for acute lung edema (ICD-9: 518.4), dyspnea (ICD-9: 786.0x) and fatigue (ICD-9: 780.79), however we will want to document the distribution of all ICD-9 codes for outpatient services by year, demographics, and physician specialty.

In providing a description of the planned analyses we are proposing a three year look-back period. This time frame is based on data in the literature which suggest that signs and symptoms of heart failure can be present at more than 2 years prior to a HF diagnosis.

We will consider a diagnosis of heart failure as present if the Medicare beneficiary has had a hospitalization for heart failure. A first inpatient HF diagnosis will be defined as the earliest HF hospitalization with no HF hospitalizations in the preceding 12 months. In providing a description of the planned analyses we are assuming that a 12 month look-back period will be sufficient to ascertain lack of prior HF-related hospitalizations and will use that convention throughout this proposal. During the analyses, we will however allow the observed distribution of time elapsed between consecutive HF hospitalizations to determine the optimal look-back period.

The encrypted beneficiary ID will be used to link claims across years of observation, creating a staggered-entry cohort of Medicare beneficiaries with a HF diagnosis. Follow-up of this “synthetic” cohort is possible only if the CMS Medicare data for the ARIC communities include the initial claim and all subsequent claims through death or the end of follow-up (December 31, 2012), whichever comes first, for all eligible (fee-for-service) Medicare beneficiaries who have lived at any time during the observation period (2003-2012) in the geographically defined ARIC communities.

Methods:

We will understand the term “patterns of healthcare utilization” to identify patterns of HF-specific inpatient and outpatient encounters including rates and time intervals between consecutive encounters. We will estimate monthly rates of outpatient visits, Emergency Department visits, and observation stays occurring within three years prior to the first HF hospitalization.

All analyses will be conducted in strata of race, gender, age, and ARIC study center. Age, estimated as age at the time of the first HF diagnosis, will be categorized as follows: 65-74, 75-84, and 85 plus years of age.

Additionally analyses will be stratified by physician specialty at the time of the outpatient visits (primary care vs. specialty care). Information concerning physician specialty will be obtained from the UPIN and NPI physician identifiers available from the CMS Medicare Carrier file.

Study size:
Most of the proposed analyses will be descriptive, therefore a formal assessment of study power is not provided here. Following is an estimate of the study size.

Estimates of study size for analyses based on the CMS Medicare data for the ARIC communities are based on Census 2000 estimates and extrapolated to all years of observation (2004-2011; the year 2003 is not considered an observation year as it provides a one year “look-back” period). We estimate that for the year 2004, 102,600 of the residents of the ARIC study communities will have been 65 years or older. We will assume an overall 40% participation in Medicare Advantage plans across all four study centers, leading to an estimate of 61,560 fee-for-service Medicare beneficiaries. Trends analyses performed by the ARIC Study Coordinating Center provide a conservative estimate of the annual incidence of hospitalized heart failure events at 10.4 per 1000. On the basis of that estimate we project an annual incidence of hospitalized heart failure among fee-for-service Medicare beneficiaries in the ARIC study communities at 640 events. We therefore, estimate that 5,120 first-ever hospitalized HF diagnoses will have occurred in the ARIC communities in the years 2004 through 2011.

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 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 ICTDER 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

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.cscce.cscce.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 MP1657 “Enumerating the community burden of heart failure”
ARIC MP1966 “Estimated burden of acute decompensated heart failure hospitalization in the United States: Applying model from the ARIC study to National Databases”

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

11. b. If yes, is the proposal
    _x_  A. primarily the result of an ancillary study (list number* AS 2013.07)
    ____  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/

12a. 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.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is your responsibility to upload manuscripts to PUBMED Central whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

References: