ARIC Manuscript Proposal #2097

PC Reviewed: 3/12/13          Status: A          Priority: 2
SC Reviewed: __________       Status: _____       Priority: ____

1.a. Full Title:
Healthcare utilization among atrial fibrillation patients

   b. Abbreviated Title (Length 26 characters):
Healthcare utilization and atrial fibrillation

2. Writing Group:
   Writing group members: Alvaro Alonso, Pamela Lutsey, Alanna Chamberlain, Laura Ross Loehr, Sally Clark Stearns, Lin Chen, Sue Duval, Anna Kucharska-Newton and Lisa Wruck

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

First author: Lindsay Smith
Address: West Bank Office Building
         1300 South Second Street, Suite 300
         Minneapolis, MN 55454
         Phone: 612-624-5238       Fax: 612-624-0315
         E-mail: smith4430@umn.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: Alvaro Alonso
   Address: West Bank Office Building
            1300 South Second Street, Suite 300
            Minneapolis, MN 55454
            Phone: 612-626-8597       Fax: 612-624-0315
            E-mail: alonso@umn.edu

3. Timeline: This proposal is part of a dissertation thesis and work will begin in early 2013 and should be completed by the fall of 2013.
4. **Rationale:**

Atrial fibrillation (AF) is a major cause of morbidity, including stroke,\(^1\) heart failure (HF)\(^3\)\(^4\) and acute myocardial infarction (AMI)\(^5\)\(^6\) as well as mortality.\(^7\) As such, healthcare utilization among AF patients is significant from both an economic and clinical perspective. Among elderly Medicare beneficiaries, the net incremental cost in 2004 dollars among those with AF was $14,199 per person in the first year following AF diagnosis.\(^8\) In the most recent annual national data, there were 467,000 hospitalizations with AF as the primary diagnosis.\(^9\) In addition to hospitalizations, outpatient or physician burden is also high with five million physician office visits, 276,000 emergency department visits and 234,000 hospital outpatient visits attributed to AF in the US in 2001.\(^10\)

Administrative claims data from the MarketScan Commercial and Medicare Supplemental research databases indicate that, compared to age- and sex- matched beneficiaries without AF, those with AF had twice as many hospitalizations during the 12-month period following initial AF diagnosis; furthermore, 21.3% of beneficiaries with AF had a CV hospitalization, which was four times greater than the 5.4% of beneficiaries without AF.\(^11\) Among Olmsted County, MN, residents diagnosed with AF between 1980 and 2000, the primary reasons for first hospitalization following AF diagnosis were AF related (26.4%), HF (21.7%), coronary or peripheral arterial causes (21.6%) and thromboembolic events (10.5%).\(^12\)

In addition to the economic and clinical burden of AF, disparities in access to and quality of healthcare between whites and African Americans as well as between men and women also exist. In the REasons for Geographic And Racial Differences in Stroke (REGARDS) Study, a national population-based longitudinal study, the odds of African Americans knowing they had AF were one third compared to whites (95% confidence interval [CI]: 0.20 – 0.52).\(^13\) There are also disparities in the access to healthcare between men and women.

Studies of healthcare utilization based exclusively on claims data have limited ability to adjust for confounders and have rarely focused on race or sex disparities. Therefore, we propose to use CMS Medicare claims data linked with the ARIC cohort data to assess the impact of AF on healthcare utilization and explore race and sex differences in healthcare utilization taking advantage of the rich information on cardiovascular risk factors available in cohort participants.

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

For phase one, we hypothesize that AF patients will have greater healthcare utilization compared to age-, sex-, race- and field center-matched non-AF patients. We hypothesize that increased healthcare utilization is not completely mediated through comorbidities.

For phase two, we hypothesize that, among AF patients, overall healthcare utilization is higher among men compared to women and among whites compared to African Americans. Additionally, we hypothesize that inpatient encounters and physician or outpatient encounters are more common among whites compared to African Americans while ED encounters are more frequent among African Americans.
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).

For both phases of the analysis, Atherosclerosis Risk in Communities (ARIC) cohort participants enrolled in fee-for-service (FFS) Medicare will be eligible for inclusion. Participants must be enrolled in both Parts A and B of FFS Medicare because Medicare Advantage (managed care) plans are not required to submit claims for beneficiaries, so claims data are incomplete for those enrolled in only Part A or risk-based managed care plans. Since we are interested in healthcare utilization following incident AF diagnosis, as well as long-term utilization, participants must be enrolled continuously in FFS Medicare for at least one year without an AF diagnosis. Centers for Medicare and Medicaid Services (CMS) administrative data on inpatient and outpatient services were first made available for research on January 1, 1991; therefore, the earliest date of incident AF will be January 1, 1992.

Definition of atrial fibrillation

AF will be defined as a diagnosis of AF on a single inpatient claim or two outpatient or physician claims between 7 and 365 days apart (in any position on the claim: international classification of disease, ninth revision, (ICD-9) code 427.3, 427.31 or 427.32; tenth revision (ICD-10) code I48). A minimum of two outpatient or physician claims at least 7 days apart will be required to reduce the likelihood of including rule-out diagnoses and to improve the algorithm specificity. The incidence date of AF will be defined as the discharge date for an inpatient claim or the claim-through date of the second qualifying outpatient or physician claim, whichever occurs earlier.

For phase one, a one-to-one matching scheme will be utilized; at the time of an AF diagnosis, one ARIC participant without AF at that time will be matched to the AF case based on age (within two years), sex, race and field center.

For phase two, analyses will be restricted to ARIC participants with incident AF diagnosis between January 1, 1992 and December 31, 2009.

Definition of healthcare utilization

Healthcare utilization will be ascertained from Medicare claims data. Healthcare utilization will be classified based on the encounter as an inpatient visit, outpatient or physician visit or ED visit. Additionally, for phase two, each encounter will be classified based on the primary ICD diagnosis as AF-related, other CV-related excluding AF, and non-CV-related. An AF-related medical encounter will be defined as described above. A CV-related medical encounter will be defined as a primary ICD-9 diagnosis code of 390-459 or a primary ICD-10 diagnosis code of I00-I99, excluding AF-related diagnosis codes.

Assessment of potential confounders

During the baseline study exam as well as follow up study exams standardized methods were used to collect data on the following factors: age, race, sex, educational achievement, cigarette smoking, ethanol consumption, height, weight, blood pressure, antihypertensive medication use, diabetes mellitus, total cholesterol, low-density

lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, previous myocardial infarction, heart failure and prior coronary heart disease. A Cornell voltage >28 mm in men or >22 mm in women on ECG was considered evidence of left ventricular hypertrophy. Data from study exams will be used to define potential confounders in adjusted analyses.

**Statistical analysis**

In phase one, characteristics of study participants will be stratified by AF status. Demographic, behavioral and clinical characteristics will be updated using data from ARIC cohort exams to reflect closest values preceding AF diagnosis or matching. A descriptive analysis of healthcare utilization stratified by AF status will be performed. Additionally, the average number of encounters, based on classification as an inpatient visit, outpatient or physician visit or ED visit, as well as the count and percent of participants utilizing healthcare at least once in each setting, will be presented in addition to age-, sex- and race-adjusted rates for each type of healthcare utilization from a Poisson regression model. The association between AF and healthcare utilization, measured by the number of encounters, will be assessed with a Poisson regression model adjusted for potential confounders. Data for potential confounders will be based on the nearest preceding value from ARIC cohort exams at the time of AF diagnosis or matching. The Poisson regression models will include an offset to account for differential exposure times. Assuming an association is present, a mediation analysis will be performed to determine the degree to which overall healthcare utilization is mediated through CV comorbidities (primary ICD-9 diagnosis code of 390-459 or primary ICD-10 diagnosis code of I00-I50, excluding AF-related diagnosis codes). The following models will be used: in model one the outcome of interest will be healthcare utilization, the exposure will be AF status and all confounding factors will be included (Model 1: Healthcare utilization = AF status + confounder₁ + ... + confounderₙ); in model two the outcome of interest will be CV comorbidities, the exposure will be AF status and all confounding factors will be included (Model 2: CV comorbidities = AF status + confounder₁ + ... + confounderₙ); in model three the outcome of interest will be healthcare utilization, both AF status and CV comorbidities as well as all confounding factors will be included (Model 3: Healthcare utilization = AF status + CV comorbidities + confounder₁ + ... + confounderₙ).

In phase two, restricted to AF patients, each medical encounter will be classified as AF-, CV- or non-CV-related based on the primary ICD code. The number of encounters per person as well as the number of patients with at least one encounter in addition to age-, sex- and race-adjusted rates will be calculated, first by sex and then in a separate analysis by race. Additionally, Cox proportional hazards regression will be used to identify factors associated with initial healthcare utilization following AF diagnosis stratified by sex and then by race; participants will be censored at time of disenrollment in FFS Medicare or death. Potential confounders, based on closest data preceding AF diagnosis, will be ascertained from ARIC cohort data and will include detailed demographic, behavioral and clinical factors. It is expected that AF patients with more comorbidities will utilize more healthcare resources; therefore, a stratified analysis by category of CHADS₂ (congestive heart failure, hypertension, age, diabetes, stroke [doubled]) score will be performed by sex and then by race. CHADS₂ was developed
from independent predictors of stroke risk in patients with nonvalvular AF\textsuperscript{17} and has been validated in a large cohort study\textsuperscript{18} and in clinical trials.\textsuperscript{19} All analyses will be performed with SAS (version 9.2, SAS Institute, Inc, Cary, NC).

**Sample size and power calculations**

There were approximately 1,900 cases of incident AF diagnosed from baseline through December 31, 2009, in ARIC. Some AF cases will be missed as a result of Medicare Advantage enrollment. To be conservative, it is estimated that there will be a total of 1,000 incident AF cases. Based on a recent analysis of administrative data from the MarketScan Commercial and Medicare Supplemental research databases, in the year following initial AF diagnosis, twice as many beneficiaries with AF (37.5\%) were hospitalized at least once compared to age- and sex-matched beneficiaries without AF (17.5\%).\textsuperscript{11} Assuming there will be 1,000 incident AF cases, matched to 1,000 non-AF cases, with 10, 15 and 20 percent of non-AF cases utilizing healthcare in years one, two and three, respectively, and an \(\alpha\) level of 0.05, the power to detect a hazard ratio of 1.5 for the hypothesis that AF patients will have greater healthcare utilization compared to age-, sex-, race- and field center-matched non-AF patients, is 0.88 for one year of follow-up after AF diagnosis and 0.99 for three years of follow-up. Additionally, based on a prior analysis, ARIC manuscript number 1997, we know there were more than 1,000 incident AF cases ascertained based on FFS Medicare data and there is very good concordance with ARIC cohort follow up data and FFS Medicare data.

**Limitations**

Several limitations of this study should be considered. ARIC participants who enrolled in Medicare Advantage do not have claims available for research and therefore will be excluded from the analysis; the percent of ARIC participants enrolled in Medicare Advantage changed during the study follow up and varied by study community. The results of this study will be less generalizable but still applicable to the FFS CMS population. Additionally, because the CMS data is linked to ARIC cohort data, detailed demographic, behavioral and clinical data will be available to assess differences in FFS and Medicare Advantage enrollees. Incident cases of AF will be identified and included in the sample, but there is no available information to further classify AF as paroxysmal, persistent or permanent. However, this study affords the opportunity to analyze healthcare utilization based on claims data augmented with detailed demographic, behavioral and clinical factors ascertained from ARIC cohort data; making this a study uniquely positioned to analyze factors related to healthcare utilization.

7.a. Will the data be used for non-CVD analysis in this manuscript?  \(\square\) Yes \(\square\) 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? \(\square\) Yes \(\square\) 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  _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)?

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/

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