

## ARIC Manuscript Proposal #2043

PC Reviewed: 12/11/12  
SC Reviewed: \_\_\_\_\_

Status: A  
Status: \_\_\_\_\_

Priority: 2  
Priority: \_\_\_\_\_

**1.a. Full Title:** Predictors of Medication Adherence in Cardiovascular Disease: Understanding the Complex Relationships Between Disease Burden, Health Literacy, and Socioeconomic Status

**b. Abbreviated Title (Length 26 characters):** Medication Adherence in Cardiovascular Disease

**2. Writing Group:** Jo Ellen Rodgers, Carla Sueta, Anna Kucharska-Newton, Sally Stearns, Patricia Chang, Mark Holmes, Hanyu Ni

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

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**3. Timeline:** Analyses to start following receipt of ARIC Visit 5 data. It is anticipated that results of this study will be presented at the American Heart Association November 2013 with manuscript submission following shortly thereafter.

#### **4. Rationale:**

Half of the 3.2 billion annual prescriptions dispensed in the United States are not taken as prescribed. (Osterberg NEJM 2005) Poor adherence to efficacious cardiovascular-related medications has led to considerable morbidity, mortality, avoidable health care costs, and deleterious consequences for workforce productivity and overall public health. (Sabate WHO 2003)

Nonadherence to medications is common for patients with cardiovascular diseases. Reports of nonadherence vary tremendously depending on the population studied, the specific medications assessed as well as the specific cardiovascular disease evaluated. (Jackevicius Circulation 2008, Vrijens BMJ 2008, Bramley J Manag Care Pharm 2006, Gislason Circulation 2007, Granger Lancet 2005) Importantly, the majority of studies focus on a single cardiovascular disease in isolation and rarely account for multiple diseases or disease severity. Heart failure is commonly accompanied by one or more additional cardiovascular diseases. (Heywood J Card Fail 2004) Study methodology (eg, electronically compiled dosing histories, claims data, clinician estimate) could also explain variable study results whereas use of a validated questionnaire to assess medication adherence would be preferred. Furthermore, a variety of additional factors may explain the large variability in estimates of adherence including characteristics of the populations studied (eg, health literacy, socioeconomic status).

Inadequate health literacy among patients and family caregivers is prevalent and directly related to medication nonadherence. (Evangelista J Cardiac Fail 2010) Many individuals with heart disease have low health literacy and poor health literacy has been associated with poor outcomes. (Murray Am J Geriatri Pharmacother 2004, Rockwell Heart Lung 2001, Morrow Gerontologist 2006, Hope Am J Health Syst Pharm 2004) Unfortunately differences in knowledge, self-efficacy and self-care do not fully explain the relationship between low literacy and worse quality of life, and thus, additional research in this area is necessary. (Macabasco-O'Connell and DeWalt 2011) There are several other potential explanations for poor adherence and outcomes: 1) an increase in disease burden or a combination of select diseases can add to the complexity of a medication regimen which may hinder medication adherence, 2) more complicated medication regimens may increase the risk for adverse effects which may further hinder medication adherence, and 3) select disease states (eg, cerebrovascular disease) may limit a patient's ability to comply with a more involved medication regimen.

Of interest in the proposed study is gaining a better insight into the predictors of medication adherence including the complex relationship between disease burden, health literacy and socioeconomic status. We propose to use data from the ARIC Visit 5, specifically survey results on medication adherence, health literacy, and socioeconomic status as well as available data on disease burden.

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

1. Hypothesis 1: Medication adherence will decrease with increasing number of comorbid cardiovascular disease and related risk factors (prevalent coronary heart

disease (CHD), cerebrovascular disease, heart failure, hypertension, hyperlipidemia, diabetes).

2. Hypothesis 2: Low socioeconomic status and low health literacy will be associated with reduced medication adherence.
3. Hypothesis 3: Low socioeconomic status and low health literacy will further explain the relationship between comorbid cardiovascular disease and related risk factors and medication adherence.

**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:

All ARIC cohort study participants with Visit 5 ascertainment of the following cardiovascular disease conditions: hyperlipidemia, diabetes, prevalent CHD, prevalent cerebrovascular disease or prevalent heart failure. We will use algorithms established by the ARIC Study Coordinating Center to identify participants with prevalent diseases.

Outcomes:

The primary outcome will be medication adherence. Medication adherence is assessed in the ARIC cohort as part of the Visit 5 Medication Survey questionnaire using the validated Morisky Scale Questionnaire. With the Morisky Scale, which consists of four questions, study participants receive one point for each positive response to a question. Zero points will represent high adherence, 1-2 points intermediate adherence, and 3-4 points low adherence.

We will use both education and income as an objective measure of socioeconomic status (SES). In addition, the MacArthur Scales of Subjective Social Status will be utilized as a subjective measure of SES. The two scales developed to capture the common sense of social status across the SES indicators. In an easy pictorial format, the scales present "social ladders" and asks individuals to place an "X" on the rung on which they feel they stand relative to traditional SES indicators (SES ladder) and relative to standing in one's community (community ladder).

Health literacy will be assessed using the Wide Range Achievement Test (WRAT-3) which measures literacy in three categories: reading recognition, spelling, and arithmetic computation. Standard scores for each of the three subtests range from < 45 to > 155, with higher scores indicating higher achievement. The following classification for standard scores are: 130 & up = Very Superior, 120-129 = Superior, 110-119 = High Average, 90-109 = Average, 80-89 = Low Average, 70-79 = Borderline, and 69 & below = Deficient.

Analytical methods:

In this analysis, medication adherence will be modeled as a categorical variable. We will use logistic regression analyses to examine cross-sectional association of prevalent cardiovascular disease and cardiovascular disease risk factors, established at ARIC Visit 5, with medication adherence. We will adjust all analyses for demographic factors (age, gender, and race) as well as the measures of socio-economic status and literacy.

Disease burden will be ascertained by using the Charlson Comorbidity Index, a validated clinical comorbidity algorithm. Consistent with previous studies, a high burden of comorbidity will be defined as a sum of  $\geq 2$  on the Charlson Index Scale whereas a low burden will be defined as a total of 0 to 1 point. (Charlson ME et al. *J Chronic Dis* 1987; 40:373–383)

Individual socioeconomic status will be determined using Visit 5 data on household income, Visit 1 (baseline) data on attained education, as well as the MacArthur scales of relative socioeconomic status obtained as part of the Visit 5 exam.

Health literacy was evaluated at the time of the Visit 5 examination using the WRAT questionnaire.

**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.csc.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)?**

Additional proposal by same investigator: Adherence and Outcomes: Mortality, Hospitalization, and Health-related Quality of Life

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

**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.csc.unc.edu/aric/index.php>, under Publications, Policies & Forms. [http://publicaccess.nih.gov/submit\\_process\\_journals.htm](http://publicaccess.nih.gov/submit_process_journals.htm) shows you which journals automatically upload articles to Pubmed central.

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