1.a. Full Title: Re-hospitalizations with heart failure: cumulative incidence rates over long term follow up and its prediction

b. Abbreviated Title (Length 26 characters)
HF re-hospitalizations – trajectory and predictors

2. Writing Group:
Writing group members (alphabetical):
Sunil K. Agarwal
Kathryn A. Carson
Patricia P. Chang
Josef Coresh
Randi Foraker
Xiaoxi Liu
Wayne Rosamond
Stuart Russell
Lisa Wruck
Others welcome

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

First author: Sunil K. Agarwal
Address: Phone: 919-265-4727
E-mail: sunilagarwal@jhmi.edu

Senior author: Patricia Chang
Phone: 919-843-5214
E-mail: patricia_chang@unc.edu

3. Timeline:
Analysis to begin immediately. Plan for manuscript within 6 months

4. Rationale:
Heart Failure (HF) remains one of the most common hospital discharge diagnosis in the US. With more than 700,000 new diagnoses and an increasing estimated prevalence
of more than 5.7 million it poses a significant economic burden amounting to a yearly
total cost of $39.2 billion in 2009.[1] 3, 4

HF is characterized by multiple relapses requiring hospitalizations with an expected
one year re-hospitalizations > 50%, and one year mortality rates >30%. Several strategies
have been suggested and are under progress to reduce re-hospitalization rates.[5]

The natural history and trajectory of HF readmissions is not well understood. In this
context this study could add to our understanding the trajectories of hospital admissions
with HF admissions with HF and as primary or secondary diagnosis with the exception of
Medicare sample. Current literature with focus on administrative database such as
Medicare has several gaps including narrow demographics and clinical attributes (HF
with reduced EF only) of patients, short term follow up, lack of event validation, clinical
trial settings etc. Further there is limited information on whether ADHF is the cause vs.
HF is comorbidity.

Further, risk stratification tools focusing on socio-demographics, clinical factors at
admission and discharge, as well as to identify patients at high risk of re-hospitalization
with ADHF or death prior to re-hospitalization can help in reducing hospitalization by
focusing resources on such higher risk strata. This is important in light of recent
Medicare’s program to reduce readmissions for HF though decreasing reimbursement for
excess admissions (proportion of expected admissions by risk score) for any readmissions
occurring with 30 days of discharge from the hospital or its sub-entity. There is a dearth
of risk scores looking at HF re-hospitalizations with no validated risk score model to
predict risk of readmission with ADHF [4]. Of the six studies that examined HF
readmission predictors only one looked at HF specific re-admissions [5]. These studies
have multiple limitations including specific patient population (stage IV HF), clinical trial
participants, single hospital, non-adjudicated HF event, all cause readmission or
mortality, limited variables –mostly biomedical only, lack of internal validation and poor
attempt to test discrimination of the risk score using modern metrics.

In brief, this study will look at trajectory of HF admissions using the richness of
information collected in ARIC cohort and ARIC HF surveillance for ARIC cohort. Also,
it will examine the predictors of frequent readmissions while attempting to derive a risk
stratification tool.

5. Main Hypothesis/Study Questions:
   a. Long term re-admissions rates - Cohort
      i. Estimate all-cause and HF specific hospital re-admission rates after an
         index HF hospitalization (ICD code at any position) since participants’
         enrollment in the ARIC cohort using death as both censoring and
         competing event.
      ii. Estimate the readmission rates for a HF patient after a documented
         admission with ADHF following year 2005 with understandable
         limitation of generalizability to elderly HF patients only.
b. Predictors of readmissions - Cohort
   i. Derive a risk prediction equation by identifying predictors of hospital readmission using data from the information from the ARIC field center visit closest to the HF admission and socio-demographic data from the baseline visit.

   ii. Using those with incident HF by visit 4, explore predictors of re-hospitalization and derive a risk prediction model for HF as well as all cause readmissions while using death as competing event.

c. Predictors of readmission: HF surveillance – Washington county only
   Derive a risk prediction equation after identifying predictors of re-hospitalization for Washington county ADHF hospitalizations (data is available for this sub-sample at current time) all and ADHF specific hospitalizations while using death as both censoring and competing event.

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 methodological limitations or challenges if present).

   Study design: Repeated outcome models with death as either censoring or competitive event.

   Outcomes:
   a) Repeat all cause hospitalizations
   b) Repeat HF specific re-hospitalization
      a. ICD code 428.x at any position – this has higher validity than at primary position
      b. Validated ADHF per ARIC adjudication panel

   Study cohorts (inclusion criteria): There are several cohorts for inclusion in the analyses
   a). ARIC cohort participants with HF at baseline
   b). ARIC cohort participants with incident HF pre-2005
   c). ARIC cohort participants with validated ADHF since 2005
   d). ARIC HF surveillance from Washington county

   Variables: predictors will depend on the cohort used but will include among following For study cohorts a). through c). as above Socio-demographics, field center, any characteristics of hospital admitted to, health insurance, individual income data, self reported quality of life, anthropometrics, physical activity level, health data including
comorbidities, cognitive function, ECG variables, serum markers including inflammatory/hemostatic markers, spirometry measured lung function etc.

For cohort d), above data from abstraction including further information about hospital characteristics (teaching vs. non-teaching), ejection fraction, BNP, creatinine, sodium level, medications at discharge etc. will be used.

We will extrapolate life course # of days of hospital stay and cost of these hospitalizations using cost and median LOS from respective year of National Inpatient Survey database.

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

8.a. Will the DNA data be used in this manuscript?  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.  Yes

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)?

Ms. # 1778: Predictors of 30-day readmission among heart failure patients (examines predictor for all-cause 30 day readmissions using cohort data)

Ms. # 1829: Trends in hospitalizations for myocardial infarction and heart failure: A comparison of national, community, and cohort data (1987-2008) – (this compares secular trend in projected # of hospitalizations through years using a combination of ARIC cohort, surveillance, and national hospital discharge database.)

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

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.


