1.a. Full Title:
Predictors of discharge to outpatient rehabilitation and physical therapy services among hospitalized heart failure patients: The Atherosclerosis Risk in Communities Study.

b. Abbreviated Title (Length 26 characters):
Heart Failure Rehab Referral

2. Writing Group:
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3. **Timeline:**

Submission to journal 1.5 years after approval of proposal.

4. **Rationale:**

Heart failure (HF) presents a significant public health concern that is expected to increase in prevalence and burden. From 2009 to 2012 reports of the National Health and Nutrition Examination Survey (NHANES), it is estimated that 5.7 million Americans aged ≥20 years had HF, and projections for 2030 estimate a 46% increase of prevalent HF resulting in more than 8 million affected adults aged ≥18 years (Heidenreich et al., 2013). Based on the Atherosclerosis Risk in Communities Study (ARIC), the 30-day, 1-year, and 5-year case fatality rate after HF hospitalization was 10.4%, 22%, and 42.3% from 1987 to 2002, respectively, and among the elderly, an increase in HF incidence and improved HF survival since the 1970’s has contributed to increased HF prevalence (Loehr et al., 2008; Barker et al., 2006). Other studies have corroborated the improvement in survival post-HF diagnosis between 1979 and 2000, and the 5-year case fatality risk has been estimated to be around 50% (Roger et al., 2004; National Center for Health Statistics). However, patients who experience nonfatal HF hospitalizations often are at risk of readmission; among US Medicare fee-for-service enrollees, 27% of patients were readmitted for HF incidents within 30 days of discharge (Jencks et al., 2009). Aside from costs attributed to treating comorbid conditions, the 2030 projected cost estimates of cardiac care for HF patients are expected to increase three-fold to $160 billion (Heidenreich et al., 2013).

Cardiac rehabilitation (CR) is a multidisciplinary approach to secondary HF prevention that includes exercise training and provides counseling and education to patients; the goal is to improve quality of living, increase exercise capacity, and reduce the risk of mortality and hospitalizations (Lavie, et al., 2013; Lavie, Milani, 2011). In a randomized control trial comparing an individualized, multidisciplinary 12-week CR program coordinated by a specialist HF nurse to standard follow-up care by a cardiologist or general practitioner, the intervention group was less likely to be rehospitalized for any cause 12 months after their HF-related hospitalization (44 vs. 69%, p = 0.01; Davidson et al., 2010). Quality of life scores showed greater improvement from baseline relative to the control group, and twelve-month survival was elevated relative to the control group (93 vs. 79%, p = 0.03; OR=3.85, 95% CI 1.03-14.42, p = 0.0042). In a separate analysis of U.S. Medicare beneficiaries receiving coronary diagnoses or procedures, patients with prevalent congestive HF receiving CR (identified using Current Procedure Terminology codes 93797 and 93798) within one year following discharge had a 15.7% lower absolute 5-year all-cause mortality rate compared to matched patients who did not engage in CR (30.9% vs. 46.6%; Suaya et al., 2009). End-stage HF patients may also benefit from physical therapy with regard to managing ventricular assist devices (Wells, 2013).

The latest guidelines for HF management recommend exercise training and CR as class I and class IIa recommendations, and the effectiveness of CR has prompted the Centers for Medicare & Medicaid to expand coverage for CR to patients with stable, chronic HF (Yancey et al., 2013; Kelly et al., 2016). However, these services remain underutilized. Based on 2005 to 2014 HF hospitalizations captured in the Get With The Guidelines-Heart Failure (GWTG-HF) registry,
only 10.4% of discharged HF patients received a CR referral at discharge (Golwala et al., 2015). The objective of this examination is to assess factors that predict the discharge of hospitalized HF patients to outpatient rehabilitation or home physical therapy services. This study will be important for understanding what type of patients receive discharge to such services and, more importantly, what type of patients do not. By better understanding predictors of rehabilitation referral, the results of this analysis will help to improve patient care by addressing why these life-preserving services may be underutilized in the HF hospitalization population.

5. Main Hypothesis/Study Questions:
Study Question: Among the hospitalized HF patient population, what are major predictors of discharge to outpatient rehabilitation or home physical therapy services?

Based on the prior work by Golwala et al., (2015) in the American Heart Association Get With The Guidelines-Heart Failure (GWTG-HF) Registry, we hypothesize that hospitalized HF patients discharged to outpatient rehabilitation or home physical therapy service will be younger, male, and have a lower burden of co-morbidities; there may also be regional differences in recommendation such that southern catchment areas (Forsyth County, North Carolina; Jackson, Mississippi) will be more predictive of referral than other sites (Washington County, Maryland; Minneapolis, Minnesota). We hypothesize that health insurance status will also be a significant predictor of discharge to outpatient services. We also hypothesize that referrals may differ by specific HF hospitalization diagnosis (e.g., HF with concurrent hypertensive disease and/or chronic kidney disease; acute cor pulmonale; chronic pulmonary heart disease; other cardiomyopathies; lung edema; dyspnea and respiratory abnormalities). With regard to HF ejection fraction (EF), we hypothesize that reduced EF cases will be referred to services more than preserved EF patients as has been suggested by Golwala et al. We will additionally evaluate various cut-offs of EF (>=55%, 40-54%, <40%, <30% etc.). We have no prior hypotheses regarding other potential predictors captured from medical chart abstraction; however, they will all be explored for inclusion in the final prediction model.

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).

The present study will utilize the surveillance component of the Atherosclerosis Risk in Communities (ARIC) Study. We will assess all individuals with abstracted and adjudicated medical charts associated with HF hospitalizations from 2010 until the latest available data, because this is when our outcome of interest was first abstracted. We will exclude individuals who were transferred to another hospital or who died during hospitalization as these patients were not eligible to be discharged alive to the community.

The primary outcome will be whether or not the patient received an appointment at discharge for outpatient rehabilitation services and/or home physical therapy as abstracted by ARIC (yes or no/not reported).
Potential predictors that will be explored include sex, race, health insurance status, and Medicaid insurance status. For selection in the final prediction model, we will also assess all variables collected from the HF hospital record abstraction which includes questions on advanced directives, screening for decompensation, history of HF, medical history (including general, respiratory, cardiovascular, gastrointestinal/endocrine, renal, and neurology), a physical exam assessing vital signs and symptoms, diagnostic tests, biochemical analyses, interventions, medications (prior or during hospitalization, and at discharge), and complications. We will code a summary score of comorbidities based on abstracted data and the Charlson Comorbidity score; most of the Charlson components are captured except for dementia, peptic ulcer disease, liver disease, hemiplegia, cancer and AIDS.

After applying standard ARIC surveillance sampling weights, we will use multivariable logistic regression with backward elimination to identify independent predictors significantly associated with discharge associated with a referral to outpatient rehabilitation services and/or home physical therapy controlling for all other predictors in the model. After backward elimination, only predictors with a p value of 0.05 or less will be retained as significant, independent predictors. We will use bootstrapping for internal validation of the model. Bootstrapping samples with replacement will allow an estimation of the consistency of predictor statistical significance across bootstrapped samples. Variables statistically significant in at least 50% of the bootstrapped datasets will be selected in the final model. We will report odds ratios, model-based predicted probabilities, and the area under the receiver operating characteristics (ROC) curve for the initial, fully inclusive predictive model and for the final model only including statistically significant predictors from at least 50% of bootstrapped samples.

Using 2010-2012 hospitalized HF cases captured in ARIC surveillance, we present logistic regression power calculations for three primary predictors (sex, center, age, and EF) that we will investigate in association with our outcome of interest. Calculations were estimated using the Demidenko algorithms published by Dartmouth (http://www.dartmouth.edu/~eugened/power-samplesize.php; Demidenko, 2007; Demidenko, 2008).
Table 1. Power calculations for sex, center, age, and ejection fraction (EF) odds ratios (ORs) based on ARIC community hospitalized heart failure patients from 2010-2012.

<table>
<thead>
<tr>
<th>1.) Predictor = Sex (male vs. female)</th>
<th>ORs:</th>
<th>Power:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.40</td>
<td>0.560</td>
<td></td>
</tr>
<tr>
<td>1.50</td>
<td>0.732</td>
<td></td>
</tr>
<tr>
<td>1.55</td>
<td>0.801</td>
<td></td>
</tr>
<tr>
<td>1.60</td>
<td>0.857</td>
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</tr>
<tr>
<td>1.70</td>
<td>0.932</td>
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</table>

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<thead>
<tr>
<th>2.) Predictor = Center (southern vs. non-southern)</th>
<th>ORs:</th>
<th>Power:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.40</td>
<td>0.585</td>
<td></td>
</tr>
<tr>
<td>1.50</td>
<td>0.752</td>
<td></td>
</tr>
<tr>
<td>1.55</td>
<td>0.817</td>
<td></td>
</tr>
<tr>
<td>1.60</td>
<td>0.869</td>
<td></td>
</tr>
<tr>
<td>1.70</td>
<td>0.938</td>
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</table>

<table>
<thead>
<tr>
<th>3.) Predictor = Age (&lt;65 years vs. ≥65 years)</th>
<th>ORs:</th>
<th>Power:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.45</td>
<td>0.565</td>
<td></td>
</tr>
<tr>
<td>1.55</td>
<td>0.724</td>
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<tr>
<td>1.60</td>
<td>0.790</td>
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<tr>
<td>1.65</td>
<td>0.845</td>
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</tr>
<tr>
<td>1.75</td>
<td>0.923</td>
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</table>

<table>
<thead>
<tr>
<th>4.) Predictor = EF (&lt;50% vs. ≥50%)</th>
<th>ORs:</th>
<th>Power:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.95</td>
<td>0.715</td>
<td></td>
</tr>
<tr>
<td>2.05</td>
<td>0.783</td>
<td></td>
</tr>
<tr>
<td>2.10</td>
<td>0.812</td>
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</tr>
<tr>
<td>2.15</td>
<td>0.838</td>
<td></td>
</tr>
<tr>
<td>2.25</td>
<td>0.882</td>
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</table>

Our calculations are based on a sample size of 4,675 hospitalized HF patients. We have adequate power (≥0.800) to detect an odds ratio (OR) of 1.55 for males vs. females at a significance level of 0.05. This is an acceptable minimal detectable OR considering the previous work by Golwala et al. (2015). From a sample of 105,619 HF patients, Golwala et al. reported that 57% of patients referred to CR services were male; this translates to an OR of 1.76 for men vs. women. We have enough power to detect a weaker association. For center location, we have adequate power to detect an OR of 1.55 for southern centers vs. non-southern centers. This minimal detectable OR may be acceptable despite our inability to assess patients in other US regions. Golwala et al. reported that 15% of patients with CR referrals were from southern and western centers while 6% were from midwestern and northeastern centers; this translates to an OR of 2.76 southern and western vs. midwestern and northeastern centers. For age, we have adequate power to detect an OR between 1.60 and 1.65 for younger (<65 years) vs. older (≥65 years) patients. Unfortunately, we are unable to compare this minimal detectable OR to the work by Golwala et al., because Golwala et al. only reported mean ages: 69±15 years vs. 72±14 years for patients referred for CR vs. patients not referred, respectively. Our EF power analysis is based on a sample size of 2,201 hospitalized HF patients, and we have adequate power to detect an OR of 2.10 for reduced EF (<50%) vs. preserved EF (≥50%). Golwala et al. did not report measures of contrast between reduced EF and preserved EF patients for comparison; however, they reported a slightly higher rate among reduced EF patients and a significant p for trend for each subgroup of HF patients and for HF patients overall. It should be noted that these power calculations are conservative for our analyses because we intend to include additional years of hospitalized cases. Therefore, we will have better power in our final analyses.

Potential limitations exist with regard to the validity of identified HF hospitalizations. The reviewed hospitalizations were first identified in the four ARIC communities based on discharge diagnosis codes for HF or related conditions or symptoms (e.g., HF concurrent with
malignant/benign/unspecified hypertensive heart disease and/or chronic kidney disease). Although a previous ARIC study reported on agreement between Medicare HF diagnostic codes and the ARIC study classification of acute decompensated HF and chronic stable HF (κ > 0.9 for codes in any position; κ < 0.8 for primary diagnostic codes), the full extent of ICD-9-CM codes used to identify hospitalizations for the present population has not been validated for this population of US adults (age ≥ 55 years; Kucharska-Newton et al., 2016). Furthermore, when comparing HF hospitalizations identified by diagnostic code (ICD-9-CM 428) to the ARIC classification of decompensated HF, ARIC investigators have reported high specificity (95%) but poor sensitivity (43%) for a primary HF code, and high sensitivity (95%) but low specificity (17%) for a HF code in any position (Rosamond et al., 2012). Results were similar when comparing code-identified hospitalizations to the ARIC classification of acute decompensated HF plus chronic stable HF: high specificity (97%) but low sensitivity (36%) for a primary HF code, and high sensitivity (95%) but low specificity (23%) for a HF code in any position. These validation results suggest that there may be misclassification and missed HF hospitalizations in these communities. We will attempt to explore the influence of HF misclassification by restricting the HF hospitalization dataset using the various ARIC classification criteria.

Another potential limitation stems from the abstraction process itself. Because observations were abstracted from medical charts, there may be opportunities for information bias due to abstractor error and because only a small proportion of records are reviewed by at least two abstractors; each abstractor re-abstracts two records each month. However, error from the abstraction process may be minimal considering that the medical abstractors are trained staff who are recertified annually. In a quality control sample, the inter-abstractor agreement for determining whether a medical record warranted a detailed abstraction was 99% (Rosamond et al., 2012).

This study may also be limited by the number of observations with an outpatient rehabilitation or home physical therapy discharge. From 2010 to 2012, 4,675 HF hospitalizations were abstracted with the outcome of interest, but only 119 observations were reported to have been discharged to such services. We will try to improve the validity of our predication models by incorporating new annual hospitalization files (for the years 2013 and 2014) as they are released by the ARIC coordinating center and by incorporating bootstrapping methods. Finally, although we have the capability to explore teaching versus non-teaching hospital status (e.g., through stratification and/or inclusion in prediction models), this study is otherwise limited in the assessment of physician-level characteristics; therefore, the goal of this study will be to focus on characteristics of the hospitalized patient.

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  ___ 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  ___ 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.

     ACKNOWLEDGED.

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://publicaccess.nih.gov/submit_process_journals.htm shows you which journals
     automatically upload articles to PubMed central.

     ACKNOWLEDGED.

13. Per Data Use Agreement Addendum, approved manuscripts using CMS data shall be
     submitted by the Coordinating Center to CMS for informational purposes prior to
     publication. Approved manuscripts should be sent to Pingping Wu at CC, at
     pingping_wu@unc.edu. I will be using CMS data in my manuscript ___ Yes  X ___ No
REFERENCES


Wells CL. Physical therapist management of patients with ventricular assist devices: key considerations for the acute care physical therapist. Phys Ther 2013;93:266–278.