1. **Full Title:** Calibration of Heart Failure as the Cause of Death in the ARIC Study

   **Abbreviated Title (Length 26 characters):** HF mortality

2. **Writing Group:** Anthony J, Sorlie P, Rosamond W, Thomas Thom, Massing M, Golden S, Heiss, G

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

**First author:** Joseph Anthony  
**Address:** University of North Carolina  
Dept. of Epidemiology  
137 E. Franklin Street, Suite 306  
Chapel Hill, NC 27514  
**Phone:** 919-966-1949  
**E-mail:** anthonyj@email.unc.edu

**Corresponding/senior author:** Gerardo Heiss  
**Address:** University of North Carolina  
Dept. of Epidemiology  
137 E. Franklin Street, Suite 400  
Chapel Hill, NC 27514  
**Phone:** 919-962-3253  
**E-mail:** gerardo_heiss@unc.edu

3. **Timeline:**  
Analysis to begin in August 2008.

4. **Rationale:**  
Heart failure (HF) is a major and escalating public health problem. Its morbidity, mortality and burden continue to increase [1, 2]. Indicators of the burden of HF are derived from hospitalization, ongoing cohort studies, and health expenditures data, but gaps exist in the literature regarding temporal trends, prevalence and incidence of HF as well as its contribution to mortality.

Data used to estimate the burden of HF mortality in the population are generally based on death certificates (DC) filed in state vital statistics offices and compiled by the Center for Disease Control and Prevention [3]. However, estimating HF mortality is complicated by the fact that the syndrome usually represents the end stage of diverse disease etiologies – typically, hypertension, coronary heart
disease, valve deformity, diabetes, or cardiomyopathy [2]. Thus, the upstream causes of HF, as opposed to the disease itself, are more likely to be reported as the underlying cause of death. This reflects death certificate instructions which specifically state: *If an organ system failure such as congestive heart failure, hepatic failure ... is listed as a cause of death, always report its etiology on the line(s) beneath it...* [4]. HF may be reported as the underlying cause when the etiology of HF cannot be determined. HF may also be mentioned on a death certificate as contributing cause. A recent editorial highlights the need to evaluate cause-of-death statistics among HF patients to improve prognosis and treatment [5]. The calibration of routinely collected information on HF mortality for use in epidemiologic surveillance of HF is one method of doing so. Additionally, information on total-mention versus HF listed as underlying cause would be informative, as well as data on the sensitivity with which death certificates ascertain prior evidence of HF in decedents.

Gold standard methods for determining the validity of mortality data include extensive reviews of medical records or autopsy studies by panels of experts, although these methods are laborious, expensive, and thus often conducted on samples of available records [6-8]. These methods have also been utilized in cohort settings [9, 10]. An alternative approach is contrasting DC information with previously collected, relevant health indicators such as hospital discharge records [11-13]. The available studies that evaluated the agreement between hospital discharge records and DC information generally report high measures of agreement (i.e. sensitivity estimates ranging between 70% and 98%) for malignancies and conditions in which diagnosis is proximal to death (e.g. lung, pancreatic, and liver cancers). However, the agreement of hospital discharge diagnosis with the DC for other chronic conditions (e.g.: kidney and cardiovascular diseases) is considerably lower, with estimates ranging from 38 to 75 percent.

The natural history of HF is such that repeat hospitalizations are frequent; almost fifty percent of incident HF hospitalization survivors are readmitted [14]. Although coding for HF across successive hospitalizations is frequent this may not be the case, whether due to diagnostic criteria [15, 16], symptomatic presentation [17], or differential diagnoses due to comorbid conditions [18]. Consequently, relying on hospital discharge records proximal to the death may be poorly sensitive. Also, a recent study among mostly Caucasians estimated that as much as sixty-four percent of HF decedents had some cardiovascular disease listed as the underlying cause of death [19].

The ARIC cohort provides the framework to extend beyond registries of hospitalizations and expand the generalizability of the current literature due to its robust follow-up, completeness of self-reported health statuses, hospital discharge diagnoses collected by surveillance, and multiethnic nature. Thus, we are able to consider natural history, estimate case fatality and address the impact on sensitivity that may be due to multiple hospitalizations. Medicare claims data add an indicator of HF to be considered in such analyses. Few studies exist that calibrate HF mortality information, although such studies are needed.

The goal of this proposal to quantify the accuracy of certification of death for HF in the ARIC cohort; to estimate the accuracy of HF case fatality determination in the ARIC cohort; and to estimate the magnitude of error in the quantification of the burden of mortality attributed to HF.

5. Main Study Questions:

   Estimate the agreement of HF death certification in the ARIC cohort with evidence of HF on hospital discharge records during the course of the cohort follow-up.

   Estimate the agreement of HF death certification in the ARIC cohort with prior indicators of HF based on self report during the course of the ARIC cohort follow-up.

   Estimate the agreement of HF death certification in the ARIC cohort with prior indicators of HF based on outpatient and inpatient Medicare claims data.
Quantify the accuracy of HF case fatality estimation in the ARIC cohort over 15 years of follow-up.

Quantify the error in one-year HF case fatality estimation in ARIC’s Community Surveillance.

Estimate the burden of HF mortality in the ARIC study communities and of HF case fatality with calibration for known sources of error.

Estimate to what degree the lapse of time between incident HF hospitalization and death and the frequency of HF hospitalizations influence the presence of HF on the DC.

Quantify the frequency of comorbid causes of death among participants that are hospitalized for HF but do not show HF on the DC.

Consider study site, demographic characteristics, comorbidity and access health care in the above estimations.

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 Size:**
Our initial analyses will be conducted on the entire ARIC cohort and will define subsets of the cohort as appropriate denominators for the different research question being addressed. As of December 2004, there are 2,534 deaths in the ARIC cohort. 816 (32%) decedents have an incident HF hospitalization.

**Dependent variable:**
- The dependent variable is the presence of an International Classification of Diseases, Ninth Revision (ICD-9), code 428 including [congestive heart failure (ICD-9 code 428.0), left heart failure (428.1), and unspecified heart failure (428.9)], 518.4 (for acute events) or ICD-10 code 150 (HF) in any position on the DC.

**Independent Variables and covariates for analysis:**
- Incident or recurrent Hospitalized HF as a binary indicator of the presence of an ICD 428 or 518.4 on any hospital discharge record.
- Self-reported HF as binary indicator reflecting a positive answer to either of the questions “Has a doctor ever said you had HF?” (from ARIC Visits 3 and 4 or AFU contact years 13 – 17) or any of the three questions about HF on AFU version L “Do you recall a HF diagnosis”, “Since we last contacted you, has a doctor said that you had HF?” or “Has a doctor ever said that your heart is weak, or does not pump as strongly as it should, or that you had fluid on the lungs?”
- The presence of a Medicare claim indicative of HF. For outpatient events, two claims will serve as a HF event, and for inpatient events, one claim will be indicative of a HF event. Medicare data is only available from 2003 through 2005; HF is observable through 2004. Thus, analyses will be restricted accordingly.
- The covariates will be age, ethnicity, sex, and study center.

**Analytic Methods**
- Percentages and kappa statistics will be used to estimate agreement. Sensitivity, specificity and positive predictive value will be calculated utilizing tabular analysis. Regression may also be utilized to estimate the odds having a DC match the various data points listed as independent variables.
Results will be organized in following general format:

<table>
<thead>
<tr>
<th></th>
<th>HF on the DC</th>
<th>No-HF on the DC</th>
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</thead>
<tbody>
<tr>
<td>HF Hospital Discharge</td>
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<tr>
<td>No-HF Hospital Discharge</td>
<td></td>
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<tr>
<td>Self-Reported HF</td>
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<tr>
<td>No-Self Reported HF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HF Medicare Claim</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No-HF Medicare Claim</td>
<td></td>
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</tbody>
</table>

I) References


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 ICTDER02 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 ICTDER02 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

b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER02 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)?

a. Ms. Proposals that consider the validation of DC data

    Ms # 956 A comparison of occupation reported on death certificate to occupation at midlife (Bidulescu)
b. **Ms. Proposals based on annual follow-up interview data**

Ms # 1282 Outpatient Surveillance of HF (Heiss)

c. **Ms. Proposals that consider hospitalized HF and/or its case fatality:**

Ms # 1376 Optimal predictors of incident hospitalized heart failure: the ARIC cohort study (Agarwal)

Ms # 1377 Relationship between pulmonary disease, lung function and incident hospitalized heart failure: The Atherosclerosis risk in communities (ARIC) study (Agarwal)

Ms #1160 Life Course Socioeconomic Exposures and Heart Failure in the Atherosclerosis Risk in Communities (ARIC) Study (Roberts)

Ms# 617 Evaluation of international classification of diseases codes to identify hospitalized heart attack patients with acute congestive heart failure: the Atherosclerosis Risk in Communities Study (Goff)

Ms# 927 Heart failure incidence and survival: 13 year follow up of the ARIC cohort (Rosamond)

Ms# 855 Retinal microvascular abnormalities and congestive heart failure (Wong)

Ms# 922 Alcohol consumption and risk of congestive heart failure (Henderson, Rosamond)

Ms# 1118 Kidney function as a risk factor for heart failure hospitalization: the ARIC Study (Kottgen)

Ms# 1182 Diet and the risk of congestive heart failure in the Atherosclerosis Risk in Communities Study (Nettleton)

d. **Ms. Proposals that consider Medicare claims data:**

Ms # 1292 Neighborhood Socioeconomic Status, Health Insurance, and Evidence-Based Pharmacologic Treatment of Myocardial Infarction: ARIC Community Surveillance (Rose)

Ms # 983 Impact of Insurance Status and Types on Inequities in Hospital Care of Acute Coronary Syndrome (Taylor)

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.cscu.unc.edu/aric/forms/](http://www.cscu.unc.edu/aric/forms/)
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.