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

_____ Yes ___**X**____ 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)?
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# 855 Retinal microvascular abnormalities and congestive heart failure (Wong)

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

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

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

ARIC Ms# 903 Lifecourse SES and systemic markers of inflammation (Pollitt)

ARIC Ms# 926 Individual and area-level lifecourse socioeconomic status and subclinical Atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) study (Carson)

ARIC Ms# 960 Individual and area-level life-course SES and decline in renal function: the Atherosclerosis Risk in Communities Study (Shoham)

ARIC Ms# 1099 SES across the life course and the metabolic syndrome (Rose)

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

11.b. If yes, is the proposal

_X_ A. primarily the result of an ancillary study (list number* __1998.02 ___)

___ 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/

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.

20) Heslop, Smith GD, Macleod J et al. The socioeconomic position of employed women, risk factors and mortality. Soc Sci Med. Aug 2001; 53(4): 477-485.

21) Claussen B, Davey Smith G, Thelle D. Impact of childhood and adulthood socioeconomic position on cause specific mortality: the Oslo Mortality Study. J Epidemiol Community Hlth. 2003; 57:40-45.

22) Smith GD, Hart C, Blane D, et al. Lifetime socioeconomic position and mortality: prospective observational study. BMJ. 1997, 314: 547-552.

23) Wamala SP, Lynch J, Kaplan GA. Women's exposure to early and later life socioeconomic disadvantage and coronary heart disease risk: the Stockholm Female Coronary Risk Study. Int J Epidemiol. 2001, 30: 275-284.

24) Franks P, Fiscella K, Beckett L, et al. Effects of patient and physician practice socioeconomic status on the health care of privately insured managed care patients. Medical Care. 2003; 41(7): 842-852.

25) Fiscella K, Franks P, Gold MR, et al. Inequality in quality: addressing socioeconomic, racial, and ethnic disparities in health care. JAMA. 2000; 283(19): 2579-84.

26) Bolton MM and BA Wilson. The Influence of Race on Heart Failure in African-American Women. Medsurg Nursing. 2005; 14(1): 8-15.

27) Wong, TY. Rosamond W., Chang PP, et al. Retinopathy and Risk of Congestive Heart Failure. JAMA. 2005; (293): 63-69.

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

8.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

6) Levy D, Larson MG, Vasan RS et al. The Progression from Hypertension to Congestive Heart Failure. JAMA. 1996; 275 (20): 1557-62.

7) Kenchaiah S, Evans JC, Levy D et al. Obesity and The Risk of Heart Failure. The New England Journal of Medicine. 2002; 347(5): 305 – 313.

8) MacIntyre K, Capewell S, Stewart S, et al. Evidence of Improving Prognosis in Heart Failure: Trends in Case Fatality in 66,547 Patients Hospitalized Between 1986 and 1995. Circulation 2000; 102: 1126 – 1131.

9) Smith GD, Hart C, Blane D, et al. Adverse socioeconomic conditions in childhood and cause specific adult mortality: prospective observational Study. BMJ. 1998; 316 (7145): 1631-5.

10) Gillum RF, Paffenbarger RSJ: Chronic disease in former college students. XVII Sociocultural mobility as a precursor of coronary heart disease and hypertension. Am J Epidemiol. 1978, 108: 289-298.

11) Robbins, GM Vaccarino V, Zhang H, et al. Socioeconomic Status and diagnosed diabetes incidence. Diabetes Res Clin Pract. 2005; 68 (3): 230-6.

12) Lawlor DA, Ebrahim S, Davey Smith G. Socioeconimc position in childhood and adulthood and insulin resistance: cross sectional survey using data from British women's heart and health study. BMJ. 2002; 325 (7368): 805.

13) Manios Y, Panagiotakos DB, Pitsavos C, et al. Implication of socio-economic status on the prevalence of overweight and obesity in Greek adults: The ATTICA Study. Health Policy. 2005; 74 (2): 224-32.

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VII) Since the cohort for this analysis consists of individuals who participated in the LC-SES survey (and thus also in Visit I of the ARIC study), selective loss-to-follow-up and also mortality may have occurred. However, at the time of the LC-SES survey ARIC personnel was able to survey 93-96% of the ARIC cohort survivors; thus, we expect the magnitude of any differential misclassification of mortality and selective loss-to-follow-up to be minimal. I will compare the characteristics at the ARIC baseline of the deceased and those lost-to-follow-up to the remainder of the cohort examined at the time of the LC-SES study to evaluate the extent of any disease misclassification or loss-to-follow-up. I may also perform a sensitivity analysis and/or correction for potential bias.

A second shortcoming of the analyses described above is the quality of the data on the heart failure outcome, since it is self-reported. I will conduct analyses of heart failure defined by hospital discharge diagnoses of HF in ARIC cohort members (restricted to those who participated in the LC-SES survey). As previously mentioned, to guard against possible selection bias, hospitalized heart failure events accrued in the full ARIC cohort prior to the LC-SES survey will be analyzed according to socio-economic status characteristics (other than life course exposures) to quantify the possible selection and/or bias.

Table 1. Method of assignment of a participant's occupational class in childhood and young and mature adulthood, utilizing an adaptation of E.O Wright class categorization schema.

Social Class	Higher Education[a]	Owns business/self-employed	Supervisory or managerial job role
Worker Class	No	No	No
Middle Class	Yes No -	No No Yes	No Yes No
Capitalist/Expert Manager Class	Yes -	No Yes	Yes Yes

[a]Higher education is some college education or more

VIII) References

1) Braunwald E. Shattuck Lecture – cardiovascular medicine at the turn of the millennium triumphs, concerns, and opportunities. New England Journal of Medicine. 1998(13):919-920.

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4) He J, Ogden LG, Bazzano LA et al. Risk Factors for Congestive Heart Failure in US Men and Women. Archives of Internal Medicine. 2001; 161.

5) Kannel WB and AJ Belanger. Epidemiology of Heart Failure. American Heart Journal. 1991; 121 (3 Pt 1): 951-7.

be the sum of the number of SES indicators that are in the lowest of each SES category (0-5). The referent group will be those with all 5 indicators in the highest categories.

2) Area-based level variable:
    a. Area-based SES: An index will be created based on census-derived measures of education, income, occupation, housing adequacy (e.g. number of people living in the household adjusted for size), and other characteristics (e.g. percentage of single parent homes) corresponding to the place of residence of the participant during the at risk period. The latter can apply to childhood (county-based), reported places of residence prior to induction into the ARIC cohort, and residence(s) over the course of the ARIC cohort follow-up. Neighborhood SES for the adult life span of the cohort members will be based on census tracts.

       In order to capture prevalent cases of HF that occurred prior to entry into the ARIC study, the risk period for the participants will begin at 45 years of age and extend through the end of the study period, the year 2003.

3) Individual-level variables:
    a. SES during childhood: It will be assessed by the parents' and/or caretakers' education and occupation during the participant's childhood from The ARIC Annual telephone follow-up (SES-AFU).
    b. SES during adulthood: Education from Visit 1, occupation from Visit 1, and family income from Visit 1 will be the indicators of adulthood SES. Social class will be a composite of the following variables from the SES-AFU: education, occupational role, and self-employment (Table 1).

IV) The covariates will be age, ethnicity, and study center. The intermediates variables will be blood pressure, antihypertensive medications, health insurance status, prior coronary heart disease, psychological conditions (i.e. depression and social support), diabetes, obesity, smoking, and alcohol. Psychological conditions will bet determined via the Maastricht Questionnaire of Vital Exhaustion, the Lubben Social Network Scale, and the Interpersonal Support Evaluation List, all of which were administered during Visit 2.

V) Participants will be excluded from the analyses if they have missing data regarding heart failure. To handle missing data from early childhood and adulthood, standard multiple imputation procedures will be utilized by combining the results of regular modeling using 5 imputed datasets where the missing data is estimated by observed data.

VI) Univariate and multivariate analysis based on a Poisson distribution will be used to estimate the incidence rates of heart failure amongst the incident cases. Hazard ratios and 95% confidence intervals will be reported. The cumulative frequency of prevalent cases of initial HF events from ages 45-80 years (in 5 year increments) will be examined via logistic regression. Prevalence odd ratios will used to quantify these associations. The lifetable method will be utilized to assess case fatality rates at 30 days 1, 2, 3, and 5 years following hospitalization from initial heart failure.

a. Is the association between the cumulative effect of individual-level SES across life course and the incidence of heart failure and case fatality following heart failure modified by area-based level SES?
b. Is the association of cumulative effect and the incidence of heart failure and case fatality in part explained by concomitant illnesses, psychological and behavioral risk factor profiles over the life course?

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).

I) The cohort for this analysis consists of individuals who participated both Visit I of the ARIC Cohort Component and in the Life Course SES (LC-SES) survey. The analyses will include HF events that occurred prior to entry into the ARIC study and HF events that occurred from 1987-2003 in African-American and Caucasian men and women. The exposure data collected by the LC-SES study is historical in nature, as is the prevalence of the outcome cumulated over the life course to the point of entry into the ARIC study. As a result, the ARIC baseline is a meaningful entry into the proposed study since information on prior events (outcomes) and prior exposure status to covariates were collected at that time.

Incidence rates and cumulative frequency will be assessed. Also, case fatality rates at 30 days and at 1, 2, and 3 years after hospitalization from the initial heart failure will be examined. [Note: We will potentially assess the case fatality rate at 5 years as well depending on whether there are enough cases to provide sufficient power for the analysis.]

II) The dependent variables are the risk of initial hospitalization for heart failure and case fatality from any cause following an initial hospitalization for heart failure. For incidence cases, these variables will be determined via surveillance of medical records and review of death certificates. Medical records with International Classification of Diseases, 9th Revision, Clinical Modification ICD-9-CM code 428 or 518.4 will be considered cases.[27] Heart failure cases will also include those with an underlying cause of death coded as heart failure on their death certificates (ICD-9-CM code 428 or ICD-10 code 150), that were not previously identified as a case via their medical records. [27] HF cases that occurred prior to baseline will be identified by using the Gothenburg criteria, which creates a score based on cardiac and pulmonary symptoms inconjunction with medicinal therapy.

III) The independent variables are:

1) Aggregate level variables:
   a. Social mobility: It is a comparison of the participants' father's working class status (manual vs. non-manual) and the participants' adulthood working class status. There will be a total of four social mobility categories: manual→manual; manual→non-manual; non-manual→manual; and non-manual→non-manual. The father's and participant's occupation will be collected from the SES-AFU.
   b. The cumulative score in childhood and adulthood: It will be compiled from caretaker's education during the participants' childhood and the participants' education, family income, occupation, and neighborhood during adulthood. It will

until it's absolutely necessary due to financial constraints[25]. Further, their time maybe constrained by obligations to their work and family[26]. In addition, individuals of lower SES may not be able to afford, and thus to comply with, their prescription medication, which could lead to worse health outcomes.

Childhood SES exposures during childhood may influence the development of risk factors that are associated with heart failure. In turn, SES measures in adulthood may influence behavioral risk factors and/or health care seeking behaviors, which may have more of an impact on the risk of heart failure. Thus, possibly the cumulative effect of individual-level SES across life course is the most indicative of the risk of heart failure than SES in childhood, SES in adulthood, or social mobility. The current literature does not address whether or how SES over the life course is associated with the risk of occurrence of heart failure. Across different age groups, the annual rates of new and recurrent events of heart failure differ for non-Blacks and Black men and women[3]. Thus, in order to detect whether our hypothesized associations apply to African-American and to Caucasian members of the ARIC cohort, we will stratify our analyses by race/ethnicity.

5. Main Hypothesis/Study Questions:

I. Are individual-level SES measures during childhood associated with the incidence of heart failure and case fatality independent of SES indicators later in life?
   a. Is the association between individual-level SES measures during childhood and the incidence of heart failure and case fatality following heart failure modified by area-based level SES?
   b. Is the association of individual-level SES measures during childhood and the incidence of heart failure and case fatality in part explained by concomitant illnesses, psychological, metabolic, and behavioral risk factor profiles?

II. Are individual-level SES measures during adulthood associated with the incidence of heart failure and case fatality independent of SES indicators earlier in life?
   a. Is the association between individual-level SES measures during adulthood and the incidence of heart failure and case fatality following heart failure modified by area-based level SES?
   b. Is the association of individual-level SES measures during adulthood and the incidence of heart failure and case fatality in part explained by concomitant illnesses, psychological, metabolic, and behavioral risk factor profiles?

III. Does social mobility from childhood to adulthood influence the incidence rate and lifetime cumulative incidence of initial hospitalized heart failure and case fatality following an initial hospitalization for heart failure?
   a. Is the association between social mobility and the incidence of heart failure and case fatality following heart failure modified by area-based level SES?
   b. Is the association of social mobility and the incidence of heart failure and case fatality in part explained by concomitant illnesses, psychological, metabolic, and behavioral risk factor profiles?

IV. Is cumulative effect of individual-level SES across life course associated with the incidence rate and lifetime cumulative incidence of initial hospitalized heart failure and case fatality following an initial hospitalization for heart failure?

between individual SES exposures and the incidence of hospitalized heart failure has rarely been assessed. Further, it appears that the relationship between cumulative effect of life-course SES measures (i.e. childhood and adulthood measures) and the incidence of heart failure have never been explored.

To our knowledge, the NHANES I Epidemiologic Follow-up Study (NHEFS) is the only study to report on the association between a SES measure and the incidence of heart failure. Heart failure was defined as any discharge diagnosis from a hospital or nursing home with an ICD-9 code of 428.0 to 428.9 or a death certificate with the underlying cause of death as ICD-9 code of 428.0 to 428.9[4]. In a cohort of 13,643 participants with 19 years of follow-up, 1,382 heart failure cases were identified in this manner. A significantly higher risk of incidence of heart failure was reported for those with low education (<HS) versus high education (≥HS). The risk was 28% higher for men and 41% higher for women, RR = 1.28 (95% CI: 1.06, 1.53) and 1.41 (95% CI: 1.13, 1.77), respectively.

A population-based cohort study in Scotland examined the effect of SES on survival after an initial diagnosis of heart failure over a 10-year period.[8] The incidence of heart failure was captured from 1986 to 1995 with a total of 66,547 patients admitted for heart failure. Deprivation was ascertained from postal codes, and a deprivation score was assigned based on neighborhood. Neighborhoods were characterized as being deprived by the proportion of unemployed residents, overcrowding, lack of access to care, and belonging to a low social class. The most deprived compared to the least deprived men were 26% times likely to not survive after heart failure within 30 days of being hospitalized [OR = 1.26 (95% CI: 1.14, 1.38)]; the odds of survival for women were 11% [OR = 1.11 (95% CI: 1.02, 1.21)]. The effect was attenuated, but remained marginally significant for both sexes when the entire length of the study, 10 years, was taken into account. The hazard rate ratio for the most deprived versus the least deprived was 1.10 (95% CI: 1.05, 1.16) for men and HR = 1.06 (95% CI: 1.02, 1.11) for women.

It is pertinent to evaluate the association between SES with the incidence of heart failure and with case fatality for several reasons. Among them, SES is demonstrably associated with the risk factors for heart failure (such as coronary heart disease,[9,10] diabetes,[11] and obesity[12,13,14]) and is plausibly an antecedent factor to an unfavorable profile of risk of heart failure. However, it is not known what epoch in one's lifetime SES would have its greatest impact on the incidence of heart failure in middle age and older adulthood. Studies have shown that early SES measures have an inverse association with the risk of CVD[15,16]. Various studies have examined the impact of social mobility from childhood to adulthood, and they have reported mixed results. Some studies have found a suggestion of an inverse relationship with CVD morbidity and mortality[17,18]. Other studies have reported that upward mobility may lead to increased risk of fatal CVD[10] and downward mobility may lead to decreased risk of CVD risk[19]. Several studies have reported that cumulative SES measures were better predictor of CVD risk factors[20], morbidity,[19,21,22,23] and mortality[19,20,21,22,23] than a single individual measure in adulthood.

Further, more educated patients are more likely to seek medical care (and have access to it), vocalize their concerns about their health at a doctor's visit, inquire about treatment and testing, ask questions about their health, and participate more in the physician-patient dialogue. Franks, et al[24] reported that patients with lower SES exposures are less likely to schedule visits to a physician, which is not surprising since people with lower income may delay going to the hospital

ARIC Manuscript Proposal # 1160r

PC Reviewed: _08__/_15__/06	**Status: __A___**	**Priority: __2__**
SC Reviewed: _08__/_17__/06	**Status: __A__**	**Priority: __2__**

1.a. Full Title: Life Course Socioeconomic Exposures and Heart Failure in the Atherosclerosis Risk in Communities (ARIC) Study

b. Abbreviated Title (Length 26 characters): Life Course SES and HF

2. Writing Group: C. Roberts, K. Rose, W. Rosamond, D. Catellier, H. Taylor, Gerardo Heiss

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

F**irst author**: Calpurnyia Roberts
Address: University of North Carolina
Dept. of Epidemiology
137 E. Franklin Street, Suite 306
Chapel Hill, NC 27514

Phone: 919-357-3108 Fax:
E-mail: calp@email.unc.edu

Corresponding/senior author (if different from first author correspondence will be sent to both the first author & the corresponding author):
Corresponding/senior author: Calpurnyia Roberts

3. Timeline:

To be completed December 2007

4. Rationale:

Heart failure is a major public health concern in the United States. It has been characterized as an epidemic by some due to its rise in morbidity, mortality, and healthcare costs over the past few decades.[1,2] In 2002, 970,000 hospital discharges were coded as due to heart failure compared to 377,000 in 1979, an increase of 157%.[3] Currently, 1 in 5 people are estimated to develop heart failure in their lifetime, and 1 in 5 are predicted to die within one year after diagnosis.[3] In 2005, $27.9 billion was spent on direct and indirect healthcare costs.[3]

Various risk factors for the incidence of heart failure have been identified in prospective studies: coronary heart disease,[4,5] diabetes[4], hypertension, [4,5,6] being overweight,[4,7] obesity,[4,7] cigarette smoking, [4] valvular heart disease,[4] and left ventricular hypertrophy[5]. By contrast, the association