THE ASSOCIATION BETWEEN SOCIOECONOMIC POSITION OVER THE LIFE-COURSE AND INCIDENT HEART FAILURE AND ITS CASE FATALITY

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ABSTRACT

Calpurnyia B. Roberts, MS: The association between socioeconomic status over the life-course and incident heart failure and its case fatality
(Under the direction of Gerardo Heiss, MD, PhD)

Background: Exposure to disadvantaged socioeconomic circumstances in specific periods over the life-course, prior to the diagnosis of heart failure in older adulthood, may increase the risk of heart failure. **Purpose:** With eighteen years of follow-up (1987-2004) in the Atherosclerosis Risk in Communities (ARIC), we investigated the impact of individual-level socioeconomic exposures from three distinct life epochs: early childhood (at age 10 years), young adulthood (at age 30 years), and older adulthood (45-64 years), individually and cumulatively, on incident heart failure (HF). Additionally, we examined the bearing of SEP in older adulthood (45-64 years of age) on case fatality in participants with incident HHF. **Methods:** Incident HF and its case fatality were ascertained via annual follow-up interviews, review of medical records, and death certificates from 1987-2002. Race-specific incidence and hazard rates and 95% confidence intervals were estimated via Cox Proportional Hazard models. Age, gender, ARIC center, and neighborhood-level SEP from each respective life epoch were adjusted for in the analyses. Traditional risk factors of incident HF and case fatality (e.g. hypertension) were treated as mediators since they occur as the result of SEP. **Results:** Age-adjusted incidence rate (per 1,000 person-years) for incident HF was higher for blacks than whites,

5.23 (95% CI: 4.32, 6.33) and 3.18 (95% CI: 2.81, 3.60), respectively. Possessing a high versus low value for the various SEP exposures across the life-course were associated with an increased risk of incident HF in blacks and whites. Overall, SEP exposures recalled from childhood were the least predictive of incident HF, and SEP exposures from young and older adulthood were among the strongest. The SEP indicators gathered in older adulthood were not significantly associated with case fatality in either blacks or whites. Health insurance was the predominant mediating risk factor in the diagnosis of HF in both blacks and whites. **Conclusions:** To curtail excess deaths due to socioeconomic inequalities affiliated with HF, more longitudinal studies in diverse populations should be implemented to confirm which life epoch(s) manifest the greatest impact on the occurrence of HF, the particular SEP measures that are the most predictive of HF, and the pathways via which SEP indicators exert their effect on HF.

To my beautiful mother and inspiration – Geraldine Tucker

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LIST OF ABBREVIATIONS

Atherosclerosis Risk in Communities Study = ARIC

Body Mass Index = BMI

Coronary Heart Disease = CHD

Heart Failure = HF

Life-Course Status, Social Context, and Cardiovascular Disease Study = LC-SES

Socioeconomic Position = SEP

United States = US

CHAPTER I. INTRODUCTION

A.Heart Failure Statistics

Heart failure (HF) is a major public health concern in the United States. It has been characterized by some as an epidemic due to its severe 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 HF compared to 377,000 in 1979, an increase of 157%.[3] Currently 1 in 5 people are estimated to develop HF in their lifetime; 1 in 5 are predicted to die within one year following hospitalization for an incident HF episode; and 1 in 2 are expected to die within five years after diagnosis.[3] In 2005, $27.9 billion was spent on direct and indirect healthcare costs.[3]

In prospective studies, coronary heart disease (CHD),[4,5] diabetes, [4] hypertension, [4-6] being overweight, [4,7] obesity, [4,7] cigarette smoking, [4] valvular heart disease, [4] and left ventricular hypertrophy[5] were identified as risk factors of heart failure. Age, [8-10] gender, [9,10] acute myocardial infarction, [10] and diabetes[10] are major health determinants of case fatality in patients with heart failure.

Coronary heart disease (CHD) is the leading risk factor for HF.[11] It attributes to 68% of HF in the United States.[11] The second leading cause of HF is idiopathic (13.20%).[11] A variety of causes (e.g. aortic stenosis, mitral regurgitation, drugs, and

alcohol) are responsible for 11.5% of HF events, and hypertension is associated with 7.5% of all heart failures.[11]

Although race/ethnicity is not identified in the literature as a HF risk factor, it is worth mentioning that black men and women have higher rates of HF than their white counterparts. According to the Heart Disease and Stroke Statistics – 2007 Update, the prevalence of HF in non-Hispanic black men and women 20 years of age or older in 2004 was 2.7% and 3.3%, respectively.[4] In non-Hispanic white men and women the prevalence of HF was 2.8% and 2.1%, respectively.[4]

B.The Physiology of Heart Failure

Heart failure, as defined by the American College of Cardiology and the American Heart Association Task Force, is "a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood".[5] There are two recognized forms of heart failure, diastolic and systolic heart failure. The prevalence of diastolic heart failure is estimated to be 20%-50%.[6] Diastolic heart failure is the presence of an elevated filling pressure in order to achieve normal end-diastolic volume due to an increased resistance to the filling of one or both of the ventricles.[7] It is often associated with hypertrophy of the left ventricle, which preserves the left ventricular ejection fraction (≥40%).[6] Approximately 60% of heart failure is classified as systolic heart failure.[6] It occurs after the heart looses contractility, which leads to a depressed left ventricular ejection fraction. [6] The loss of contractility may be due to previous damage such as a myocardial infarction. [6] The heart eventually remodels to take on a globular shape and the ventricle walls become thin. [6]

Table 1 shows the clinical profile of patients with diastolic and systolic heart failure. Patients with diastolic HF are more likely to be older and female than patients with systolic HF.[6] Patients with diastolic HF are usually hypertensive, diabetic, obese, have chronic lung disease, and are on long-term dialysis more so than patients with systolic dysfunction. There is some evidence suggesting that among African-Americans that diastolic heart failure is more prominent than systolic heart failure due to a higher prevalence of left ventricular hypertrophy[8-11] and hypertension in this population. The converse has been observed for White Americans.[8-11]

Table 1. Characteristics of patients with diastolic and systolic heart failure.

Characteristic	Diastolic Heart Failure	Systolic Heart Failure
Age	Frequently elderly	All ages, typically 50-70yr
Sex	Frequently female	More often female
Left ventricular ejection fraction	Preserved or normal, ~ ≥ 40%	Depressed ~ < 40%
Left ventricular cavity size	Usually normal, often with concentric LVH	Usually dilated
Chest radiography	Congestion with or without cardiomegaly	Congestion and cardiomegaly
Hypertension	Usually	Often
Diabetes mellitus	Usually	Often
Previous Myocardial Infarction	Occasionally	Usually
Obesity	Usually	Often
Chronic Lung Disease	Often	Not
Sleep Apnea	Often	Often
Long-term dialysis	Often	Not
Atrial fibrillation	Occasionally	Occasionally

Adopted from Jessup, M. New England Journal of Medicine 2003.(6)

C.Socioeconomic and Health Inequalities

In the United States, access to wealth confers health and consequently longevity. As of 2007, individuals in the highest income bracket in the United States (≥$82,600 for a family for four) are projected to live on average, six and half years longer than

those in the lowest bracket (<$41,300 for a family for four), and two years longer than those in the middle category.[20] Moreover, attaining a college degree is associated with living an average of 5 years longer than those with who did not finish high school.[21]

It is well understood that adverse individual-level socioeconomic exposures are inversely related to a variety of risk factors for heart failure. For instance, diabetes is twice as prevalent in adults in the lowest compared to those in the highest income; heart disease is approximately 50% greater.[21] Additionally, income, education, and occupation obtained by adulthood are highly associated with an increased risk of coronary heart disease,[22,23] and obesity.[24-26] Furthermore, social class at birth is negatively correlated with carotid intima thickness[27] and myocardial infarction.[(12] Father's occupation (manual vs. non-manual) during the participant's childhood was demonstrated to be strongly related to an elevated risk of coronary heart disease in women[29] and men.[30-32] SES exposures in adulthood have been shown to be correlated with compliance to medications and health behavior which are indicative of survival following an heart failure episode.

Socioeconomic inequities lead to poor health through several avenues. Access to health care is the largest factor stymieing Americans from seeking healthcare. It is currently estimated that 50 million Americans (15.3% of the population) are not insured. Even the type of health insurance can lead to differential outcomes. Patients with non-private insurance are more likely to receive less specialized health care than patients with higher levels of SES.[33] Time constraints and family

obligations are other obstacles that prevent individuals of lower SES from attending regular check-ups or seeking medical attention.[34]

D.Significance of research

The prevalence of heart failure is expected to rise as the baby boom population ages, and treatment for coronary heart disease continues to advance. The number of uninsured people is also expected to rise. Currently, there is a lack of studies which have ascertained the association between SES and the onset of heart failure or its case fatality. Research in this area could provide clinical and public awareness of individuals who should be targeted for early intervention to prevent the onset of heart failure, and inform future research to incorporate SES risk factors into their studies of heart failure in order to risk residual confounding.

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CHAPTER II. LITERATURE REVIEW

There is a dearth of studies which have examined the association between socioeconomic status and incident HF and/or its case fatality. Between April 1970 and June 2008, 11,427 published articles related to risk factors of heart failure (HF) were listed in Pubmed. Of these 8131 articles, thirty-six, less than 1%, were dedicated to deciphering the association between SES and HF. The majority of these studies were conducted in European white males, and relied on individual and contextual-level attained solely in adulthood.

Below, I present a review of the literature on these associations by the different types of SES measures. The first section summarizes the relation between individual-level SES exposures and incident and prevalent HF and its case fatality. The next section is a review of the literature on the relation between contextual-level SES and these health outcomes. The last section covers the studies on the association between cumulative level indicators of SES and these health outcomes.

A.Individual-level SES

1.Individual-level SES with Incident HF

To our knowledge, three studies[13-15] have presented the effect of individual-level SES indicators in adulthood on the incidence of hospitalized HF (Table 2). All of the studies used prospective-study designs, and two of the three studies were

conducted in the United States. Various socioeconomic measures were employed to evaluate exposure to SES.

The Cardiovascular Health Study reported in individuals 65 years of age or older who self-reported annual income was less than $25,000 had a higher incidence of hospitalized HF than their counterparts whose annual income was $25,000 or greater.[15] The results were significant among men ($p<0.0001$) and women ($p=0.0002$).

Occupation was categorized into three levels (i.e. laborers, semi-skilled, and professionals) in the Uppsala Longitudinal Study of Adult Men based in Sweden.[13] The highest occupational role was significantly associated with lower hazard of incident HF compared to laborers and semi-skilled employees, [(HR=1.55 (95% CI: 1.03, 2.35)] and [(HR=1.47 (95% CI: 0.97, 2.23)], respectively. The similar hazard ratios signify that there is a lack of a gradient as the level of occupation increases. Education was used an indicator of SES in all three studies.[13-15] In both the First National Health and Nutritional Examination Survey (NHANES I)[14] and the Cardiovascular Health study[15], education was dichotomized into: acquiring less than high school and achieving an high school education or higher. In the Uppsala Longitudinal Study of Adult Men, education was categorized into elementary, secondary school, and three years or more of college or graduate exam.[13] Education was negatively associated with incident HF in all three studies. [13-15] Investigators from the NHANES I reported a significant association between education and incident HF in the total population; however, the association was not significant by gender.[14] In the Cardiovascular Health Study, education was

associated with incident HF in men ($p<0.001$) and women ($p<0.0001$).[15] In the adjusted analysis by the Uppsala Longitudinal Study of Adult Men, education was significantly related to incident HF.[13] There was some evidence of a gradient as the educational attainment increased: elementary vs. 3+ years of college or grad exam [(HR=1.98 (95% CI: 1.07, 3.68)] and secondary versus college or grad exam [(HR=2.31 (95% CI: 1.06, 5.05)].[13]

2.Individual-level SES and Prevalent HF

Five studies have reported the relationship between individual-level SES indicators and prevalent HF (i.e. any recorded HF event including death) (Table 3).[16-20] Of the five studies, two are prospective[17, 19] and three are cross-sectional[16, 18, 20], and three of them[16-18] were conducted in the United States.

The investigators from the Cardiovascular Health Study reported a negative unadjusted association between annual income (≤$25,000 vs. > $25,000) and the prevalence of HF in the total population (x^2, $p=0.001$), for men (x^2, $p=0.003$) and women (x^2, $p=0.001$).[16]

Housing (i.e. public, private, and community) was not significantly related to prevalent HF in the 10-year community-based study conducted in Connecticut (x^2, $p=0.23$).[17]

Unadjusted and adjusted analyses were presented for the relationship between any HF event and education in a community based study and a cross-sectional study. In the community based study, education (i.e. elementary, HS, < College, or Unknown) was inversely related to incident hospitalized HF or HF mortality (x^2, $p=0.40$).[17] A slight inverse yet null association between education and prevalent HF

was detected for those with a high school education compared to less than a high school education in the adjusted analysis presented by the study of 64 centers in the United States [OR: 0.96 (95% CI: 0.75, 1.24)].[18] Participants with more than an high school education possessed 25% lower odds of prevalent HF than participants with less than an high school education [OR: 0.75 (95% CI: 0.56, 0.99)].[18] A significant inverse association between those with greater than high school vs. those with less than high school education was observed for men [(OR: 0.69 (95% CI: 0.48, 0.99)], but not women [OR: 0.77 (95% CI: 0.48, 1.23)].[18]

In a Swedish longitudinal study, the type of profession (i.e. unskilled, semi-skilled, foremen, non-manual, or professional) of men was related to prevalent HF.[19] The occupational role and the hazard of incident HF were negatively associated with hazard of incident HF, secondary HF, or HF mortality.[19] Of the groups with similar occupations, non-manual workers had a 28% increased hazard of having the outcome compared to professionals after adjusting for confounders [HR=1.28 (95% CI: 0.98, 1.67)].[19] The greatest disparity in hazard of primary HF, secondary HF, or HF mortality was evident for the two groups that were the most disparate in terms of occupational roles, unskilled workers vs. professionals, [HR=1.72 (95% CI: 1.34, 2.20)].[19]

3.Individual-level SES and Case Fatality

There are no studies to our knowledge which have examined the relation between individual-level SES and case fatality.

B.Contextual-level SES

1. Contextual-level SES and incident HF

There is a dearth of studies that have assessed the effect of contextual-level SES on incident HF (Table 4). To our knowledge, two prospective studies, both conducted in Scotland that have investigated this association.[21, 22] Although both studies used the Carstairs-Morris Deprivation Category, which is based on postal codes; one modeled the variables in quintiles[21] and the other into 7 categories[22]. In both studies, investigators detected a significant negative association between contextual-level SES and incident HF in the overall population after adjusting for confounders.[21, 22] In one of the studies, the results were reported by gender, and the hazard ratios were not found to be statistically significant by gender (Table 3).[22]

2.Contextual-level SES and HF case fatality

The majority of the studies examining the association between contextual-level SES and case fatality were conducted in European populations[23-25] with the exception of a recent publication by Rathore et al.,[26] which was based in the United States (Table 5).

Contextual-level data was ascertained via census data in the four studies.[23-26] The data were grouped by census blocks in two of the studies,[23, 26] postal codes in one study,[24] and by ward (i.e. British area of residence) in another study[25]. Different indices (e.g. family size and home value) in the census data were chosen to represent contextual-level SES in each study. The contextual-level variables were categorized in two studies[23, 24], treated as quintiles in one study[25], and represented via z-scores in another study[26].

Overall the results were null, and the effect of contextual-level SES on HF case fatality was modest, approximately less than 10% in the studies that presented adjusted effect estimates.

C.Life-Course SES

There are no studies to our knowledge which have examined the association between SES over the life-course and incident or prevalent HF or its case fatality.

D.Summary

Individual-level SES

Overall in the published studies regarding the association between individual-level SES and incident HF, education, income, and occupation were found to be negatively associated with incident and prevalent HF, regardless of how the variables are categorized. However, the magnitude of the association differed between the studies, and that may reflect spatial and temporal differences in benefits conferred by income, education, or occupation. The differences among these studies may also be due to recall, selection, and survival bias as well as the definition and ascertainment of heart failure events. The study population, the method used to model the SES constructs, and the covariates controlled in the model are also factors that could have varied the results. The null findings in some of the studies may have been contributed to a lack of study power.

In the aforementioned studies, childhood-level SES was not assessed nor was it controlled for as an effect measure or as a cofounder. Thus, the effect estimates purely reflect the influence of SES in adulthood on the various HF outcomes.

Controlling for childhood SES is debatable, and is based on the type of life-course model one adheres to in the analysis. In the accumulation model that is based on clustering the different levels of SES emerge from a common source (e.g. family's SEP).[27] Therefore adjusting for childhood SES in addition to adulthood-level SES, could introduce biases between the two SES constructs since they cluster together. Adulthood-level SES is considered to be an intermediate variable between childhood-level SES and chronic disease according to the pathway model;[27] thus, including both measures of SES in the model would be erroneous and cause the main effect estimate to be underestimated. In contrast, the accumulation of risk model holds that indicators of SES are independent.[27] Therefore, childhood-level SES and adulthood-level SES could confound each other. By not controlling for the other SES variable, the estimates would be biased towards the null since childhood-level SES and adulthood-level SES are both have a positive association with the onset of HF. In this model, it is also possible that the independent variables are highly collinear; thus, the effect estimates would be unreliable.

A preponderance of the studies identified heart failure events by examining the medical records for an ICD-8, 9, 10 codes. Due to financial incentives, upcoding to HF permeates hospitals in the United States; thus, the prevalence and incidence of HF events in these studies could be inflated, which could bias the estimates away from the null.[28] Also, changes in the diagnostic codes (e.g. ICD-9 and ICD-10) may have caused an increase in the incidence of HF. Consequently, there may be some degree of differential misclassification that could bias the estimates towards or away from the null.

With the exception of the study based in Nigeria[20], which was conducted among people of African descent, the remainder of the studies solely reported results for participants of European descent.

Contextual-level SES

Based on the literature neighborhood-level SES may share an inverse association with incident HF and a null association with HF case fatality. Of all the studies using contextual-level SES as the main exposure, the study by Rathore et al. is the sole study that adjusted for potential clustering, and to do this the investigators used hierarchical analysis to adjust for the clustering.[26] It is pertinent to assess and adjust for clustering since the risk of a disease maybe related to the areas of residence. Failure to adjust for clustering could overestimate the variance, which would increase the precision of the confidence intervals. Thus, the significant findings from the studies that did not adjust for clustering may actually be null.

A comparison of these studies is made difficult by the fact that they were conducted in diverse study populations, during different time periods, and the estimates were adjusted for different covariates. In addition, the contextual-level measures were derived from different indices, which may themselves affect the results.

Since the majority of these studies were conducted in European countries the results may not be generalizable to neighborhoods in the United States in part because of the lack of universal healthcare in the United States; thus, the effect might be stronger in the United States.

Table 2. A summary of results from studies of individual-level SES and incident heart failure.

Authors, (Year)	Dura-tion	Study Population	Study Design	SES exposure(s)	Outcome	Cases	Results U = Unadjusted A = Adjusted
Ingelsson E et al (2006) [2] *Uppsala Longitudinal Study of Adult Men*	32 yrs (1970-2002)	Sweden ≥ 50 yrs N = 2314	Longitudinal	Occ: Low (laborers), Middle, and High (professionals) Edu: Elementary, 2° School, and 3+ years of college or grad exam	Incident HHF	N=346	(A) HR (95% CI) ***Occ for Men*** Low vs. High 1.55 (1.03, 2.35) Mid vs. High 1.47 (0.97, 2.23) ***Edu for Men*** Elementary vs. College or grad exam 1.98 (1.07, 3.68) 2° School vs. College or grad exam 2.31 (1.06, 5.05)
He Jiang et al (2001) [1] *NHANES I Epidemiologic Fup Study*	Avg. 19yrs (1971-1992)	U.S. N=13,643 n=5545 M n= 8098 W Avg. age 52.2 yrs in M 48.1 yrs in W	Prospective, population based	Edu: <HS vs. ≥HS	Incident HHF or nursing home stay HF	N=1382 n=741 M n=641 W	(A) HR (95% CI) ***Edu Overall*** 1.22 (1.04, 1.42) ***Edu for Men*** 1.20 (95% CI: 0.99, 1.45) ***Edu for Women*** 1.25 (95% CI: 0.99, 1.57)
Gottdiener JS et al (2000) [3] *Cardiovascular Health Study*	Avg. 5.5 yrs (1989-1996)	NC, CA, PENN, & MD ≥ 65 yrs N = 5,625 n= 2,368 M n = 3,257 W	Prospective, community-based	Income: ≥$25,000 vs. <$25,000/yr Edu: ≥HS vs. <HS	Incident HHF: Physician diagnosis or trt for HF	N = 597 n= 329M n = 268W	(U) IR/1,000py (95% CI) ***Income for Men*** 31.9% vs. 19.7% p<0.0001 ***Income for Women*** 17.7% vs. 10.4 % p=0.0002*:* ***Edu for Men*** 35.0% vs. 23.0% p<0.0001 ***Edu for Women*** 20.9% vs. 12.3% p<0.0001

*Incidence hospitalized heart failure = Incident HHF

Table 3. A summary of results from studies of individual-level SES and any heart failure event.

Authors, Year	Duration	Study Population	Study Design	SES exposure(s)	Outcome	Cases	Results U= Unadjusted A = Adjusted
Schaufelberger et al (2007) [7] *Multifactor Primary Prevention Study*	28 yrs (1970-1998)	Sweden 47-55 yrs N = 6999 M	Longitudinal	Occ: Unskilled and semi-skilled; skilled workers; non-manual employees; employees; and professionals, higher civil servants, and executives	1^{o} or 2^{o} hosp. or death from HF	N = 1004	(A) HR (95% CI) ***Unskilled vs. Professionals*** 1.72 (1.34, 2.20) ***Semi-skilled and skilled vs. Professionals*** 1.48 (1.15, 1.89) ***Foremen vs. Profess.*** 1.57 (1.22, 2.03) ***Non-manual vs. Profess.*** 1.28 (0.98, 1.67)
Mukamal KJ et al (2004) [6] *Part of the Determinants of Myocardial Infarction Onset Study*	7yrs 1989-1996	64 Centers in the US N= 3800 T n= 2567 M n= 1233 W	Cross-Sectional	Edu: < HS, HS, > HS	A recorded HF event in medical records after having an AMI	N=499	(A) OR (95% CI) ***Edu Overall*** *HS vs.< HS:* 0.96 (0.75, 1.24) *> HS vs.< HS:* 0.75 (0.56, 0.99) ***Edu Men*** *HS vs < HS:* 0.81 (0.58, 1.14) *> HS vs. < HS:* 0.69 (0.48, 0.99) ***Edu Women*** *HS vs.< HS:* 1.09 (0.74, 1.60) *> HS vs. < HS* 0.77 (0.48, 1.23)
Kitzman DW et al (2001)[4] *Cardiovascular Health Study (CHS)*	1yr 1994-1995	NC, CA, PENN, MD ≥ 65 years N= 4,842* n= 1,922 M n= 2,920 W	Cross-Sectional	Income: ≤$25,000/yr vs. >$25,000/yr	At least 1 adjudicated episode of hosp. or outpatient HF	N=425 n=204M n=221W	(U) HF vs. no HF ***Income Overall*** 23% vs. 33% p=0.001 ***Income Men*** 32% vs. 43% p=0.003 ***Income Women*** 15% vs. 27% p =0.001

***of which 783 were AA**

Table 3 (cont.) A summary of results from studies of individual-level SES and any heart failure event.

Authors, Year	Duration	Study Population	Study Design	SES exposure(s)	Outcome	Cases	Results U= Unadjusted A = Adjusted
Chen Y et al (1999) [5]	10 years (1982-1992)	Connecticut N= 1749 n = 718 M n = 1031 W ≥ 65yrs	Community-based population study	Educ: Elementary, HS, College or more, Unknown Housing: Public, Private, and Community	Incident hosp. or death from HF	N =173 n = 85 M n = 88 W	(U) p-value ***Edu Overall*** p-value 0.40 ***Housing Overall*** p-value 0.23
Falase AO et al (1983) [8]	--	Nigeria N=196 ≥ 20 yrs	Cross-Sectional	Occ: 8 categories	Presence of any HF	N= 78	Chi-square Test for the 8 categories x^2 = 16.50, 7 d.f. 0.02<p<0.05

Table 4. A summary of results from studies of contextual-level SES and incident heart failure event.

Authors, (Year)	Duration	Study Population	Study Design	SES exposure(s)	Outcome	Cases	Results U= Unadjusted A = Adjusted
McAlister et al (2004) [9]	1yr (1999-2000)	Scotland N=307,741	Prospective, population-based	Postal codes of residence in quintiles (Q5 = most deprived) based on Carstairs-Morris Deprivation category	Incident HHF entered in medical records	N=609T	(U) OR ***Q5 vs. Q1*** 1.33 p for trend 0.002 (A) OR ***Q5 vs. Q1*** OR 1.44 p for trend 0.0003
Stewart S et al (2004) [10] *Renfrew/Paisley Study*	20 yrs (1977-1996)	Scotland N=15,402 n=7048 M n=8354 W 45-64 years	Prospective, community based	Postal code of residence 7 categories based on Carstairs-Morris Deprivation category	Incident HHF	N=628T	(A) HR (95% CI) ***Area SES Overall*** Cat 7 vs. Cat 1* 1.39 (1.04, 2.01) ***Area SES for Men*** Cat 7 vs. Cat 1* 1.53 (0.92, 2.85) ***Area SES for Women*** Cat 7 vs. Cat 1* 1.64 (0.96, 2.32)

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Table 5. A summary of results from studies of contextual-level SES and heart failure case fatality.

Authors, (Year)	Duration	Study Population	Study Design	SES exposure(s)	Outcome	Cases	Results U= Unadjusted A = Adjusted
Rathore SS et al (2006) [14]	1 yr (1998-1999)	U.S. Medicare recipients ≥ 65 years N=25,086 T n =10,611 M n=14,475 W	Retrospective Cohort	Census block data.. Used z-scores and standard deviation.	CF after hosp. HF	N=18,062T	(A): Relative Risk (95%CI) ***30-day mortality*** Lower vs. Higher: 1.13 (0.92, 1.38) Lower-middle vs. Higher: 1.03 (0.87, 1.22) Higher-middle vs. Higher 1.01 (0.85, 1.20) ***1-year mortality*** Lower vs. Higher: 1.10 (1.02, 1.19) Lower-middle vs. Higher 1.12 (1.05, 1.18) Higher-middle vs. Higher 1.04 (0.97, 1.11)
Forastiere F et al (2006) [11]	3yrs (1998-2001)	Rome ≥35 yrs n=83,253	Case-Crossover	Census Block data.	CF after Hosp. HF at least once 29days to 2 years before death	N=7785T	(U): Prevalence Ratio ***Income:*** Low/High = 1.61 ***SES (categories based on percentiles):*** Low/High = 1.56

Case fatality = CF

Table 5 (cont.). A summary of results from studies of contextual-level SES and heart failure case fatality.

Authors, (Year)	Duration	Study Population	Study Design	SES exposure(s)	Outcome	Cases	Results U= Unadjusted A = Adjusted
Blackledge HM et al (2003) [13]	8 yrs (1993-2001)	Leicestershire, England ≥ 40 yrs N=12,200 T n= 6055 M n= 6164 W	Retrospective Cohort	Ward of residence using the index of multiple deprivation. Quintiles (Q5 = most deprived)	CF after 1st hosp. † HF	N=7818	(A) HR (95% CI) Q5 vs. Q1: 0.94 (0.87, 1.01) Q4 vs. Q1: 1.00 (0.91, 1.08) Q3 vs. Q1: 0.98 (0.89, 1.07) Q2 vs. Q1: 1.03 (0.93, 1.12)
MacIntyre K et al (2000) [12]	10 yrs (1986-1995)	Scotland Median age =72 yrs M =78 yrs W N= 66,547 T n=31,277 M n=35,270 W	Retrospective Cohort	Used 1991 census data from postal codes Carstairs Deprivation category. 5 categories (C5 = most deprived).	CF after hosp. HF‡	N=58295	(A) HR (95% CI) (30 days - 10 yrs) ***Area for Men*** C5 vs. C1: 1.10 (1.05, 1.16) C2 vs. C1: 1.03 (0.98, 1.08) ***Area for Women*** C5 vs. C1: 1.06 (1.02, 1.11) C2 vs. C1: 1.03 (0.98, 1.08)

Case Fatality = CF

*Lower SES = more than 1 SD below national mean; lower-middle SES = within 1 SD below the national mean; higher-middle SES = within 1 SD above the national mean; and Higher SES = more than 1 SD above the national mean

†excluded participants with a recorded HF diagnosis before the start of the observation period.

‡excluded patients with a hosp. related to HF 5-years prior to the start of the observation period.

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CHAPTER III. STUDY QUESTIONS

The overarching goal of this research project is to evaluate the direct and indirect effects of SES exposures over the life course on incident HF and its case fatality. The specific research questions are as follow:

1) Are individual-level SES measures during childhood (at 10 years of age), individually and cumulatively, associated with incident HF?
    a. Is the association between individual-level SES measures during childhood and incident HFF modified by contextual-level SES?
    b. To what degree is the association of individual-level SES measures during childhood and incident HHF explained by concomitant illnesses, metabolic, and behavioral risk factor profiles?
2) Are individual-level SES measures during young adulthood (at 30 years of age) associated with incident HF?
    a. Is the association between individual-level SES measures during young adulthood and incident HHF by contextual-level SES?
    b. To what degree is the association of individual-level SES measures during young adulthood and incident HHF explained by concomitant illnesses, metabolic, and behavioral risk factor profiles?

3)Are individual-level SES measures during older adulthood (45-64 years of age) associated with incident HF and case fatality in participants with an incident HHF?

a. Is the association between individual-level SES measures during older adulthood and incident HHF by contextual-level SES?

b. To what degree is the association of individual-level SES measures during older adulthood and incident HHF explained by concomitant illnesses, metabolic, and behavioral risk factor profile.

4) Is the cumulative effect of individual-level SES across life course associated with the incident HF?

a. Is the association between the cumulative effect of individual-level SES across life course and incident HHF modified by contextual-level SES at the time of HF?

b. To what degree is the association of cumulative effect and incident heart failure explained by concomitant illnesses, metabolic, and behavioral risk factor profiles over the life course?

5)Do these associations differ in Blacks and Whites?

CHAPTER IV. STUDY DESIGN

A.Study Population

The study population consists of the participants from the Atherosclerosis Risk in Communities (ARIC) study. The ARIC study is a longitudinal cohort study conducted in four communities: Washington County, Maryland (MD); Forsyth County, North Carolina (NC); Jackson, Mississippi (MS); and Minneapolis, Minnesota (MN). Area sampling and random-digit dialing identified eligible households in NC; participants in MS, MN, and MD were identified via driver's licenses, identification cards, and voter registration cards. Participants were enrolled at baseline from 1987 to 1989 (i.e. Visit 1) during which 15,792 men and women between the ages 45-64 years were enrolled into the study. Re-examination visits occurred in 1990-1992 (Visit 2), 1993-1995 (Visit 3), and from 1996-1998 (Visit 4). Home interviews were conducted during each visit with information being collected on SES factors, family medical history, and behavioral and psychological risk factors. At these interviews, participants were extended an invitation to attend the clinic examination where information was obtained on the following: sitting blood pressure, anthropometry, venipuncture, pulmonary function, and medication use. Since Visit 1 annual-contact was maintained via telephone interviews as part of the ARIC Annual Follow-up.

To study the association between SES over the life-course and incident HHF, data from an ancillary study to ARIC, the Life Course Socioeconomic Status, Social

Context, and Cardiovascular Disease Study (LC-SES) were also utilized. The LC-SES Study was conducted from 2001-2002 to obtain information regarding socioeconomic factors from the participants childhood into adulthood. Of the original cohort members, approximately 95% of the ARIC participants were alive at the time of enrollment in to the LC-SES study. Of original cohort, 80.5% (n=12,712) of them were enrolled into the study.

The exclusions for the two health outcomes of interest were similar. Asians (n=34) and American Indians (n=14) were excluded due to small sample sizes. African-Americans that were not recruited in Jackson, MS (n =349) were excluded in the first manuscript, but not the 2nd manuscript. After these exclusions were made, n=12,332 men and women of African or European descent remained for inclusion into the analyses. Of the 12,332 participants, the majority of European American women 41.9% (n = 5,170), followed by European American men 34.7% (n = 4,284), African-American women 15.2% (n= 1,876), and African-American men 8.1% (n =1,002). Participants with prevalent HF or those taking medication for HF at baseline were also excluded. After all of the exclusions n=11,890. To analyze the effect of SES over the life-course on incident HHF for the first manuscript, ARIC participants who did not enroll into the LC-SES study were also excluded. To analyze the association between SES in older adulthood and case fatality, only participants with an incident HF from 1987-2002 were included. Participants who were not hospitalized for at least one day were excluded as well.

A complete case analysis was conducted; thus participants with missing data for the main outcome, main exposure, and the covariates were excluded.

B.Definition of Incident Heart Failure and Case Fatality

The primary outcome is incident hospitalized HF. The HF events were ascertained via annual contacts from ARIC personnel and by epidemiologic surveillance of the hospital records and death certificates over a fifteen-year period, 1987-2002. Incident HHF was ascertained via annual contacts and review of medical records for all hospitalizations over an fifteen-year study period from enrollment, 1987-89 through December 31, 2002. Incident hospitalized HF was defined as the first occurrence of either an ICD-9 428 coded hospital discharge diagnosis or an underlying cause of death of 428 or ICD-10 150 among those without a previous record of a hospitalization with an ICD-9-CM code 428.[29] Underlying causes of death based on records from the US Vital Statistics Office will not be used since the National Center for Health Statistics has stringent rules that HF could never be listed as the underlying cause of death. Information regarding vital status and hospitalizations for CVD is complete with <1% of missing data as of 1998. These definitions have been used in previous ARIC study.[30]

The secondary outcome is case fatality, to be defined as a fatal event in participants with an incident HHF event, and who hospitalized for at least one day.

In order to assess the incident HHF events, the prevalent HF events must be excluded. Currently, there is no gold standard in determining prevalent HF. Heart failure is normally detected by echocardiogram, which assesses systolic function (i.e. normal ejection fraction).[6] However, echocardiograms were not available for all of the participants before baseline. There are various instruments that define prevalent HF: Framingham (1971), Gheorghiade (1983), Boston (1985), NHANES

(1992), Walma (1993), ESC (1995), CHS (1995), Gothenburg Criterion ≥Grade 1 (latent) (1987), Gothenburg criterion ≥ Grade 2 (declared) (1987), and Gothenburg criterion ≥Grade 3 (declared) (1987).[31] These different criteria are based on point scale that incorporate cardiac, pulmonary dysfunction, and medication use. In a review of seven instruments by Fonseca et al, the Gothenburg criterion ≥Grade 1 (latent) had the best sensitivity, 84.3%+/- 3.38 and the Boston ≥ 8 (probable) had the best specificity, 99.1% +/- 0.17. However, Gothenburg had the best balance of sensitivity, 83.5% +/- 4.34 and specificity, 80.9%+/-5.17. Thus the Gothenburg was used to determine whether a participant had a HF event prior to baseline.

Table 6. The definition of prevalent HF using the Gothenburg criterion as defined by the ARIC Coordinating Center.

Gothenburg Score	Cardiac	Pulmonary	HF therapy
3	1	1	1
2	1	1	0 or Missing
	1	0 or Missing	1
1	1	0 or Missing	0 or Missing
0	0	N/A	N/A
Missing	Missing	N/A	N/A

The Gothenburg criterion is based on cardiac, pulmonary symptoms, and heart failure therapy. In order to be positive for prevalent HF, cardiac, pulmonary, and heart failure therapy must all be present (i.e. score = 3) (Table 5). To receive a positive cardiac score (i.e. 1 or higher), at least one of the following were present at baseline: previous coronary heart disease, angina, edema, paroxysmal nocturnal dyspnea, rales, and atrial fibrillation. A positive pulmonary score (i.e. 1 or higher) is based on having at least one of the following: history of bronchitis, history of asthma, chronic cough, or rhonchi. Self-reported use of either digitalis or diuretics for HF

therapy will constitute as having a value of 1. Self-reported use of HF medication(s) two weeks prior to the baseline interview, 1987-1989, independent of the Gothenburg criterion, will be used in conjunction with the Gothenburg criterion to determine the prevalence of HF at baseline.

Table 7. Itemization of the Gothenburg Score.

Category	Gothenburg Components	Score
Cardiac	Coronary heart disease	1 point if ever 2 points if w/in last yr
	Angina	1 point if ever 2 points if w/in the last yr
	Leg edema	1 point
	Shortness of breath at night	1 point
	Rales on lung exam	1 point
	Atrial fibrillation on electrocardiography	1 point
Pulmonary	History of bronchitis	1 point
	History of asthma	1 point
	Cough, phlegm, or wheezing	1 point
	Rhonchi on lung exam	1 point
Therapy	Treatment with digoxin	1 point
	Treatment with diuretics	1 point

Adopted from Loehr et al. 2007[1]

C.Measurement of Individual-level SES indicators

There are three life epochs each will be explored in this analysis: childhood, early adulthood, and older adulthood. Education, occupation, managerial role, and home ownership from at least one of the life epochs were used as proxies for SES. These variables were chosen since data are available for each of them in at least one of the three life epochs.

Each variable employed to represent SES has its distinct limitations. Occupation may not easily be defined for individuals that are unemployed, homemakers, or retired. In order to alleviate the limitation of using occupation, it will be classified into manual or non-manual. Retired participants were grouped into as non-manual

positions since this position allows more flexible and have a higher connotation in society than manual workers. Homemakers in young adulthood or older adulthood were treated as a separate group from manual and non-manual workers since their risk of heart failure was different than these two groups. Other ARIC studies have treated homemakers as distinct groups because they noted the risk was different in these groups than in manual and non-manual employees.[5,6] Rose et al. reported that the risk among homemakers for all cause mortality and diseases related to the CVD system is significantly lower than among non-manual and manual female workers.[5] Carson et al. weighted homemakers because she believed they had a different risk for subclinical atherosclerosis.[6] For some of the items concerning SES, "unknown" was a potential response. All "unknown" responses were coded as missing since the value of it is not ascertainable.

SES during childhood (at 10 years of age)

Data was collected retrospectively from the participants during the LC-SES Study regarding the participants' parental (i.e. mother, father, or caretaker) SES when the participant was 10 years of age. Approximately 6% of the participants were raised by a caretaker until age 5 (n = 33). The education (<8th grade, 9-11th grade, >11th grade), occupation (manual or non-manual), managerial occupational role (yes or no), and home ownership (yes or no) of the primary caretaker was used. A score was created for SES during adulthood by summing across the variables, and it ranged from 0 to 5. The score was split at the median separately for blacks and whites inconsideration of discrimination in wages.

SES during early adulthood (age 30 years)

The indicators for this age group will be education (< 11th grade,12-16 years , 17+) occupation (manual or non-manual), managerial occupation role (yes or no), and home ownership (yes or no) at 30 years of age, which were also collected retrospectively during the LC-SES Study. A score was created for SES during adulthood by summing across the variables, and it ranged from 0 to 6. The score was split at the median separately for blacks and whites inconsideration of discrimination in wages.

SES during older adulthood (45-64 years)

Annual income (<$25,000, $25-49,999, ≥ $50,000), occupation (manual or non-manual), managerial occupation role (yes or no), and owned home (yes or no) during older adulthood were used as the exposures for this age group. Data for these exposures were collected at the baseline ARIC visit. A score was created for SES during adulthood by summing across the variables, and it ranged from 0 to 6. The score was split at the median separately for blacks and whites inconsideration of discrimination in wages.

Table 8. Categorization of the variables used as proxies for socioeconomic variables in the LC-SES study, 2001.

Socioeconomic Exposure	Category	Score
Childhood		
Parental Education	≤ 8th grade	0
	9-11 grade	1
	≥ 12th grade	2
Parental Occupation	Manual	0
	Non-manual	1
Parental Occ. Role		
	Not a Manager	0
	Manager	1
Home Ownership		
	No	0
	Yes	1
Young Adulthood		
Education	≤11th grade	0
	HS Graduate	1
	Some College or Greater	2
Occupation	Manual	0
	Homemaker	1
	Non-manual	2
Occupational Role	Not a Manager	0
	Manager	1
Home Ownership	No	0
	Yes	1
Mid- Adulthood		
Income	≤$25,000	0
	$25,000-$50,000	1
	≥$50,000	2
Occupation	Manual	0
	Homemaker§	1
	Non-manual	2
Occupational Role	Not a Manager	0
	Managerial	1
Home Ownership	No	0
	Yes	1

*The possible range for the cumulative SES score = 0 to 17.

†Parental education wad determined by using the education obtained by the parent or caretaker with the highest value when the participant was 10 years of age.

D.Measurement of Cumulative SES indicator

There are four recognized models to conceptualize SES over the life-course: the latent effects model, pathway model, social mobility model, and the cumulative model.[7] Briefly, the latent effects model involves a series of biological chains of events initiating in utero and early infancy that have irrevocable, sustained effects, which can lead to deleterious health outcomes. The pathway model predicts that events early in life lead to risk factors and health behaviors later in life that give rise to health outcomes in adulthood. The social mobility model suggests that changes in SES circumstances from generation to generation can predict health outcomes. Lastly the cumulative model asserts that negative events accumulate over one's life and the exposures, independently or in clusters, lead to health outcomes. Of the four postulated models to conceptualize SES over the life-course, we decided to use the cumulative model and the pathway model for several reasons. We could not utilize the latent effects model because we didn't have information from when the participant was in utero or early infancy. Due to a lack of individuals possessing lower SES values than their parents, we did not have the power to use the social mobility model. A cumulative SES score was created to reflect the cumulative SES exposure across one's life course. It was formulated by summing the values for each of the individual variables in each of the life epochs. The values for the individual cumulative score ranged from 0 to 17 with lower values indicating lower individual-level SES over the life course. Life course SES was dichotomized into high and low due to a lack of heterogeneity. Assessing the independent effect of childhood level SES at the age of 10 was how we used the pathway model.

E.Collection of Contextual-Level SES

In the LC-SES study, information on place of residence during childhood, at 10 years of age, and during adulthood, at ages 30, 40, 50, 60, and 70 was linked with study census-based socioeconomic indicators from 1930-1990.[32] Residence during childhood and adulthood was gathered from 12,681 of the participants in the LC-SES study.

Of the 12,681 participants, 304 were excluded since they were born outside of the United States. The place of residence during childhood was linked with county-level socioeconomic census-based data for approximately 98.5% (n = 12,187) of the participants that reported childhood residence in the U.S.[32] Linkage did not vary by race, gender, birth cohort, or level of educational attainment.[32] Childhood residential data was geocoded and linked to county-level census data since it is the smallest geographical unit for which census data was available.[32]

Childhood residential data at 10 years of age was linked to county-level socioeconomic census data since it was the smallest geographical unit for which census data was available for that period. Place of residence at ages 30, 40, 50, 60, and 70 years were linked with tract-level socioeconomic census data. Census tracts are subdivisions of a county with an average size of 4,000 residents; they represent areas with homogenous economic and living conditions.

The amount and quality of the geocoding was high. The percentages of addresses that were successfully geocoded increased with each census decade: 66% in 1960, 76% in 1970, 85% in 1980, and 95% in 1990.[33] In a subset of LC-SES

participants (n = 1,032), the repeatability of geocoding addresses collected at age 50 years was assessed. The repeatability was found to be high (kappa = 0.90).[34]

Incident HHF and contextual-level SEP

In a prior factor analysis, six socio-economic census variables in older adulthood from the 1990 US Census Bureau were identified as the strongest predictors of coronary heart disease in the ARIC cohort study.[33]

Table 9. Neighborhood characteristics from the 1990 US Census that were used.[33]

Neighborhood Indices
Older Adulthood census variables from Diez-Roux
% of Adults with ≥ 4 years of high school
% of Adults ≥ 4 years of college
% of Adults with managerial/professional occupations
% of Households with interest, dividend, or rental income
Median household income
Median value of owner-occupied dwelling

Similar census variables were also are significantly associated with Coronary Heart Disease, CVD mortality[35] and intima media thickness in the ARIC study population.[36] Thus, we used comparable census variables for these two manuscripts. To correct for changes in definitions and availability across censuses, a z-score, a measure of the deviation from the mean, was created for each census variable within each life epoch, separately for Blacks and Whites. The z-scores were summed in each life epoch in order to render a cumulative neighborhood-level z-score for each distinct life epoch. Since the z-scores were not normally distributed, each neighborhood-level SES measure was split at the median in order to create a binary variable. A life-course neighborhood z-score was generated by summing the neighborhood z- scores from each life epoch, separately for Blacks and Whites, and

was dichotomized at the median to produce a binary life-course SES neighborhood-level variable. Childhood neighborhood-level SES was based on the indices from age 10. Young adulthood contextual-level SES was based on data collected at 30 years. For mid-adulthood, the census level variables at ages 40 and 50 years were averaged.

Table 10. Neighborhood characteristics from the US Census that were used in this study.

Childhood census variables used in this study
% of Adults 25+ years with ≥ 4 years of high school
% of Adults 25+ years with ≥ 4 years of college
% of Adults 14+ years with managerial/professional occupations
Median family income
% housing units owner-occupied
Young Adulthood census variables used in this study
% of Adults 25+ years with ≥ 4 years of high school
% of Adults 25+ years with ≥ 4 years of college
% of Adults 16+ years with managerial/professional occupations
Mean value owner occupied house
Mean family income
% housing units owner-occupied
Older Adulthood census variables used in this study
% of Adults 25+ years with ≥ 4 years of high school
% of Adults 25+ years with ≥ 4 years of college
% of Adults 16+ years with managerial/professional occupations
Median value owner occupied house
Median household income
% housing units owner-occupied

Case Fatality and contextual-level SEP

To determine the impact of contextual-level SES on the association between the main exposures and the outcome, census data was collected and geocoded for the residence of the participants at ages 50 and 60 years. Census block groups were used as proxies for neighborhoods. The following census variables: median

household income; median value of housing units; the percentage of households with interest, dividend, or rental income; the percentage of adults residents who completed high school; the percentage of adult residents who completed college; and the percentage of employed residents with executive, managerial, or professional occupations were used in approximating contextual-level SES. For each race group, a z-score, a measure of the deviation from the mean, was estimated for each census variable. The z-scores were summed to create neighborhood summary score. Since the z-scores were not normally distributed, each neighborhood-level SES measure was split at the median in order to create a binary variable.

F.Covariates

All covariates were obtained at the initial visit for studying incident HHF. For case fatality the covariates closest visit prior to the death were utilized. Sitting blood pressure was measured three times and the last two measurements were averaged to determine systolic and diastolic blood pressure levels. Systolic and diastolic blood pressures were each treated as continuous. Pulse pressure was defined as systolic blood pressure minus diastolic blood pressure. Hypertension was defined as a systolic blood pressure ≥ 140 mm/Hg or diastolic blood pressure ≥ 90 mm/Hg or antihypertensive medication use during the previous two weeks. Prevalent coronary heart disease was determined by the presence of at least one of the following: myocardial infarction from adjudicated Visit 1 ECG data, history of myocardial infarction diagnosed by a physician, coronary bypass, or angioplasty of coronary arteries. Type II diabetes was defined as fasting blood glucose level ≥ 126mg/dL,

non-fasting blood glucose level ≥ 200 mg/dL, use of hypoglycemic medications in the last two weeks, or self-reported history of physician diagnosis. Fasting total plasma cholesterol (mmol/L) was collected using standardized methods[37] and was modeled as continuous. Weight and height were measured by trained interviewers, and body mass index was calculated as weight (kilograms) divided by height squared (meters) and categorized into underweight (≤18.5 kg/m^2), normal (18.5-25 kg/m^2) and overweight (≥25kg/m^2). Smoking cigarettes and drinker status were self-reported, and were categorized as: ever or never. The Cornell criterion was used to identify left ventricular hypertrophy via electrocardiograph.

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CHAPTER V. ANALYTICAL DESIGN

A.Assessment of confounders

Directed Acyclic Graphs (DAG) was used to illustrate the pathways through which SES impacts HF (Figures 1-5). Variables that are independently associated with the SES measure and the outcome will be identified as confounders. Age at the time of the event, gender, and community center (for whites) are the only variables in the DAG, which are considered to be confounders of the association between life course SES, and the outcomes of interest. The confounders for childhood SES are age at baseline and center (only for whites).

B.Assessment of mediators

Variables that are in the intermediate pathway between the SES measure and the outcome in the DAGs will be considered mediators. In the DAGs (Figures 1-5), age at the time that the incident HF event occurred, hypertension, antihypertensive medications, health insurance status, prior coronary heart disease, left ventricular hypertrophy, type II diabetes, BMI, smoking status, and alcohol status are the potential intermediate variables. The recorded value of the mediators at baseline will be used in the analyses concerning incident HF. For case fatality, the latest measurement (from Visit 1 to Vist 4) for the variables will be used.

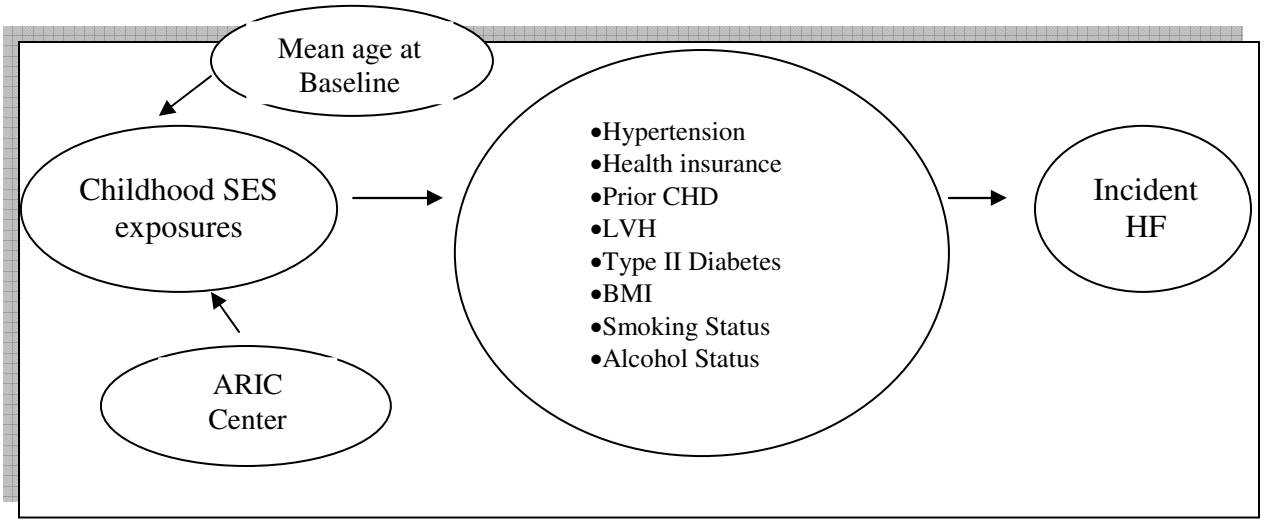

Figure 1 Postulated pathway via which indicators of childhood-level SEP (i.e. parental level SES when participant is age 10 years) (e.g. education and occupation) are hypothesized to influence on incident heart failure (HF).

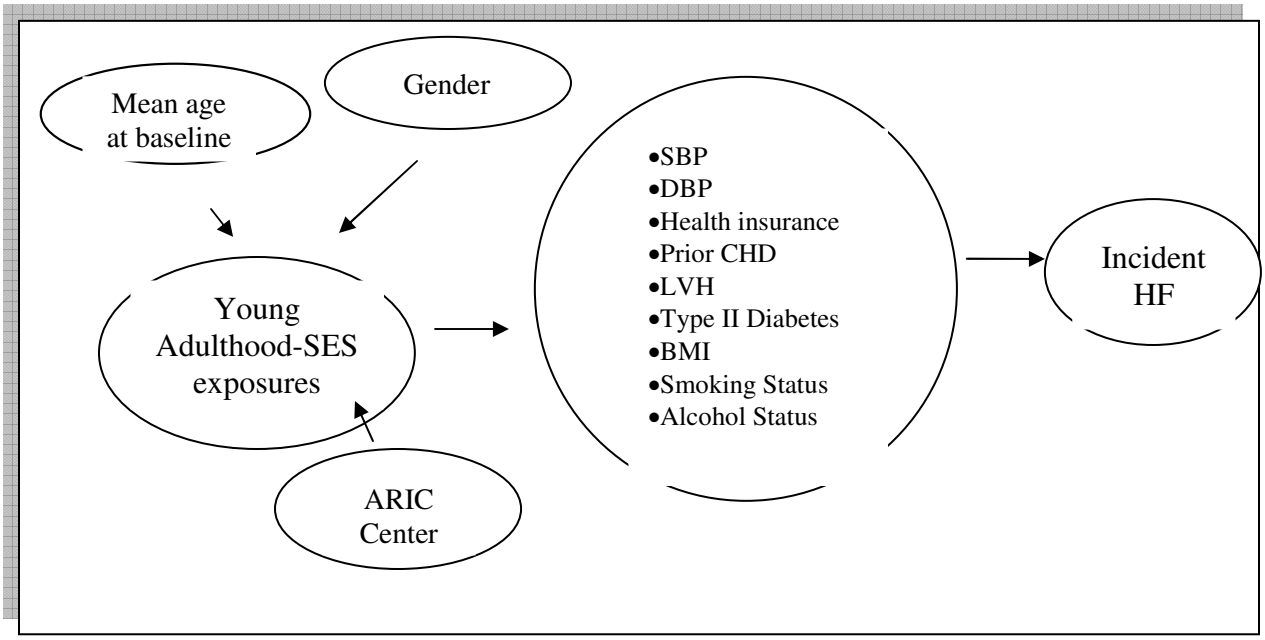

Figure 2 Postulated pathway via which young-adulthood SEP indicators (e.g. education and occupation) at age 30 years exert an effect on incident hospitalized heart failure (HF).

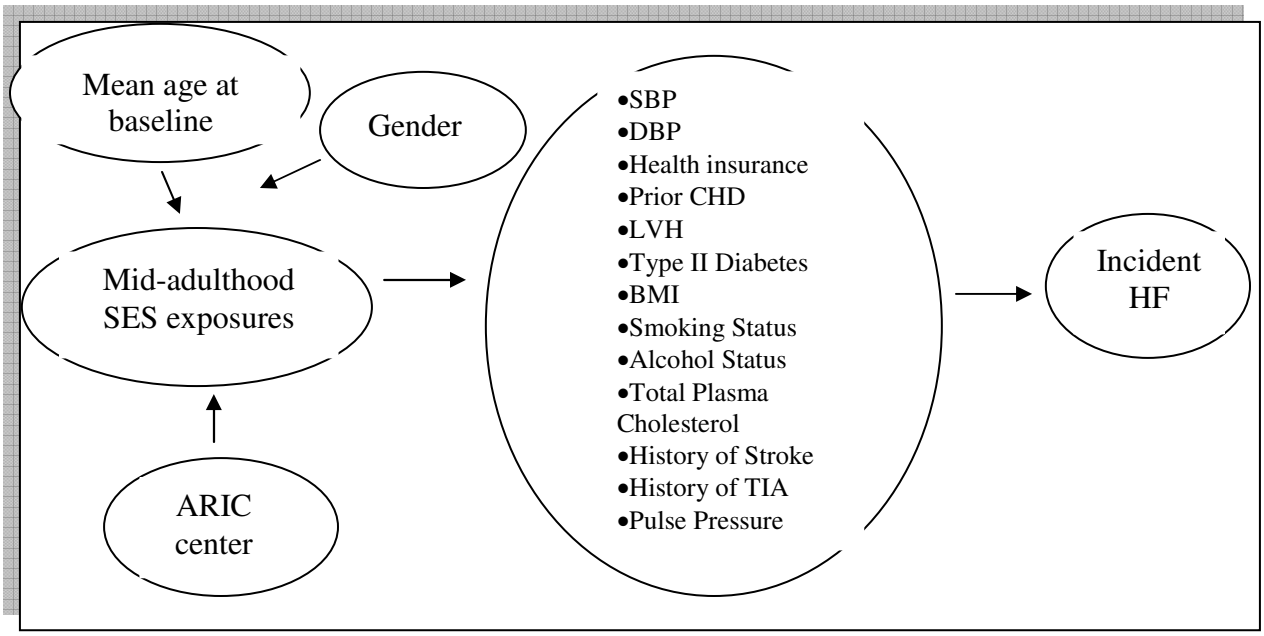

Figure 3 Postulated pathway via which indicators of mid-adulthood level SEP (e.g. occupation and income) at age 45-64 years are hypothesized to influence incident hospitalized heart failure (HF).

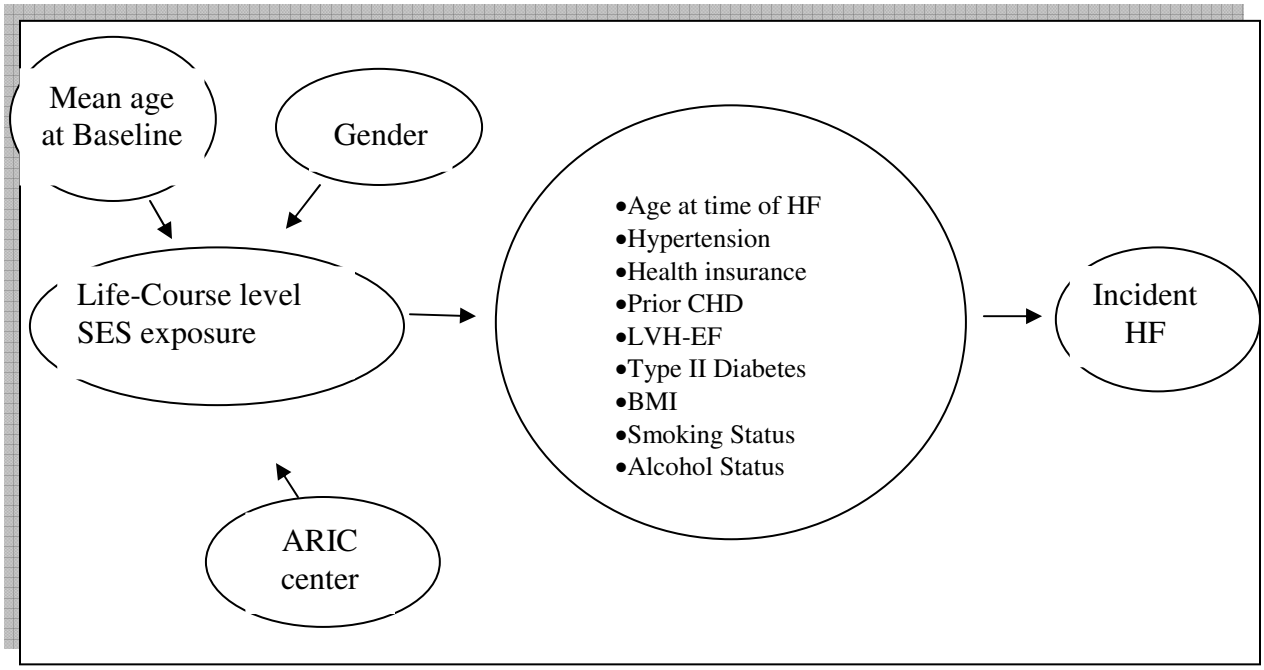

Figure 4 Postulated pathway via which indicators of life-course SEP (e.g. occupation and income) from 10years to 64 years of age are hypothesized to influence incident hospitalized heart failure (HF).

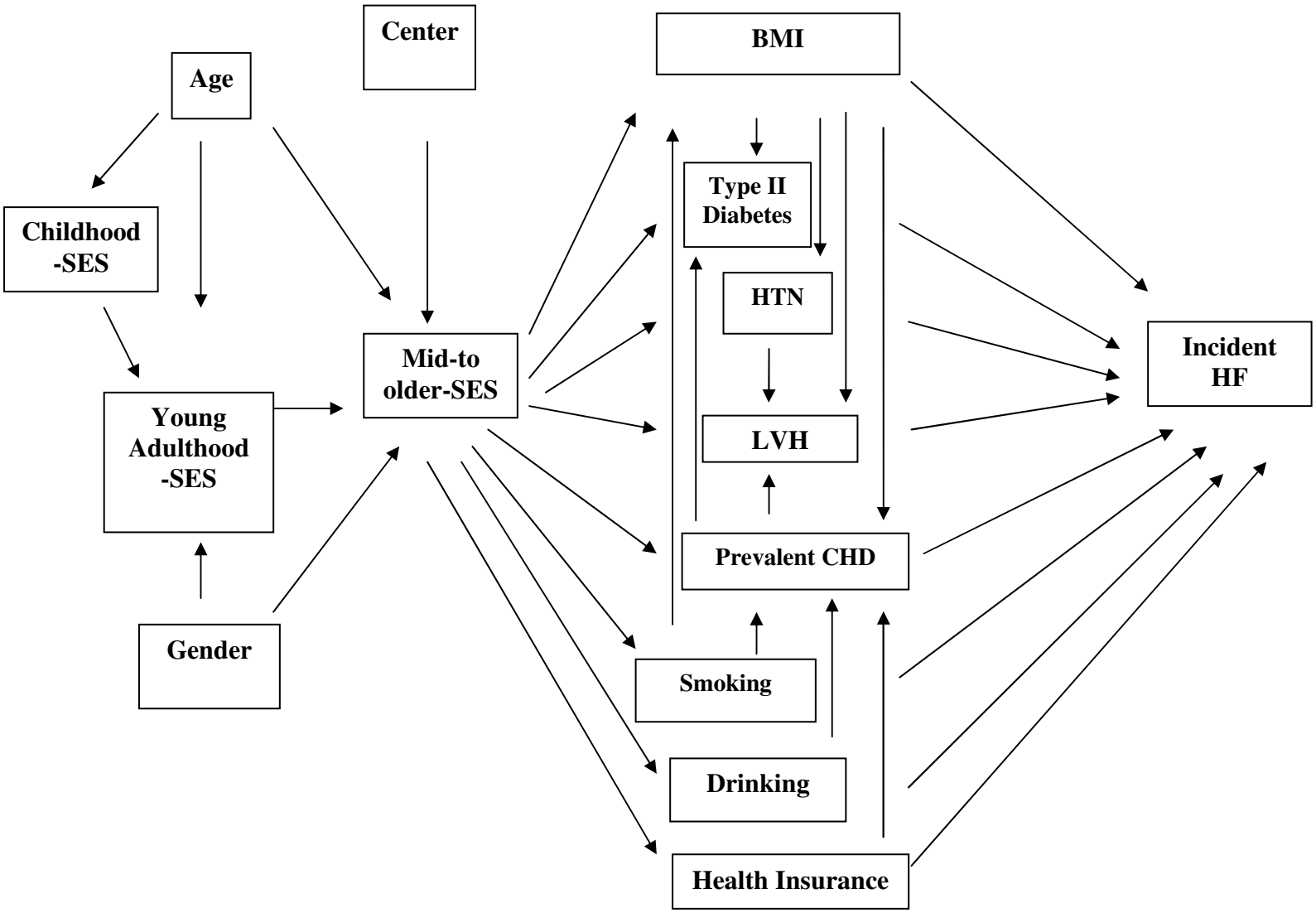

Figure 5 Directed Acyclic Graph of the relation between SEP and incident heart failure.

C. Survival Analysis

Cox Proportional Hazards[38] (p. 187-200) were utilized to estimate the unadjusted and adjusted hazard ratios and 95% confidence intervals for the association between the different life-course variables and the outcomes of interest using SAS version 9.1. The proportional hazards assumption was tested to ensure that the PH assumption over the 15-year period was not violated. The proportional hazards assumption was verified by examining continuous time interactions and log(-log) survival plots.[39] The proportional hazards assumption was not violated for any of the associations between the SES variables and the outcomes of interest, which indicates that the hazard of the outcomes occurring was constant over time in those with high versus low SES.

D. Hierarchical Analysis

Hierarchical analysis was not used since ARIC previous studies did not find any clustering by neighborhoods.

E.Effect Decomposition

In order to delineate the percentage of excess risk explained by SES beyond controlling for the intermediate variable (e.g. CHD), we used a technique known as effect decomposition as described by Szklo and Nieto[40] (p. 184-187). By using effect decomposition, we were able to detect which intermediate variables should be targeted for potential intervention or policy to reduce the burden of HF. The proportion of excess risk explained by SES was computed for each intermediate variable, individually, which allowed us to determine through which pathways SES exerted the most influence on incident HHF. The results of the decomposition analyses distinguished the direct

pathways through which SES impacts incident HHF from the indirect pathways (i.e. the effect of SES via intermediate variables) (Figure 1 and 2). Intermediate variables that greatly reduced the effect estimate between SES and the outcomes of interest were considered to be the most influential. Intermediate variables that resulted in a minimum change in the hazard ratio were considered to not play an important role in the pathway between the SES exposures and the outcome. Prior studies examining the association between adulthood SES and HF incidence and its case fatality treated the adjusted risk factors as confounders (rather than as possible mediators); thus potentially underestimating the effect. The proportion of the excess risk explained by the SES indicators were calculated by subtracting the adjusted hazard ratio (HR_A) from the unadjusted HR (HR_U) using the following equation and dividing the difference by the unadjusted hazard ratio.

$$\%\text{Excess Risk Explained} = \left[\frac{\left(HR_A - HR_U\right)}{\left(HR_U - 1.0\right)}\right] x100$$

The model rendering the HR_A included the SES indicator of interest and an intermediate variable while controlling for confounders (i.e. gender, age, and ARIC center). The model computing the HR_u is similar except it does not contain the mediator.

F.Multiple Imputation

Data was missing for some of the individual-level and contextual-level SES measures. For all of the individual-level SES measures except parental education in adulthood for both Whites and Blacks; and income for Blacks in adulthood, the amount of missing data was negligible, (<10%). however, 15.5% of the contextual-level SES in childhood was missing, largely due to the lack of availability of census data from the

earlier time periods. Thus, multiple imputation was utilized to compensate for the missing neighborhood-level SES data.[41, 42] Multiple imputation applies a series of possible data points from a set number of trials with an algorithm to obtain a single estimate for a missing data point, while factoring within and between variance of the imputation.[43] Gibbs sampling and Multivariate Imputation by Chained Equations were used to perform the multiple imputation with 10 iterations and five imputations using SAS version 9.1. It was also used to aggregate the estimates and incorporate between- and within-imputation variance for the summary estimates and 95% confidence intervals. All of the models converged.

G.Power Calculation

Since there is a lack of studies, which have investigated the association between individual SES in the context of neighborhood SES, pertinent information (i.e. R^2 and intra-class correlation) that is needed to calculate power for this dissertation proposal was unavailable. Thus, power calculations for the association between individual-level SES and incident HF were estimated for time-to-event analysis via N_Query Advisor 4.0. The power calculation presented was conducted for the primary aim, which was to assess the association between SES indicators and incident HHF. In the manuscript version with latest defintion for incident HHF, there were 168 events among blacks and 418 among whites. In Figure 6, the power attainable at different hazard ratios is indicated for whites and blacks, by the blackened and dotted lines, respectively. For whites, the minimum hazard ratios that can be detected with 80% and 90% power are 1.32 and 1.38 respectively. Among blacks, the minimum hazard ratios that can be detected at 70%, 80%, and 90% power are 1.48, 1.55, and 1.65, respectively.

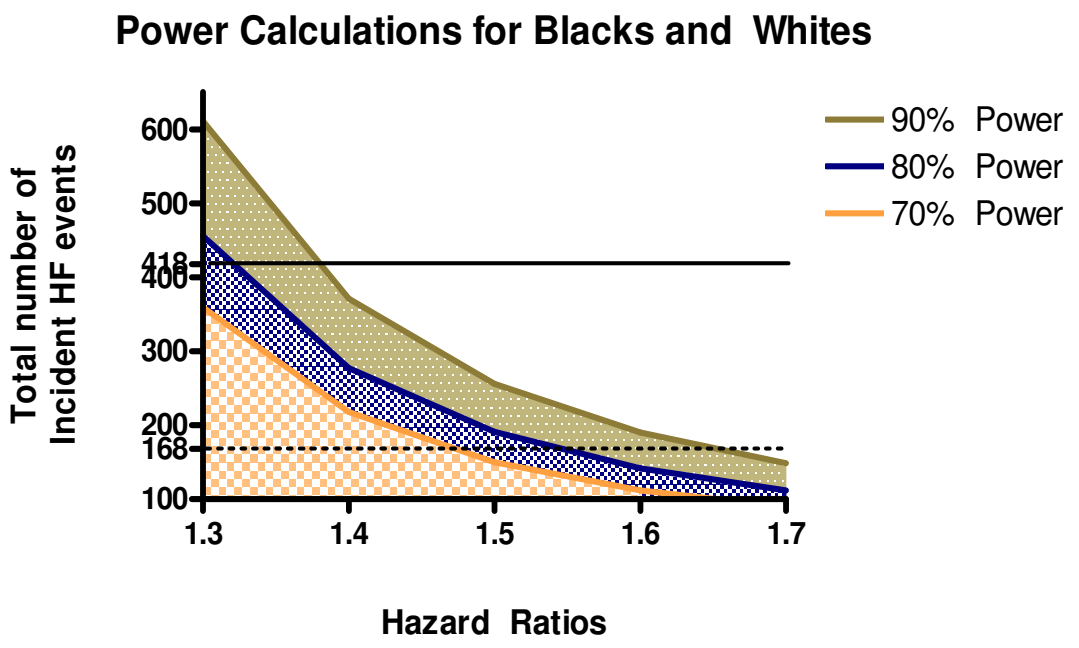

Figure 6 The level of power available to assess the association between SEP and incident HF for Blacks and Whites in the ARIC Study.

The following equation was used to generate the power. It is based on the log rank test and holds that assumption that the hazard ratio is constant throughout the course of the study.

$$n = \frac{(z_{\alpha/2} + z_{\beta})^2 (h+1)^2}{(2 - p_1 - p_2)(h-1)^2}$$

In the equation, p_1 and p_2 represent the proportion of participants who did not experience a HF event by the end of the study among those with high or low SES scores, respectively. The hazard ratio, h, is the natural log of p_1 divided by the natural log of p_2. The z_{β} and $z_{\alpha/2}$ symbolize the power and two-sided alpha level, respectively. The n symbolizes the total number of participants.

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CHAPTER VI. RESULTS

A.Manuscript 1: *"*Socioeconomic Position across the life-course and incident heart failure in Blacks and Whites: The ARIC Study*"*

1.Abstract

Background: The impact of socioeconomic position (SEP) over the life-course on incident heart failure (HF) is unknown. **Methods and Results:** The relation between SEP indicators over the life course and incident HF was assessed in black (n=2503) and white (n=8519) participants of the Atherosclerosis Risk in Communities (ARIC) study (1987-2004). Individual- level SEP was obtained for early childhood (at age 10 years), young-adulthood (at age 30 years), and mid-adulthood (45-64 years). Life-course SEP was generated by summing these SEP variables. Each SEP measure was dichotomized at the median. Race-specific hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox Proportional Hazard models and adjusted for pertinent confounders. The percentage of mediation contributed by intermediate variables was also estimated. After eighteen-years of follow-up there were 758 incident HF episodes (blacks n = 221; whites n = 537). SEP from young-adulthood had the greatest impact on incident HF in blacks [adjusted HR = 1.55 (95% CI: 1.14, 2.12)] followed by SEP in mid-adulthood then life-course SEP [adjusted HR = 1.29 (95% CI: 0.96, 1.72)]. For whites, young and mid-adulthood SEP were equally important predictors of HF as SEP over the life-course [adjusted HR = 1.45 (95% CI: 1.17, 1.80)]. Childhood SEP was not significantly associated

with the outcome. The impact of life-course SEP on HF was primarily mediated through access to health insurance in blacks and type II diabetes in whites.

Conclusions: SEP attained as early as in young-adulthood and over the life-course are important contributors of incident HF.

2.Introduction

Numerous studies have identified biological risk factors[3, 14, 17, 44-48], trends[24, 49-54], or medical therapies[55] for heart failure (HF). In contrast, few studies[13, 14, 21, 22] have addressed the associations between indicators of socioeconomic position (SEP) and incident heart failure despite the mounting evidence that socioeconomic attainment in early life and in adulthood are inversely related to salient biological risk factors (e.g. coronary heart disease[56, 57], hypertension[14, 45, 46], diabetes[14, 58, 59], and obesity[14, 46, 57]), behavioral characteristics (e.g. smoking, increased alcohol consumption, and lack of physical activity)[57], and access to medical care[60-62] which can exacerbate the risk of incident heart failure. Prior studies that have investigated the relation between socioeconomic exposures and incident HF have focused exclusively on individual-level[13-15] or contextual-level[21, 22] socioeconomic indicators attained mainly in mid- to older-adulthood. While HF is primarily diagnosed in older adulthood,[3] HF is considered to be a progressive and chronic syndrome that may originate decades prior to diagnosis[6] . Consequently, SEP that reflects socioeconomic circumstances in earlier life epochs (i.e. childhood or young-adulthood) or a SEP measure that captures the accumulation of socioeconomic exposures over the life course may exert a greater influence on the risk of incident heart failure than SEP in mid-to older adulthood taken alone. Hence, clarifying the predictive power of socioeconomic variables across the life-course could improve the ability to identify at-risk individuals.

Based on eighteen-years of follow-up in the bi-ethnic Atherosclerosis Risk in Communities Study, we investigated the impact of socioeconomic position at

childhood (at age 10 years), young-adulthood (at age 30 years), mid-adulthood (age 45-64 years), and over the life-course on the incidence of heart failure. We also ascertained the whether contextual-level SEP from each life epoch modifies these associations, and the pathways via which SEP mediates the onset of incident heart failure.

3.Materials and Methods

Study population

The Atherosclerosis Risk in Communities (ARIC) Study is an on-going bi-ethnic longitudinal cohort study designed to investigate the etiology of atherosclerosis and cardiovascular diseases. At baseline (1987-1989), 15,792 men and women, aged 45-64 years, were enrolled into the study from four communities: Forsyth County, North Carolina; Jackson City, Mississippi; Minneapolis, Minnesota; and Washington County, Maryland. Follow-up examinations occurred every three years after baseline until 1996 to1998. Telephone-calls have been made annually since 1987 to maintain contact with the participants and to ascertain their health status.

The Life Course Socioeconomic Status, Social Context, and Cardiovascular Disease (LC-SES) study is an ancillary study to, ARIC, which was conducted to evaluate the association between individual-level and contextual-level socioeconomic exposures over the life course and cardiovascular diseases. Of the 15,792 original ARIC cohort study members, n=12,716 (80.5%), were recruited into the LC-SES Study (2000-2001). Due to small sample size non-blacks and non-whites were excluded (n = 35). Blacks who did not reside in Jackson, Mississippi or Forsyth, North Carolina were also excluded since their numbers (n = 55) were

insufficient to control for possible heterogeneity by community. Participants with prevalent heart failure (defined using the Gothenburg criterion[31] (n= 752) or missing HF status (n=287) at the initial ARIC visit were also excluded in order to focus exclusively on incident heart failure events. Participants with missing data for any confounder or intermediate variable were also excluded for this complete case analysis. The final sample size consisted of 2503 blacks and 8519 whites.

Socio-economic Position

Twelve individual-level socioeconomic measures were collected for three life epochs to assess the impact of socioeconomic exposures across the life-course on incident heart failure. The socioeconomic indicators during childhood (at 10 years of age) and young-adulthood (at age 30 years) were collected retrospectively during the LC-SES study. Mid-adulthood socioeconomic measures were collected at the ARIC baseline visit when the participants were 45-64 years of age. Socioeconomic indicators during childhood were based on the educational level of the parent or caretaker who attained the highest degree (<8th grade, 9-11th grade, ≥12th grade); occupation status (manual or non-manual) and managerial occupational role (yes or no); and whether the participants' parent(s) or caretaker(s) owned their home (yes or no). The socioeconomic indicators in young adulthood were based on the participants' education (≤11th grade, high school graduate, some college or more), occupation (manual, homemaker, non-manual), managerial occupation role (yes or no), and home ownership (yes or no). SEP exposures in mid-adulthood consisted of household income (<$25,000, $25,000-50,000, ≥ $50,000), occupation (manual,

homemaker, non-manual), managerial occupation role (yes or no), and home ownership (yes or no).

The four socioeconomic indicators within each life epoch were summed in order to evaluate the relation between aggregate-level SEP from each life epoch and the outcome. The sum of the scores ranged from 0 to 5 in childhood, 0 to 6 in young-adulthood, and 0 to 6 in mid-adulthood with the higher values indicating lower SEP. The totals were dichotomized at the median separately for blacks and whites in order to control for any residual confounding due to race-related economic inequalities. Persons with values above the median served as the referent group.

A life-course SEP measure was created by summing the SEP indicator across the three life epochs. The total score ranged from 0 to 17 with the higher values indicating lower SEP. The variable was dichotomized at the median separately for blacks and whites. The median value for blacks was nine and seven for whites.

Contextual-level SEP

Residential information was obtained retrospectively during the LC-SES study for when the participants were 10, 30, 40, and 50 years of age. Childhood residential data at 10 years of age was linked to county-level socioeconomic census data since it was the most finite geographical unit for which census data was available for that period. Place of residence during young adulthood (age 30 years) and mid-adulthood (age 40 and 50 years) were geocoded and linked with tract-level census data. The SEP indices used for each life epoch were chosen based on indices from older adulthood that were found to be significantly predictive of coronary heart disease, [33] CVD mortality,[35] and ankle-branchial index[36] in the ARIC study

population. A z-score was created for each census index, and the z-scores were summed within each life epoch. Then the measures were dichotomized at the median into low and high contextual-level SEP separately for blacks and whites. For mid-adulthood the z-scores for the census level variables at ages 40-50 years were averaged. The life-course neighborhood z-score was created by summing the z-scores in each life epoch and dichotomizing the variable at the median by race.

Due to the minimal clustering within neighborhoods, hierarchical modeling was not used. Since there as a lack of interaction between individual-level SEP and neighborhood-level SEP, neighborhood-level SEP was treated as a potential confounder.

Covariates

The covariates age, ethnicity, and study center were collected at the initial ARIC visit. Age at the time of the ARIC baseline study was modeled as linear. The intermediate variables were also collected at baseline and included: hypertension, prevalent coronary heart disease, type II diabetes, body mass index (BMI), smoking status, drinking status, and left ventricular hypertrophy (LVH). Hypertension was defined as systolic blood pressure ≥ 140 mm/Hg or diastolic blood pressure ≥ 90 mm/Hg or taking antihypertensive medication. Prevalent coronary heart disease was determined by the presence of at least one of the following: Q waves on the Visit 1 ECG, history of myocardial infarction diagnosed by a physician, coronary bypass, or angioplasty of coronary arteries. Type II diabetes was defined as having fasting blood glucose level ≥ 126mg/dL, nonfasting blood glucose level ≥ 200 mg/dL, use of hypoglycemic medications, or self-reported physician diagnosis. BMI was calculated

as weight (kilograms) divided by height squared (meters) and categorized into normal (≥18.5-25 kg/m^2), overweight (≥25-30 kg/m^2) and obese (≥30kg/m^2). Smoking and drinker status at baseline (i.e. current, former, or never) were both self-reported. Cornell voltage left ventricular hypertrophy was evaluated by electrocardiograph.

The institutional review board for research on human subjects at the University of North Carolina approved the data collection protocol and the secondary data analyses for the present study.

Outcome

Incident HF was ascertained via annual contacts and review of medical records for all hospitalizations over an eighteen-year study period, baseline (1987-1989) through December 31, 2004. Incident HF was defined as the first occurrence of either an ICD-9 428 coded hospital discharge diagnosis or an underlying cause of death of 428 or ICD-10 150 among those without a previous record of a hospitalization with an ICD-9-CM code 428.[29]

4.Statistical Analysis

Cox proportional hazards regression was used to estimate the unadjusted and adjusted hazard ratios and 95% confidence intervals. Continuous time-covariate interactions were created and log(-log) survival plots were viewed to ensure that the proportional hazards assumption was not violated over the 18-year study period.

The proportion of excess risk explained by life-course SEP was computed for each intermediate variable to determine the likely biological and behavioral pathways for SEP. The proportion of the excess risk explained by SEP indicators

was calculated by subtracting the unadjusted hazard ratio (HR_U) from the hazard ratio obtained from the model adjusted for an intermediate variable (HR_A) and then dividing the difference by the unadjusted hazard ratio minus 1.0. [40]

$$\%\text{Excess Risk Explained} = \left[\frac{(HR_U - HR_A)}{(HR_U - 1.0)}\right] x100$$

Although the percentages of addresses successfully geocoded increased with each census decade (66% in 1960, 76% in 1970, 85% in 1980, and 95% in 1990)[34] nearly 20% of the contextual-level SEP data were missing. Multiple imputation was used to reduce selection bias due to missing values. The multiple imputation method applied a series of possible data points from a set number of trials with an algorithm to obtain a single estimate for a missing data point while factoring within and between variance of the imputation.[41, 42] A Bayesian Gibbs sampling algorithm was used to perform the multiple imputation with 500 iterations and 10 imputations. Statistical analyses were conducted using SAS, version 9.1.3 (SAS Institute, Inc., Cary, North Carolina).

5.Results

Selected health and demographic characteristics of the participants at baseline are shown in Table 1. Over the eighteen year follow-up period, more blacks (9 percent (221/2503)) than whites (6.3 percent (537/8519)) were diagnosed with incident heart failure. White and black participants who were diagnosed with incident HF were significantly older, and were more likely to be diabetic, hypertensive, overweight or obese, smokers, and more likely to have left ventricular hypertrophy and coronary heart disease, and to drink alcohol than those free of HF. Blacks with

incident HF during the study period were less likely have health insurance than those without HF.

As shown in Table 2, the overall age-adjusted incidence rate for incident HF was greater in blacks than whites, 5.23 (per 1,000 person-years) and 3.18 (per 1,000 person-years), respectively. The age-adjusted incidence rates of HF were higher in those with low compared to high SEP in each life epoch, irrespective of race.

Table 3 shows the adjusted hazard ratios for the association between incident heart failure each individual-level socioeconomic variable from childhood into adulthood. The majority of the individual-level socioeconomic variables in each life epoch were inversely related to the outcome. Socioeconomic variables in early life were the least predictive of incident heart failure. Of the socioeconomic exposures obtained for childhood SEP, parental education ($\leq 8^{th}$ vs. $\geq 12^{th}$ grade) had the greatest impact on incident HF. Education and income were the socioeconomic measures most predictive of HF in adulthood, irrespective of race. Blacks with $\leq 11^{th}$ grade compared to those with some college or greater in young-adulthood had nearly a 2-fold increase in incident HF during the study period [HR = 1.82 (95% CI: 1.30, 2.55)] and more than 2-fold in Whites [HR = 2.16 (1.71, 2.73)].

Figure 1 displays covariate-adjusted associations between the individual-level SEP variables aggregated in each life epoch, and incident HF. Each SEP measure was inversely associated with the outcome, although, the effect SEP in early childhood was not statistically significant. Of the SEP measures, SEP attained in young-adulthood showed the strongest association with incident HF [HR = 1.55 (95% confidence interval: 1.14, 2.12)] among blacks. For whites, SEP in young or

mid-adulthood and cumulative life-course SEP [adjusted HR = 1.45 (1.17, 1.80)] showed a similarly increased hazard of incident heart failure.

Table 4 summarizes the estimated excess risk for the unadjusted association between life-course SEP and incident HF as explained by each of the candidate intermediate variables. In blacks, the magnitude of the association between life-course SEP and incident HF was attenuated the most after adjusting for health insurance followed by type II diabetes, which resulted in 32.7% and 30.6% reduction, respectively. In whites, mediation through the candidate intermediate variables was not as strong as in blacks, but the findings for type II diabetes, alcohol drinking status, and hypertension suggested mediation effects. Adjusting for age, gender, center and all of the intermediate variables listed in Table 4 accounted for the association between life-course SEP and incident HF in blacks (100%) and more than half of the relation in whites (60.3%).

6.Discussion

Heart failure is a growing public health concern. The findings from this study highlight that SEP attained in early life can predict an increased hazard of incident heart failure.

Individual-level measures of childhood socioeconomic exposures, in particular parental education in whites and parental home ownership in blacks, were associated with approximately a 50% increase in the risk of incident HF. Parental education (≤ 8^{th} grade versus ≥12^{th} grade) was marginally associated with the outcome in blacks. However, an aggregate measure of childhood SEP was not significantly related to the outcome. This suggests that the etiology of HF may be

differentially related to socioeconomic factors in childhood. Parental education may have the greatest influence through healthier behaviors and/or greater opportunities for the offspring to achieve health promoting life trajectories. We are not aware of any prior studies that have examined this association, but our results are consistent with previous studies showing that parental social class, education, and occupation were inversely associated with the risks of other CVD outcomes, including coronary heart disease, myocardial infarction, stroke mortality, and CVD mortality.[12, 63-68]

As observed in other studies, individual-level socioeconomic exposures adulthood were significantly inversely associated with incident HF.[13-15] However, this is the first study to distinguish between SEP in young adulthood versus mid-to older adulthood. This is pertinent since experiences in young adulthood may have a longer lasting effect than SEP in mid-to older adulthood and it may determine an individual's experiences in mid- and older adulthood. In our data on blacks, we observed that an aggregate SEP measure in young-adulthood has a stronger effect than SEP in mid-adulthood. These differences were not evident for whites. The increased risk observed in young-adulthood for blacks, but not whites is in congruence with national statistics which indicate that blacks have a higher prevalence of hypertension at younger ages than their white counterparts.[69, 70] This is also in accordance with the manifestation of heart failure at younger ages in blacks than whites in this study. These findings suggest that critical periods for HF susceptibility may vary by race.

Life-course SEP was a strong predictor of incident HF in blacks and whites, supporting the proposition that there is a cumulative effect of diverse socioeconomic

experiences over the life-course. However, the effect of life-course SEP was not greater than the effects for SEP in mid-adulthood, which indicates that adulthood-level SEP may be an adequate measure of SEP for these purposes.

To our knowledge this is the first study to incorporate individual-level and contextual-level SEP in studies of incident HF. We observed that contextual-level SEP was not associated with incident HF, and that it slightly modified the effects of the individual-level SEP variables (results not shown). Other studies have reported in the absence of individual-level measures that neighborhood-level SEP is an independent predictor of HF. [21, 22] The lack of association seen in our study could reflect limited heterogeneity between the neighborhoods in our study. Supporting the accuracy of our neighborhood-level SEP measure the kappa statistic was 0.90 in a sample of 1,000 LC-SES participants.[34]

Mediation is pertinent to understanding the pathways in which SEP affects incident HF since SEP is reflected in behaviors or risk factors that antecede HF. The findings from this study reveal that there maybe ethnic differences in the way that life-course SEP operates to influence incident HF. Our observations that health insurance is the leading mediating factor for the risk of incident HF in blacks suggests that limited access to resources and/ or health care adversely affects the natural history of heart failure outcomes. If replicated, this finding has implications for policies in the areas of health disparities. In whites, type II diabetes and alcohol consumption at baseline were the prominent mediating factors. Participants who were diabetics or current drinkers at baseline were more likely to have coronary heart disease, and be overweight, obese, and hypertensive (results not shown).

Alcohol intake has been linked to elevated blood pressure[71], and to increased risk of coronary heart disease[71] and left ventricular mass[72], which are risk factors of incident heart failure.

There are several limitations to this study. Inherent in collecting SEP retrospectively there is the chance of recall and self-report bias, although we expect that the observed estimates would be biased toward the null since it is more likely that disadvantaged participants inflated their SEP. Approximately 95% of ARIC cohort members were alive at the time of the LC-SES survey, and although the majority of the participants from the ARIC cohort (80.5%) were enrolled into the LC-SES survey, there is a chance of selection bias. The cohort members who did not enroll into the LC-SES survey were older, more frequently male, and had lower education and family income. This may have biased the estimates towards the null. Lastly, only southern blacks were included in the study, thus, the findings may not be representative of blacks living in other regions of the United States.

This study has several strengths worth highlighting. This is the first study to document the association between SEP in childhood and also over the life-course. In addition, various individual-level and contextual-level socioeconomic measures were collected across three life epochs, which allowed for multiple comparisons and an opportunity to synthesize a life-course measure. To our knowledge, this is also the first study to report the association between SEP and incident HF in blacks, a group particularly susceptible to this condition. Lastly, cohort follow-up was high and incident HF events were ascertained from medical reports, thus reducing the chance of bias.

In the face of an aging population and increasing life expectancy and economic inequality in the United States, [73] these results provide opportunities for strategies toward reducing the burden of this disease in all segments of the US population.

Table 11. (Manuscript 1, Table 1) Selected health and demographic characteristics of participants measured at the ARIC baseline examination by ethnic group and incident heart failure status, ARIC LC-SES study.

Characteristics	Blacks			Whites		
	With HF (n=221)	Without HF (n=2282)	p-value	With HF (n= 537)	Without HF (n=7982)	p-value
Age (yrs) (mean) ± SD	55.2±5.7	52.6±5.6	<0.0001	56.7±5.2	53.7±5.6	<0.0001
Male (%)	38.5	35.9	0.4472	57.4	45.0	<0.0001
Body Mass Index (kg/m^2)						
≥25 – 30 (kg/ m^2)	34.8	39.5	<0.0001	40.2	40.4	<0.0001
≥30 (kg/ m^2)	54.3	38.3		38.6	19.7	
Type II Diabetes (%)	38.5	12.3	<0.0001	19.6	6.2	<0.0001
Hypertension (%)	67.4	48.9	<0.0001	42.8	22.3	<0.0001
Left Ventricular Hypertrophy‡ (%)	12.2	4.7	<0.0001	2.6	0.8	<0.0001
Prevalent CHD (%)	7.2	1.8	<0.0001	13.6	2.6	<0.0001
Current Smoker (%)	32.1	24.8	0.0170	30.5	20.3	<0.0001
Current Drinker (%)	22.2	32.8	0.0012	59.0	66.8	0.0002
Health Insurance (%)	68.8	80.3	<0.0001	94.4	96.0	0.0774
Center:						
Jackson City (%)	92.8	90.2	0.2213	--	--	<0.0001
Washington County (%)	--	--		41.5	33.0	
Minneapolis Suburbs (%)	--	--		27.8	36.5	
Forsyth County (%)	7.2	9.8		30.7	30.4	

*All exposure variables were measured at the cohort baseline examination (Visit 1).
†P-values were generated by chi -square for categorical variables and t-test for continuous exposures.
‡Left Ventricular Hypertrophy was determined by electrocardiograph.

Table 12. (Manuscript 1, Table 2) Age-adjusted incidence rates per 1,000 person-years and 95% confidence intervals.

Life Epoch	Blacks (n= 2503)				Whites (n=8519)			
	HF	Person-years	HF incidence	95% CI	HF	Person-years	HF incidence	95% CI
Overall	221	39,554	5.23	(4.32, 6.33)	537	136,510	3.18	(2.81, 3.60)
Childhood SEP*								
Low	151	26,212	5.31	(4.29, 6.28)	255	58,627	3.63	(3.18, 4.15)
High	70	13,342	5.07	(4.00, 6.42)	282	77,883	3.38	(2.99, 3.82)
Young-Adulthood SEP†								
Low	165	24,671	6.01	(4.96, 7.28)	213	43,339	4.06	(3.51, 4.71)
High	56	14,883	3.91	(2.88, 5.31)	324	93,171	3.22	(2.86, 3.62)
Mid-Adulthood SEP‡								
Low	167	25,346	5.98	(4.87, 7.34)	272	51,993	4.34	(2.86, 3.62)
High	54	14,208	3.87	(2.76, 5.41)	265	83,977	2.96	(2.55, 3.42)
Life-course SEP§								
Low	149	23,104	5.76	(4.67, 7.07)	296	58,716	4.19	(3.62, 4.85)
High	72	16,450	4.48	(3.80, 5.92)	241	83,194	2.95	(2.54, 3.43)

Adjusted to mean age at baseline.

*Childhood SEP was generated by summing four individual-level socioeconomic indicators pertaining to the participant's parents SEP collected retrospectively during the LC-SES study in 2001 for when the participant was 10 years of age, and dichotomized at the median.

†Young-adulthood SEP was generated by summing four individual-level socioeconomic indicators during young-adulthood which were collected retrospectively during the LC-SES study in 2001 for when the participants were 30 years of age, and dichotomized at the median.

‡Mid-adulthood SEP was ascertained by summing four individual-level socioeconomic indicators at the time of the ARIC baseline study, and dichotomized at the median.

§Life-Course SEP was created by summing individual-level SEP in childhood, young-adulthood, and mid-adulthood, and then dichotomized at the median.

Table 13. (Manuscript 1, Table 3) Adjusted* hazard ratios and 95% confidence intervals (CI) for the association between individual-level socioeconomic exposures over the life-course and incident heart failure by ethnic group in the ARIC LC-SES study.

Socioeconomic Exposures	Blacks Hazard Ratio (95% CI) (N=2503)	Whites Hazard Ratio (95% CI) (N=8519)
Childhood †		
Parental Education		
≤ 8th grade	1.49 (0.99, 2.23)	1.56 (1.24, 1.90)
9-11 grade	1.10 (0.64, 1.89)	1.31 (1.01, 1.70)
≥ 12th grade	1.00	1.00
Parental Occupation		
Manual	1.45 (0.84, 2.47)	1.16 (0.96, 1.40)
Non-manual	1.00	1.00
Parental Occ. Role		
Not a Manager	0.93 (0.69, 1.25)	1.19 (1.00, 1.41)
Manager	1.00	1.00
Home Ownership		
No	1.42 (1.08, 1.87)	0.95 (0.78, 1.15)
Yes	1.00	1.00
Young Adulthood‡		
Education		
≤11th grade	1.82 (1.30, 2.55)	2.16 (1.71, 2.73)
HS Graduate	1.42 (0.98, 2.06)	1.26 (1.03, 1.55)
Some College or Greater	1.00	1.00
Occupation		
Manual	1.60 (1.15, 2.20)	1.18 (0.96, 1.44)
Homemaker	1.46 (0.90, 2.37)	0.95 (0.73, 1.25)
Non-manual	1.00	1.00
Occupational Role		
Not a Manager	1.31 (0.80, 2.17)	0.99 (0.80, 1.24)
Manager	1.00	1.00
Home Ownership		
No	1.02 (0.78, 1.33)	1.22 (1.02, 1.47)
Yes	1.00	1.00
Mid- Adulthood§		
Income		
≤$25,000	1.98 (0.97, 4.07)	1.87 (1.47, 2.39)
$25,000-$50,000	1.42 (0.66, 3.05)	1.30 (1.03, 1.64)
≥$50,000	1.00	1.00
Occupation		
Manual	1.05 (0.79, 1.39)	1.42 (1.18, 1.72)

Homemaker§	1.44 (0.92, 2.27)	1.22 (0.88, 1.69)
Non-manual	1.00	1.00
Occupational Role		
Not a Manager	1.74 (1.17, 2.58)	1.25 (1.00, 1.55)
Managerial	1.00	1.00
Home Ownership		
No	1.50 (1.10, 2.04)	1.74 (1.33, 2.29)
Yes	1.00	1.00

*Age was adjusted for in examining the association between each individual-level childhood SES measure and incident heart failure in Blacks. Age, gender, and center were adjusted for in examining the association between individual-level SES measures in young and mid-adulthood in Blacks and Whites.
†Parental socioeconomic indicators were collected from the participants retrospectively during the LC-SES study in 2001 for when the participants were 10 years of age.
‡Socioeconomic indicators during young-adulthood were collected retrospectively during the LC-SES study in 2001 for when the participants were 30 years of age.
§Socioeconomic indicators during mid-adulthood were collected during baseline of the ARIC study for the age of the participant at baseline.

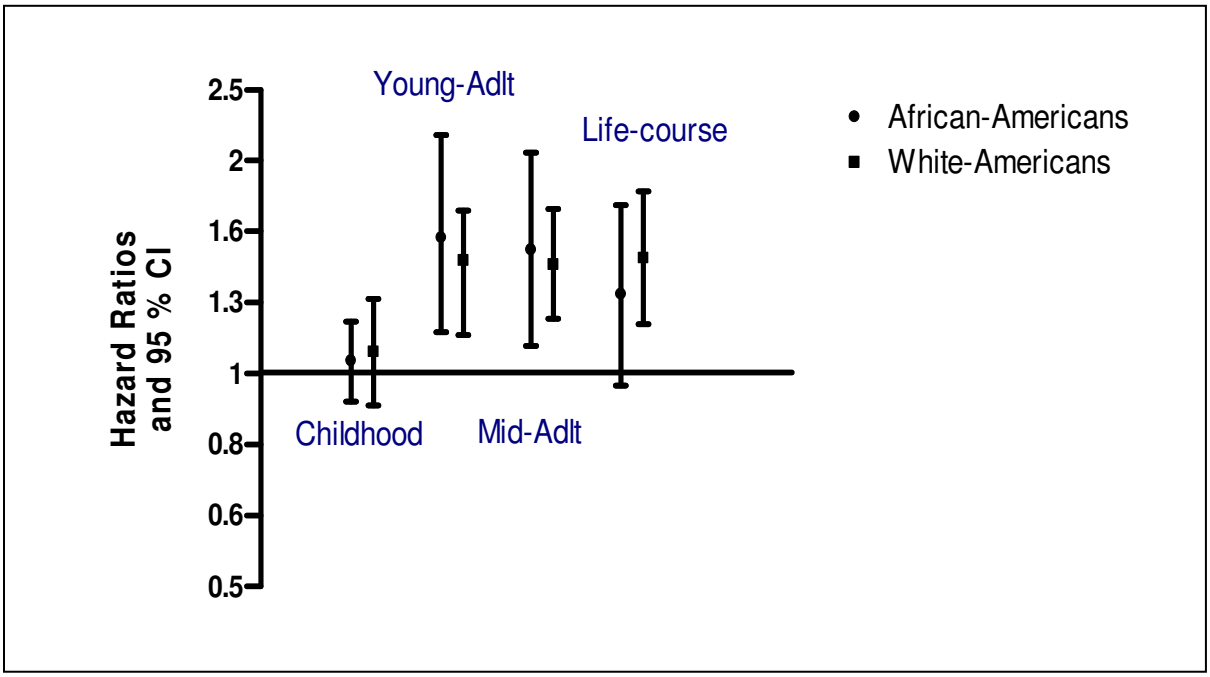

Figure 7 The adjusted hazard ratios for the association between aggregate-level SEP in each life epoch and incident heart failure by ethnicity among Blacks and Whites in the ARIC study (1987-2004).
Circles and squares represent the adjusted hazard ratios for Blacks and Whites, respectively. Bars, 95% confidence interval (CI). Hazard ratios are adjusted forage, gender, center, and neighborhood level SEP.
*Young-Adlt = Young Adulthood
†Mid-Adlt = Mid-Adulthood

Table 14. (Manuscript 1, Table 4) Estimated percentage of the hazard ratio and 95% confidence intervals (CI) between life-course (low vs. high) socioeconomic position (SEP)* and incident heart failure explained by candidate intermediate variables for blacks and whites in the ARIC LC-SES study.†

Covariate	Blacks	% Δ§	Whites	% Δ§
	HR (95% CI)		HR (95% CI)	
Unadjusted (Low/High):	1.49 (1.12, 1.97)		1.63 (1.37, 1.93)	
Fully adjusted (Low/High)‡:	1.00 (0.75, 1.34)	100.0	1.25 (1.04, 1.51)	60.3
Intermediate variables adjusted for:				
Body Mass Index	1.39 (1.05, 1.85)	20.4	1.56 (1.32, 1.85)	11.1
Type II Diabetes	1.34 (1.01, 1.78)	30.6	1.55 (1.30, 1.83)	12.7
Hypertension	1.40 (1.06, 1.86)	18.4	1.56 (1.32, 1.85)	11.1
Left Ventricular Hypertrophy	1.46 (1.10, 1.93)	6.1	1.61 (1.36, 1.91)	3.2
Prevalent coronary heart disease	1.47 (1.11, 1.95)	4.1	1.61 (1.36, 1.91)	3.2
Current Smoker	1.47 (1.11, 1.95)	4.1	1.58 (1.33, 1.88)	7.9
Current Drinker	1.41 (1.06, 1.87)	16.3	1.55 (1.30, 1.85)	12.7
Health insurance	1.33 (1.00, 1.78)	32.7	1.61 (1.36, 1.91)	3.2

* Life-Course SEP was created by summing the individual-level SEP variables in childhood, young-adulthood, and mid-adulthood, and then dichotomized at the median.

† % Δ is the Excess Risk explained by each intermediate variable, and was calculated as: [HR (unadjusted) – HR (adjusted)] / [HR (unadjusted)-1] x 100%.

‡ Adjusted for age, gender, body mass index, type II diabetes, hypertension, left ventricular hypertrophy, prevalent coronary heart disease, current smoking status, current drinking status, health insurance, and center.

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B. Manuscript 2: "The impact of socioeconomic position in adulthood on survival post-hospitalization for incident heart failure: The Atherosclerosis Risk in Communities (ARIC) Study"

1.Abstract

Background: The influence of individual-level socioeconomic position (SEP) on survival following an incident heart failure (HF) event has yet to be elucidated. **Methods and Results:** Age-adjusted Cox proportional hazards regression was utilized to compare the effect of individual-level indicators of SEP (e.g. income, occupation, occupational role, health insurance) and neighborhood-level SEP at ages 50 and 60 years on 10-year case fatality in middle-aged black (n = 406) and white (n=882) participants in the Atherosclerosis Risk in Communities (ARIC) study who were hospitalized for an incident HF event between1987-2004. The association between traditional risk factors of HF and HF case fatality were also reported. Fifty-seven percent of blacks and 50.3% of whites died during the study period. Age-adjusted ten-year case fatality was similar for black and white men, 96.2% and 97.4%, respectively, but remained significantly higher in black woman (82.7%) than in white women (77.3) (p=0.01). Health insurance (no versus yes) showed the strongest association with long-term survival (i.e. 10 years) in blacks [HR = 1.26 (95% CI: 0.97, 1.65)] and in whites who survived for three or more years [HR = 2.12 (95% CI: 1.29, 3.51)]. Neighborhood-level SEP was not predictive of survival. Type II diabetes, history of stroke or transient ischemic attack, and drinking status were the strongest predictors for blacks, while gender, prior coronary heart disease, type II diabetes, and body mass index were the strongest predictors in whites. **Conclusion:** A lack of health insurance may have a major role in explaining excess case fatality.

2.Introduction:

Despite significant improvements in survival in patients with heart failure (HF)[24, 44, 50, 53] case fatality remains high.[74] The association between low socioeconomic position and shorter survival following myocardial infarction is well-established.[75] In contrast, the association between socioeconomic exposures (e.g. income) and case fatality following an incident heart failure event is less clear. Several studies have found that census-based neighborhood-level socioeconomic position (SEP) shares a modest to null relation with short to long-term case fatality following an incident heart failure event.[23-26] However, to our knowledge, no study has investigated the influence of individual-level SEP on survival in patients following an incident HF event. Since individual-level SEP indicators directly reflect one's access to health promoting resources and prestige[76] they may exert an even greater influence on survival after an incident HF event than neighborhood-level SEP characteristics since the latter are merely an indicator of surrounding social and economic resources.

With fifteen-years of follow-up, we estimated the impact of income, occupation, occupational role, and health insurance attained in adulthood on case fatality in participants with an incident hospitalized heart failure occurring between 1987-2004 in middle-aged blacks and whites in the Atherosclerosis Risk in Communities (ARIC) study. In addition, we compared the influence of the SEP variables with neighborhood-level SEP and traditional behavioral and clinical risk factors of HF. Lastly, we determined whether neighborhood-level SEP modifies these associations.

3.Materials and Method

Study population

The Atherosclerosis Risk in Communities (ARIC) Study is an on-going bi-ethnic longitudinal cohort study designed to investigate the etiology and community burden of atherosclerosis and cardiovascular diseases. At baseline (1987-1989), 15,792 men and women, aged 45-64 years, were enrolled into the study from four communities: Forsyth County, North Carolina; Jackson City, Mississippi; suburbs of Minneapolis, Minnesota; and Washington County, Maryland. Follow-up examinations occurred every three years after baseline until 1996 to1998. Telephone-interviews have been made annually since 1987 to maintain contact with the participants and to ascertain their health status.

To evaluate the relation between SEP and case fatality, several exclusions were made. Non-blacks and non-whites were excluded (n = 48) due to a small sample size. Blacks who did not reside in Jackson, Mississippi (n=538) were also excluded since the majority of the black participants (87.4%) were recruited from Jackson, Mississippi. Participants with missing HF status (n=279) or participants with prevalent heart failure at the time of baseline (n=695), defined as a score of 3 or more on the Gothenburg criterion,[31] were excluded. After these exclusions the study population consisted of 13,035 participants. During the course of the study there were 1,362 HF events. Participants who were not hospitalized for at least one day after the onset of the HF event (n=74) were excluded. Thus, the final study size consisted of 1,288 participants who were diagnosed with an incident hospitalized HF event (n = 406 blacks and n=882 whites).

Outcome

Case fatality, was defined as a death occurring from any cause following an incident hospitalized HF event with at least an one day hospital stay for HF from 1987 through December 31, 2004. Incident HF was defined as the first occurrence of either a hospitalization which included an International Classification of Diseases, 9th revision, discharge code 428 (428.0 to 428.9) in any position or a death certificate with a 428 (HF) or International Classification of Diseases, 10th revision, code I50 (HF) in any position from baseline (1987-1989) until December 31, 2004.[29]

Individual-level Socio-economic Status

The individual-level socioeconomic measures for adulthood (45-64 years) were ascertained at ARIC baseline (1987-1989). The SEP exposures included health insurance (yes vs. no), family income (low vs. high), occupation (manual and non-manual), and managerial occupation role (yes vs. no). Income was dichotomized at the median into low and high groups separately for blacks and whites in order to control for any residual confounding that may exist between blacks and whites due to historical racial inequalities. The median income category for blacks was from $8,000 to $11,999 and it was $25,000 to $34,999 for whites. Homemakers constituted 11.1% of the participants, and were grouped with the manual workers since the risk of CF was similar in these two groups.

In order to generate an aggregate measure of SEP in mid-adulthood, the four individual-level socioeconomic indicators were summed. The sum of the scores ranged from 0 to 4. The total was dichotomized at the median into low versus high SEP, again separately, for blacks and whites.

Contextual-level SEP

Census data was collected and geocoded for the residence of the participants at ages 50 and 60 years. Census block groups were used as proxies for neighborhoods. The following census variables were used in approximating contextual-level SEP: median household income; median value of housing units; the percentage of households with interest, dividend, or rental income; the percentage of adults residents who completed high school; the percentage of adult residents who completed college; and the percentage of employed residents with executive, managerial, or professional occupations. These six variables were identified as the strongest SEP predictors of coronary heart disease using factor analysis in a previous analysis,[33] and were significantly related to CVD mortality[35] and ankle-branchial index[36] in the ARIC cohort. A z-score, a measure of the deviation from the mean, was estimated for each census variable separately for blacks and whites. The z-scores were summed to create neighborhood summary score (i.e. neighborhood-level SEP). Due to a minimal degree of clustering within neighborhoods and a lack of interaction between neighborhood-level SEP and individual-level SEP, the neighborhood-level SEP variables were treated as potential confounders.

Covariates

Covariates at the closest visit prior to the incident HF event were included in the analysis. Sitting blood pressure was measured three times and the last two measurements were averaged to determine systolic and diastolic blood pressure levels. Pulse pressure was defined as systolic blood pressure minus diastolic blood pressure. Hypertension was defined as a systolic blood pressure ≥ 140 mm/Hg or

diastolic blood pressure ≥ 90 mm/Hg or antihypertensive medication use during the previous two weeks. Prevalent coronary heart disease was determined by the presence of at least one of the following: myocardial infarction from adjudicated Visit 1 ECG data, history of myocardial infarction diagnosed by a physician, coronary bypass, or angioplasty of coronary arteries. Participants with fasting blood glucose level ≥ 126mg/dL, non-fasting blood glucose level ≥ 200 mg/dL, use of hypoglycemic medications in the last two weeks, or self-reported history of physician diagnosis were considered to have type II diabetes. Fasting total plasma cholesterol (mmol/L) was collected using standardized methods.[77] Weight and height were measured by trained interviewers, and body mass index was calculated as weight (kilograms) divided by height squared (meters). Smoking cigarettes and drinking status (ever vs. never) were self-reported. The Cornell criterion was used to identify the presence of left ventricular hypertrophy via electrocardiograph.

The institutional review board for research on human subjects at the University of North Carolina approved the data collection protocol and the secondary data analyses for the current study.

4.Statistical Analysis

Comparisons of demographic and socioeconomic measures were stratified by race. Age-adjusted case fatality percentages and 95% confidence intervals were generated for race and gender groups using Cox proportional hazards regression. Age-adjusted hazard ratios and 95% confidence intervals stratified by race were also estimated via Cox proportional hazards regression. The proportional hazards assumption was verified by examining continuous time interactions and log(-log)

survival plots. Due to the violation of proportional hazards assumption for type II diabetes, BMI, LVH, and health insurance, the hazard ratios are presented for time points before and after the log(-log) survival curves crossed.

Although the percentages of addresses successfully geocoded increased with each census decade, nearly 30% of the census level variables were missing due in part to inaccurate or insufficient address information. To reduce potential selection bias, multiple imputation was used to compute values for missing census level variables by applying a series of possible data points from a set number of trials with an algorithm to obtain a single estimate for a missing data point, while factoring within and between variance of the imputation.[41, 42] A Bayesian Gibbs sampling algorithm was used to perform the multiple imputation with 750 iterations and fifty imputations. All statistical analyses were conducted using SAS, version 9.1.3 (SAS Institute, Inc., Cary, North Carolina).

5.Results

Over the course of the follow-up period, 57.1% (232/406) blacks and 50.3% (444/882) whites had died (Table 1) after being diagnosed with incident HF. The median survival following an incident hospitalized HF event was 2.08 ± 2.61 years and 2.16 ± 2.87 years for blacks and whites, respectively. Table 1, shows the demographic and clinical characteristics measured at the latest visit prior to hospitalization for an incident heart failure. Those who died were significantly older compared to participants who survived during the study period. There were also a few apparent racial differences between survivors and non-survivors. For instance, among white decedents cardiovascular disease risk factors such as pre-existing

CHD, type II diabetes, obesity, and gender were more common. This was not evident for blacks. In blacks, other cardiovascular disease risk factors (i.e. hypertension and drinking status) were more prevalent among survivors. Survivorship was also higher in blacks with health insurance and whites with a manual occupation at baseline.

In Table 2, age-adjusted short to long-term case fatalities following an incident hospitalized HF episode are shown by race and gender. The 6-month case fatality was nearly identical for race and gender groups: 19.7% in black men and 19.8% in white men (p= 0.2628); 18.7% in black women and 17.6% in white women (p=0.6446). Case fatality began to diverge at three-years, with blacks having a greater case fatality than their white counterparts. By the five-year case fatality, black men had a higher case fatality than their white counterparts after adjusting for age, but the results were not statistically significant (p=0.1985). For women, at five years there was a significantly higher proportion of black women dying than white women (p=0.0301). As survival time approached the 10^{th} year, case fatality became more comparable in black and white men, 96.2% and 97.4%, respectively. However, 10-year case fatality was still significantly higher in black women (82.7%) than white woman (77.3%) (p=0.0129).

In Table 3, the age-adjusted hazard ratios and 95% confidence intervals are presented for the association between the SEP indicators and incident hospitalized HF. The age-adjusted hazard ratios varied for the different socioeconomic indicators with health insurance being one of the more predictive variables in both blacks and whites. There was a 26% increased hazard of 10-year case fatality in blacks (95%

CI: 0.97, 1.65) and more than 2-fold increase in whites for three or more years of survival following an incident HF event [HR = 2.12 (95% CI: 1.29, 3.51)]. The aggregate measure of SEP (i.e. cumulative SEP) in blacks was marginally associated with a reduction in survival [HR = 1.19 (95%CI: 0.92, 1.54)]; however, the results were not statistically significant. For whites, the aggregate measure had no relation with the outcome. The magnitude of the effect for the participants' neighborhood at ages 50 and 60 years were close to null. Traditional cardiovascular risk factors exhibited different effects in black and whites. For instance, age, gender, prior CHD, and BMI were significantly associated with 10-year case fatality in whites, but not in blacks. Type II diabetes and history of stroke or TIA were the most influential risk factors of long-term survival in blacks while obesity was in whites [HR= 4.41 (95% CI: 1.46, 9.90)]. Prior CHD, being overweight, and type II diabetes also significantly reduced survival in whites.

In Figures 1a-b, the probability of survival in patients hospitalized with incident HF is shown by race for health insurance and cumulative SEP. The survival curves were statistically different for blacks and whites with and without health insurance (p=0.0242). This was also evident for cumulative SEP (p = 0.0415). For each SEP variable, whites and blacks with an adverse value had a lower survival than compared to participants with higher values. Moreover, blacks with high or low value for each SEP measure had a lower probability of survival than whites.

6. Discussion

To date, studies of the association between socioeconomic variables and survival post-hospitalization for an incident heart failure event have used neighborhood-level

variables,[23-26] and with the exception of the National Heart Failure Project, these studies were conducted in predominantly white populations.[26] In the current study, the effects of four individual-level variables, income, health insurance, occupation, and occupational role were examined to determine whether they were predictive of survival in patients hospitalized with incident HF. The relations between the individual-level variables and the outcome were observed to be heterogenous. Health insurance showed the greatest association with 10-year case fatality in both blacks and whites. This is an important finding since it suggests that survival after being admitted to a hospital for heart failure is predicated on health insurance status. In prior studies, the type of health insurance has been linked to properties of HF admissions which could affect survival, such as hospital length of stay[78] and being the recipient of specialty cardiac care.[79] The association between the individual-level SEP variables was not altered significantly after adjusting for all of other traditional risk factors of HF (results not shown), which suggests that these variables do not confound their relation with HF case fatality.

In this study, individual- and neighborhood-level SEP were independently related to the outcome. Neighborhood-level SEP at ages 50 and 60 years did not influence survival in this study population. In subsequent analyses, adjusting for neighborhood-level SEP did not attenuate or increase the association between each individual-level SEP variable and the outcome (results not shown). The null effect of census block neighborhood-level SEP at ages 50 and 60 on survival in addition to lack of modification between individual-and neighborhood-level SEP indicate that factors within neighborhoods did not influence survival.

The association between neighborhood-level SEP and the outcome has been examined in several European studies and in US medicare recipients. Multi-level analysis was not used in these studies. A modest to null inverse association, was also seen in prior studies.[23-26, 80] In a large prospective hospital based study conducted in Scotland, MacIntyre et al. reported that neighborhood deprivation (most deprived compared to the least deprived) based on the Carstairs Deprivation scale was slightly associated with 30days to 10-year CF in men [HR = 1.10 (95% CI: 1.05, 1.16)] and women [HR = 1.06 (95% CI: 1.02, 1.11).[24] In another study conducted in the United Kingdom, residents of the least deprived did not significantly have a greater hazard of HF case fatality [HR = 0.94 (95% CI: 0.87, 1.01)].[25] In a population of US medicare recipients, neighborhood SEP, defined using census block data, was associated with 1-year mortality [HR = 1.10 (95% CI: 1.02, 1.19)] in men and women.[26] Short-term case fatality (less than two years) was higher in Italian neighborhoods (block groups) with low (11.6%) versus high income (7.2%).[23] It should be noted that neighborhood-level SEP specifically at ages 50 and 60 years were examined in this study, and that other studies used census data from a larger age range; hence the comparability across studies is uncertain. Moreover, different indices (e.g. percent of residents with at least an high school education) were utilized in these studies to define neighborhood-level SEP.

Since the impact of the individual-level SEP variables were not significant additional comparisons were made between the outcome and the traditional risk factors of HF. Overall, clinical and demographic variables measured at the closest visit prior to the incident HF event were shown not be predictive of survival after an

incident HF event in blacks and whites. In the Framingham study, history of hypertension, SBP, DBP, and cigarette use which were measured at the latest examination prior to HF were also not significantly related to survival in univariate analysis. As in the Framingham study for women, type II diabetes was a pertinent predictor of reduced survival post-hospitalization.[52] In other studies, baseline characteristics were utilized and the results are mixed with a history of coronary heart disease, type II diabetes, and hypertension being significant in some[24], but not others[51, 81]. In all of these studies, and in this study (except for blacks) increased age was a potential harbinger of reduced survival.

Short-term case fatality percentages (i.e. less than 3 years) in this study were similar for the different race and gender groups, but diverged thereafter. Case fatality began to converge again for black and white men as they neared the ten-year mark after being hospitalized for incident HF. However, white women consistently had lower case fatality than black women. A comparison of short-term case fatality (i.e. less than 5 years) in blacks and whites by gender has been reported previously by Loehr et al. in an ARIC study.[82] This is the first study to report race-specific long-term (i.e. greater than five years) case fatality estimates. Moreover long-term case fatality has been reported in only a few studies.[24, 51, 52] In the Rochester Epidemiology Project (mean age = 75.0 ± 14.7 years), observed that for men that 10-year case fatality was 100% and approximately 75% in women. In the Framingham Heart study (mean age = 41.0 ±10years), case fatality was also worse in men (85%) than in women (71%). A large Scottish hospital study (median age = 72 in men and 78 years in women) reported that 10-year case fatality was similar in

men (87%) and women (88%). Long-term case fatality in these studies was also relatively high, pointing to the generally grim prognosis for heart failure in older populations.

There are several limitations in this study. The Gothenburg criterion was used to define prevalent heart failure events at baseline. It has a sensitivity of 84% and a specificity of 81% and was assessed only in White men in an earlier study[31]; thus, there is a chance of potential misclassification for this biracial cohort. Additionally, there was a lack of heterogeneity in the SEP variables, especially for blacks. This may have reduced our ability to detect an association between the SEP indicators and CF. Since the SEP variables were collected at ARIC baseline (1987-1989), the SEP variables may not be representative of the participants' SEP at the time of the HF event, which constituted the baseline in this study. Lastly, the findings may not be applicable to blacks outside the Southern region of the United States since all of the black participants in this study were recruited from Mississippi.

A major strength of this study is the inclusion of various individual-level socioeconomic exposures to determine the effect of SEP on case fatality, allowing for a fuller assessment of the associations of interest. In addition, this is the first study to compare short to long-term case fatality percentages in black and white participants. Misclassification on the outcome was reduced by using incident HF events obtained from medical records. Further, a large number of Black men and women were included, allowing for stratified estimation by race and gender.

To further clarify the association between HF and SEP, future studies should incorporate the severity of the HF event, type of heart failure (systolic versus

diastolic), ejection fraction, diet, and the potential etiology of heart failure (e.g. coronary heart disease, hypertension, and valvular heart diseases).

In summary, low SEP, especially lack of health insurance, may play a leading role in explaining the poor prognosis in patients hospitalized with incident HF. In future studies, disparities in survival beyond three-years post-hospitalization should be examined across race and gender groups and multiple individual-level SEP variables should also be used.

Table 15 (Manuscript 2, Table 1). Selected health and demographic characteristics by race and vital status in ARIC participants with incident hospitalized heart failure event between1987-2004, ARIC study. Participants died or were censored between1987-2004.

Characteristics	Blacks			Whites		
	Died (n=232)	Censored (n=174)	p-value	Died (n=444)	Censored (n=438)	p-value
Age, mean ± SD (yrs)	64.8±6.28	68.1±6.22	<0.0001	67.6±6.15	69.2±6.31	0.0002
Male (%)	44.0	35.6	0.0904	65.6	51.4	<0.0001
Body Mass Index (%)						
≥ 30 (kg/m^2)	51.7	58.1	0.1406	36.9	47.7	0.0009
≥ 25-30 (kg/ m^2)	29.7	30.5		36.5	34.5	
Type II Diabetes (%)	53.1	53.6	0.9213	36.7	28.2	0.0066
Hypertension (%)	82.2	74.0	0.0471	57.9	59.4	0.6559
Systolic Blood Pressure, mean ± SD	141.9±27.6	141.2±24.3	0.8115	132.6±21.9	130.5±19.8	0.1462
Diastolic Blood Pressure, mean ± SD	78.4±14.1	78.2±15.4	0.9342	69.6±11.5	69.1±10.7	0.5185
Pulse Pressure, mean ± SD	142.1±25.0	142.9±24.0	0.7576	128.7±18.4	128.0±16.2	0.5069
Left Ventricular Hypertrophy[‡] (%)	19.9	15.6	0.2656	6.6	5.7	0.5742
Prevalent CHD (%)	15.2	10.9	0.2087	31.5	22.7	0.0037
History of Stroke or Transient Ischemic Attack (%)	5.6	2.9	0.1860	6.8	6.6	0.9357
Total plasma cholesterol (mmol/L), mean ± SD	5.49±1.37	5.45±1.08	0.7633	5.31±1.14	5.26±1.14	0.5597
Current Smoker (%)	63.2	57.1	0.2181	74.3	69.4	0.1043
Current Drinker (%)	51.3	63.5	0.0150	77.7	75.6	0.4543
Married (%)	50.0	51.3	0.8086	81.2	82.0	0.7761
Center						
Jackson (%)	100.0	100.0	--	--	--	0.7683
Washington County (%)	--	--		41.2	42.7	
Minneapolis Suburbs (%)	--	--		33.3	31.1	
Forsyth County (%)	--	--		25.5	26.3	
Socioeconomic Measures						
Low income[§] (%)	67.7	59.2	0.0782	43.5	37.9	0.0923
No health insurance (%)	39.7	28.7	0.0224	7.9	6.4	0.3902

Manual occupation (%)	54.1	62.6	0.0896	33.8	42.4	0.0102
Non-managerial occupational role (%)	89.2	90.6	0.6311	86.4	82.4	0.1053
Low Cumulative SEP§ (%)	53.5	45.4	0.1086	58.1	55.9	0.5147
Cumulative SEP category						
0 (Highest)	17	9	0.2595	66	74	0.6816
1	22	26		120	119	
2	69	60		167	146	
3	76	47		78	83	
4 (Lowest)	48	32		13	16	

*All exposures were measured at the closest exam visit prior to the recorded hospitalized incident HF event except for the socioeconomic measures which was obtained from exam Visit 1, and age which was at the time of the HF event.
†P-values were generated by chi -square for categorical variables and t-test for continuous exposures.
‡Left Ventricular Hypertrophy was determined by electrocardiographic Cornell Index.
§Dichotomized separately at the median for blacks and whites.

Table 16 (Manuscript 2, Table 2). Age-adjusted* 6month to 10-year case fatalities and 95% confidence intervals in participants with incident hospitalized heart failure by race and gender, The ARIC study (1987-2004).

	6-month	1-year	3-year	5-year	10-year
Black Men (n=164)	n=32	n=39	n = 70	n=86	n=102
	19.7 (13.3, 25.5)	24.3 (17.4, 30.6)	48.4 (39.1, 56.2)	63.2 (53.3, 70.8)	96.2 (84.5, 99.1)
White Men (n=517)	n=102	n=129	n = 196	n=237	n=292
	19.8 (16.3, 23.2)	25.4 (21.5, 29.1)	41.1 (36.5, 45.5)	53.3 (48.2, 58.1)	97.4 (87.1, 99.5)
Black Women (n=242)	n=45	n=59	n = 92	n=108	n=130
	18.7 (13.7, 23.5)	24.9 (19.2, 30.2)	42.4 (35.2, 48.7)	54.5 (46.2, 61.5)	82.7 (71.1, 89.7)
White Women (n=365)	n=64	n=80	n = 112	n=127	n=152
	17.6 (13.6, 21.4)	22.3 (17.9, 26.6)	33.9 (28.4, 38.9)	41.4 (35.2, 47.0)	77.3 (56.9, 88.0)

***Mean age at time of HF event for black men= 66.3; black women = 66.1; white men = 68.4; whites women= 68.4 years.**

Table 17 (Manuscript 2, Table 3). Age-adjusted* hazard ratios and 95% confidence intervals for the association between all-cause mortality and socioeconomic variables in black and whites participants, The ARIC study (1987-2004).

Socioeconomic Variable	Blacks (n = 406)	Whites (n = 882)
Income (low vs. high)†		
Low	1.02 (0.77, 1.34)	1.08 (0.89, 1.30)
High	1.00	1.00
Health Insurance‡		
Yes	1.26 (0.97, 1.65)	
< 3 years	--	0.69 (0.42, 1.12)
≥ 3 years	--	2.12 (1.29, 3.51)
No	1.00	1.00
Occupation		
Manual	0.90 (0.69, 1.16)	0.84 (0.69, 1.03)
Non-manual	1.00	1.00
Occupational role		
Non-managerial	0.96 (0.63, 1.45)	1.30 (0.98, 1.71)
Managerial	1.00	1.00
Cumulative SEP§		
Low	1.19 (0.92, 1.54)	1.01 (0.84, 1.22)
High	1.00	1.00
Neighborhood-level SEP (at age 50 years)		
Low	0.90 (0.68, 1.19)	0.97 (0.79, 1.19)
High	1.00	1.00
Neighborhood-level SEP (at age 60 years)		
Low	0.95 (0.73, 1.23)	1.01 (0.84, 1.22)
High	1.00	1.00

*All variables adjusted for the age at time of heart failure event.
†Income in mid-adulthood ranged from $8,000 to $11,999 for blacks and from $25,000 to $34,999 among whites. Income was dichotomized at the median into low and high groups, separately for blacks and whites.
‡ Due to violation of the proportional hazards assumption at three years, time was divided into dying <3 years and ≥ 3 years after having an initial heart failure event.
§Cumulative SEP was created by summing the individual-level SEP variables (i.e. income, health insurance, occupation, and occupational role), and then dichotomized at the median separately for blacks and whites.

Table 18 (Manuscript 2, Table 4). Age-adjusted* hazard ratios and 95% confidence intervals for the association between all-cause mortality and socioeconomic variables† and selected risk factors‡ in black and whites participants, The ARIC study (1987-2004).

Characteristics	0-10years	
	Blacks (n=406)	Whites (n=882)
Age	1.00 (0.98, 1.02)	1.02 (1.00, 1.04)#
Gender (female vs. male)	0.83 (0.64, 1.07)	0.78 (0.64, 0.95)¶
Hypertension (yes vs. no)	1.34 (0.96, 1.88)	--
<3 years	--	0.87 (0.69, 1,09)
≥ 3years	--	1.30 (0.91, 1.86)
Systolic Blood Pressure (per10 mmHg)	1.00 (0.95, 1.05)	1.04 (0.99, 1.09)
Diastolic Blood Pressure (per10mmHg)	0.97 (0.89, 1.06)	1.02 (0.94, 1.11)
Pulse Pressure (per10mmHg)‡	1.00 (0.94, 1.05)	1.00 (0.94, 1.06)
Prior CHD (yes vs. no)	1.12 (0.78, 1.61)	1.28 (1.04, 1.56)#
Type II diabetes (yes vs. no)		
< 3 years for Blacks < 2 years for Whites	0.81 (0.59, 1.10)	1.08 (0.85, 1.38)
≥ 3 years for Blacks ≥ 2 years for Whites	1.83 (1.12, 2.99)#	1.57 (1.15, 2.16)
BMI (Obese vs. Normal) (kg/m^2)		--
< 1 year for Blacks <7 years for Whites	1.81 (0.62, 5.26)	2.83 (1.67, 4.81)§
≥ 1 year for Blacks ≥7 years for whites	2.13 (0.44, 10.16)	4.41 (1.96, 9.90)¶
BMI (Overweight vs. Normal) (kg/m^2)		--
<1 year for Blacks <7 years for Whites	1.35 (0.79, 2.29)	1.68 (1.29, 2.19)§
≥ 1 year for Blacks ≥7 years for Whites	1.58 (0.55, 4.54)	2.62 (1.46, 4.72)¶
LVH (yes or no)¶	--	1.04 (0.71, 1.52)
< 2 years for Blacks	1.17 (0.75, 1.84)	--
≥ 2 years for Blacks	1.50 (0.55, 4.13)	--
Married (yes vs. no)	1.14 (0.86, 1.50)	0.93 (0.72, 1.19)
Total Plasma Cholesterol (per 5mmol/L)	0.94 (0.55, 1.61)	0.98 (0.64, 1.51)
History of Stroke or TIA (yes or no)	1.85 (1.05, 3.24)#	0.94 (0.65, 1.37)
Current Drinker (yes vs. no)	0.73 (0.56, 0.95)#	1.14 (0.91, 1.43)
Current Smoker (yes vs. no)	1.07 (0.82, 1.40)	1.03 (0.83, 1.28)

*All variables adjusted for the age at time of heart failure event.
†Socioeconomic variables were obtained at baseline when the participants were 45-64 years of age.
‡The risk factors were measured at the closest exam visit prior to the diagnosis of the incident hospitalized heart failure event.
§p<0.0001
¶p-value <0.01
#p-value <0.05
†† Left Ventricular Hypertrophy was determined by electrocardiographic Cornell Index.

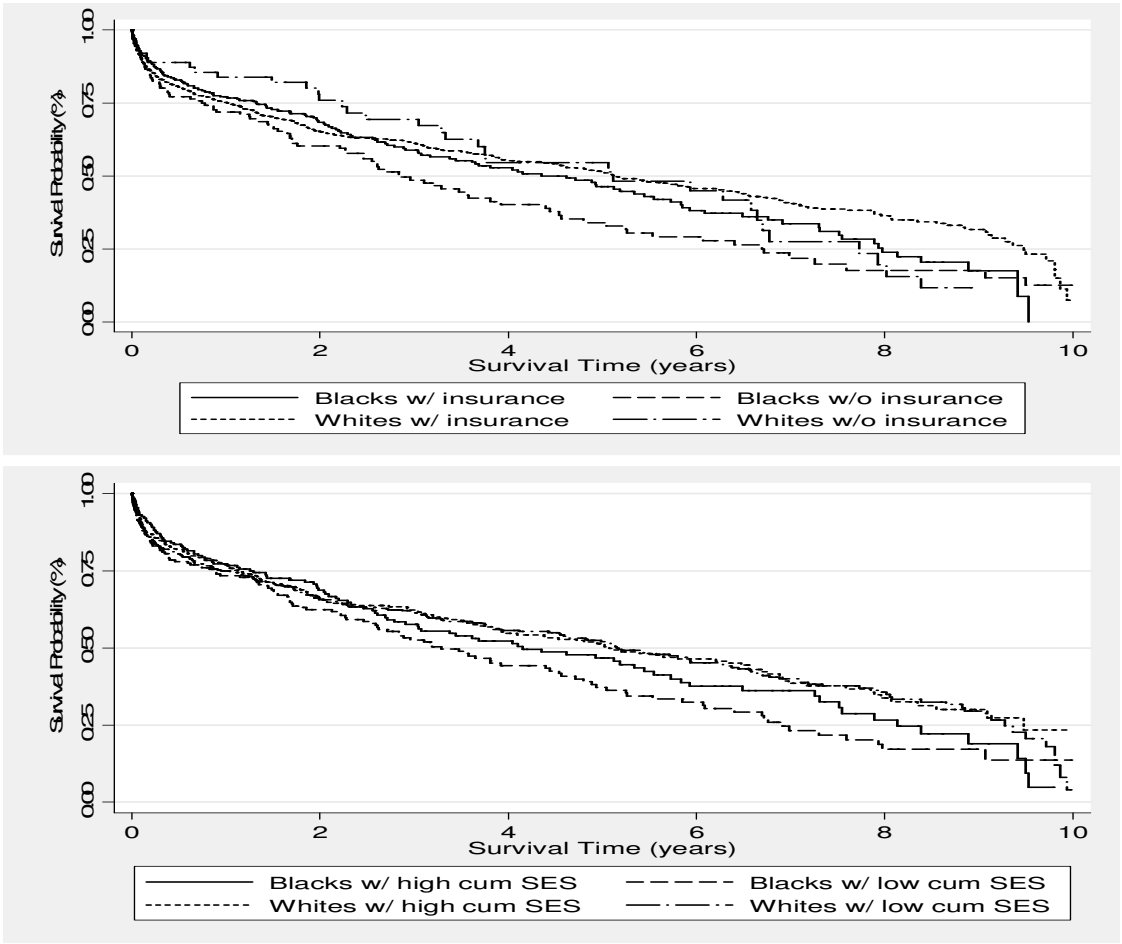

Figure 8 (Manuscript 2, Figure 1) Kaplan-Meier graphs of the survival probability for blacks and whites with incident hospitalized heart failure for occupation, health insurance status, and cumulative SEP, The ARIC study (1987-2004).

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CHAPTER VII. CONCLUSIONS

A. Recapitulation of overall study questions, findings, and degree to which the goals of the doctoral research have been met

The overarching goals of the doctoral research were to:

- Evaluate whether SES circumstances in distinct life epochs (i.e. childhood, young-adulthood, and older-adulthood), individually and cumulatively, are associated with incident hospitalized heart failure in the Atherosclerosis Risk in Communities (ARIC) study.
- Examine whether exposures of SES in adulthood (ages 45-64 years) are predictors of case fatality in participants with incident hospitalized heart failure.
- Assess whether neighborhood level SES modified these associations
- Examine the pathways via which the SES measures influence these outcomes.
- Determine whether the associations differed by race.

Results

The findings from Manuscript #1 suggest that various single and aggregate individual-level socioeconomic indicators over the life-course are significant predictors of incident heart failure. The strength of the association between SES and

incident HHF varied by life-epoch and race. Parental SES indicators from the participants' childhood (at age 10 years) had the weakest association in both Blacks and Whites. SES exposures in young and mid-adulthood and over the life-course SES showed the strongest association with incident HHF. In African-Americans, SEP in young-adulthood had the greatest effect on incident HF while cumulative life-course SEP was moderately associated with incident HF. In contrast among Whites, SEP in young and mid-adulthood resulted in similar increases in the hazard of incident HF as cumulative life-course. Adjusting for neighborhood-level SEP attenuated the associations of the individual-level measures of SEP and incident HHF only slightly.

The impact of life-course SEP on incident hospitalized HF was mediated primarily by access to health care, type II diabetes, and BMI in Blacks. Drinking status, type II diabetes, BMI, and hypertension were the more salient mediators for Whites.

In the second manuscript, SES circumstances assessed at 45-64 years of age were shown not be significantly related to case fatality in unadjusted and adjusted analyses. Neighborhood-level SES did not modify the effect estimates. This is contrary to the results for incident HHF, in which SES exposures in older-adulthood were strongly, significantly related to the outcome.

We postulate that the lack of association could be contributed to additional unmeasured factors, which may confound or interact with SES including severity of the HF event, the efficacy of medical care, medication use, compliance to medicinal therapy, and type of heart failure, and the etiology (e.g. valvular heart disease or

coronary heart disease). Thus, SES factors occurring earlier in life or over the life course may serve as better predictors of case fatality in patients with incident HHF.

The inverse associations between various socioeconomic indicators and different CVD outcomes and the results observed in the study for SES over the life-course suggest that individuals with lower education, income, occupation and a lack of health care have an increased risk of incident HHF. This is also supported by the significantly higher prevalence of hypertension, type II diabetes, obesity, and coronary heart disease in persons with heart failure. These findings also support findings from previous studies, in which individuals with more deprived SES measures show a significantly higher risk of risk factors that may eventually lead to heart failure – coronary heart disease, hypertension, and obesity.

B. Satisfying the goals of the doctoral program

I believe that I have satisfied the requirements and expectations of the doctoral program. As stated in the Epidemiology Academics Policies Manual the doctoral research needs to achieve a high level of originality, depth, scholarship, and writing skills. The manuscripts that I along with my committee members have prepared are original in scope since no other studies to our knowledge have published research on this particular topic. Thus, we are making a significant contribution to the literature on the association between SES exposures and incident heart failure and its case fatality. By using higher level statistical analysis including survival analysis, I believe that I have achieved the expectation of depth. In terms of scholarship, I have completed an unpublished systematic review in which I have examined the work of previous studies which have explored similar relations between SES and

these outcomes. In addition, my scholarship has been demonstrated when presented posters and presentations based on this research area at the American Heart Association and National Heart Lung and Blood Institute conferences. Lastly, I believe that I have demonstrated a competency in scientific writing in writing these two manuscripts and by having a previous manuscript accepted by a peer-reviewed journal.

C. Strengths

The major strengths of this study is that we are among the first to present the relation between SES circumstances over the life course and incident HHF. Moreover, we are among the first to report the findings for Black men and women. Prior studies have focused mainly White men and women in European countries. As a result, our work will provide important contributions to public health research. Prior studies have of SES and various health outcomes have included risk factors for heart failure as confounders, but our work shows that they serve as mediators. Thus, potentially the findings may influence other researchers to explore the pathways by which SES influences these health outcomes.

In a clinical setting SES could be used as a means to identify patients who may have an increased risk of heart failure.

D. Limitations

The limitations of the study included a lack of power to assess short-term case fatality. In addition, all of the Blacks were from Jackson, Mississipii, which reduces the generalizability of our study results. Further, there was a lack of heterogeneity in the SES variables, especially for Blacks. This may have attenuated our ability to

detect an association between the SES indicators and CF. Survival bias may have arisen in our study of SES circumstances and incident HHF since only participants of the LC-SES study were included. Thus, less robust individuals may have died prior to enrolling in the LC-SES study. This would have caused our results to be underestimated.

E. Future Directions

Our results highlight that SEP measures for young and mid-adulthood, as well as cumulative life-course SEP are significant predictors of incident hospitalized heart failure, for both Blacks and Whites, and thus represents windows of opportunity for researchers and clinicians to collaborate in reducing the burden of this disease in all segments of the US population. Moreover, additional studies are needed to evaluate the mechanisms (i.e. pathways) via which SES influences the occurrence of heart failure. The lack of association with SES in mid-life and case fatality suggests that future research should include SES indicators from earlier in life and over the life-course in order to better determine whether SES is a determinant of case fatality in those with heart failure, and in order to avoid any residual occurring by not adequately controlling for SES measures. In addition, future studies should also incorporate exploring heart failure in the outpatient setting in order to further illuminate the impact of socioeconomic disparities on these important health outcomes in the United States.

CHAPTER VIII. APPENDICES

A.IRB Certification

TO: Calpurnyia Roberts
Epidemiology
CB: 8050

FROM: Public Health-Nursing IRB

DATE: 5/16/2007

RE: Determination that Research or Research-Like Activity does not require IRB Approval
Study #: 07-0219

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

This submission was reviewed by the above-referenced IRB. The IRB has determined that this submission does not constitute human subjects research as defined under federal regulations (45 CFR 46.102 [d or f] and OHRP guidance) and does not require IRB approval.

No further review of this research is required unless your study changes in such a way that this determination would no longer apply, at which time resubmission to the IRB should be undertaken. Call the IRB at 966-3113 if you have any questions. You can now access IRB status information at https://my.research.unc.edu/.

Study Description:
The purpose of this study is to deduce the impact of socioeconomic exposures over the life course on hospitalized incident heart failure (HF) and its case fatality. This sstudy will use a dataset from the ARIC study.

CC:
Gerardo Heiss, Epidemiology, CB:8050 Bank Of America Suite 306, Faculty Advisor

B.Supplemental results, Manuscript 1

Table 19 (Supplemental results, MS1) Sociodemographic Composition (%) of ARIC Baseline Cohort and LC-SES participants and the proportion of ARIC participants verified as deceased through December 2001 (adapted from Katherine Rose grant).

	Baseline ARIC Participants		LC-SES participants		Percentage of ARIC Participants Verified Deceased from baseline to December 2001:	
Race-Gender	N	%	N	%	N	%
Black Women	2635	17	2090	17	388	15
Black Men	1631	10	1137	9	392	24
White Women	6050	38	5170	41	515	9
White Men	5428	35	4284	34	814	15
Age at Visit 1						
44-49	4235	27	3751	30	237	6
50-54	4097	26	3453	27	396	10
55-59	3852	24	3013	24	589	15
60+	3608	23	2499	20	891	25
Education						
<12 years	3767	24	2671	21	822	22
12 years	6412	41	5250	41	760	12
>12 years	5586	35	4774	38	527	9
Family Income						
<12,000	2342	16	1561	13	599	26
12,000-23,999	3341	23	2587	22	550	16
24,000-34,999	2653	18	2184	18	320	12
35,000-49,000	2871	19	2456	21	262	9
50,000+	3658	25	3217	27	245	6

"The LC-SES participants were modestly more likely to be female, younger, and to have higher levels of educational attainment and higher family incomes than the baseline ARIC cohort. Markedly higher proportions of blacks, men, older participants, those with less than a high school education and those with lower incomes were verified deceased." - Katherine Rose.

Table 20 (Supplemental results, MS1) Selected health and demographic characteristics of participants measured at the ARIC baseline examination by race group and incident heart failure status in participants enrolled into the ARIC study.

Characteristics	Blacks			Whites		
	With HF (n=396)	Without HF (n=2661)	p-value	With HF (n=871)	Without HF (n=9064)	p-value
Age (yrs) (mean)	55.8±5.5	53.0±5.8	<0.0001	57.4±5.1	53.4±5.7	<0.0001
Male (%)	38.6	38.4	0.9187	61.1	46.3	<0.0001
Body Mass Index (kg/m^2)						
≥25 – 30 (kg/ m^2)	39.4	40.7	<0.0001	31.6	37.5	<0.0001
≥30 (kg/ m^2)	37.0	20.1		39.5	53.0	
Type II Diabetes (%)	44.7	13.4	<0.0001	22.5	6.7	<0.0001
Hypertension (%)	70.7	50.2	<0.0001	45.6	22.9	<0.0001
Left Ventricular Hypertrophy¥ (%)	15.4	4.9	<0.0001	4.4	0.9	<0.0001
Prevalent CHD (%)	8.3	2.2	<0.0001	16.7	3.1	<0.0001
Current Smoker (%)	33.3	27.3	0.0130	34.4	22.1	<0.0001
Current Drinker (%)	22.7	34.1	<0.0001	57.8	66.7	<0.0001
Health Insurance (%)	67.7	79.5	<0.0001	93.5	95.6	0.0031
Center:						
Jackson City (%)	92.7	88.9	0.0232	--	--	<0.0001
Washington County (%)	--	--		41.9	32.3	
Minneapolis Suburbs (%)	--	--		27.3	37.0	
Forsyth County (%)	7.3	11.1		30.8	30.7	

*All exposure variables were measured at the cohort baseline examination (Visit 1).
§P-values were generated by chi -square for categorical variables and t-test for continuous exposures.
¥Left Ventricular Hypertrophy was determined by electrocardiograph.

Table 21 (Supplemental results, MS1) Adjusted* hazard ratios and 95% confidence intervals (CI) for the association between individual-level socioeconomic exposures in older-adulthood and incident heart failure by race group in participants enrolled into the ARIC.

Socioeconomic Exposures	Blacks Hazard Ratio (95% CI) (N=3057)	Whites Hazard Ratio (95% CI) (N=9935)
Mid- Adulthood		
Education		
≤11th grade	2.05 (1.58, 2.66)	2.09 (1.74, 2.52)
HS Graduate	1.46 (1.09, 1.96)	1.36 (1.15, 1.60)
Some College or Greater	1.00	1.00
Occupation		
Manual	0.94 (0.76, 1.17)	1.24 (1.05, 1.45)
Homemaker	1.54 (1.19, 2.12)	1.24 (0.96, 1.61)
Non-manual	1.00	1.00
Occupational Role		
Not a Manager	1.94 (1.40, 2.67)	1.44 (1.20, 1.73)
Manager	1.00	1.00
Home Ownership		
No	1.71 (0.67, 4.40)	3.79 (1.83, 7.85)
Yes	1.00	1.00
Income		
≤$25,000	1.86 (1.08, 3.22)	2.13 (1.74, 2.60)
$25,000-$50,000	1.06 (0.59, 1.92)	1.38 (1.14, 1.67)
≥$50,000	1.00	1.00

* Age at baseline, gender, and center adjusted

Table 22 (Supplemental results, MS1) Selected health and demographic characteristics of participants measured at the ARIC baseline examination by race group for non-participants and participants of the LC-SES study.

Characteristics	Not in LC-SES study		LC-SES study	
	Blacks (n=554)	Whites (n=1416)	Blacks (n= 2503)	Whites (n=8519)
Age (yrs) (mean)	55.7±5.8	56.5±5.5	52.7±5.7	53.9±5.6
Male (%)	48.7	58.4	36.1	45.8
Incident Heart Failure (%)	31.6	23.6	8.8	6.3
Body Mass Index (kg/m^2)				
≥25 – 30 (kg/ m^2)	35.6	41.2	39.1	40.5
≥30 (kg/ m^2)	39.0	25.2	39.7	20.9
Type II Diabetes (%)	32.5	14.5	14.6	7.0
Hypertension (%)	63.2	32.6	50.5	23.6
Left Ventricular Hypertrophy¥ (%)	10.7	2.9	5.3	1.0
Prevalent CHD (%)	6.3	10.2	2.2	3.3
Current Smoker (%)	40.1	36.4	25.5	21.0
Current Drinker (%)	35.9	62.8	31.8	66.3
Health Insurance (%)	71.8	92.9	79.3	95.9
Center:				
Jackson City (%)	84.7	--	90.5	--
Washington County (%)	--	31.1	--	33.6
Minneapolis Suburbs (%)	--	36.9	--	36.0
Forsyth County (%)	15.3	32.0	9.5	30.5

Complete case analysis.

*All exposure variables were measured at the cohort baseline examination (Visit 1).

§P-values were generated by chi -square for categorical variables and t-test for continuous exposures.

¥Left Ventricular Hypertrophy was determined by electrocardiograph.

Table 23 (Supplemental results, MS1) Selected health and demographic characteristics of participants measured at the ARIC baseline examination by ethnic group for non-participants and participants of the LC-SES study.

Characteristics	Not in LC-SES study		LC-SES study	
	Blacks (n=885)	Whites (n=1817)	Blacks (n=2967)	Whites (n=8987)
Age (yrs) (mean)	55.8±5.8	56.5±5.6	52.7±5.7	53.9±5.6
Male (%)	49.4	57.4	35.9	45.6
Incident heart failure (%)	8.8	6.3	9.2	6.6
Body Mass Index (kg/m^2)				
≥25 – 30 (kg/ m^2)	34.3	40.5	38.4	40.3
≥30 (kg/ m^2)	37.4	20.9	40.1	21.2
Type II Diabetes (%)	31.1	15.6	15.0	7.1
Hypertension (%)	62.3	33.7	50.7	23.7
Left Ventricular Hypertrophy¥ (%)	10.9	2.9	5.3	1.0
Prevalent CHD (%)	6.0	10.3	2.1	3.3
Current Smoker (%)	42.1	38.5	26.4	21.6
Current Drinker (%)	35.5	60.6	31.8	65.9
Health Insurance (%)	70.1	92.4	78.3	95.8
Center:				
Jackson City (%)	83.5	--	90.5	--
Washington County (%)	--	32.0	--	34.3
Minneapolis Suburbs (%)	--	35.0	--	35.1
Forsyth County (%)	16.5	33.0	9.5	30.6

Not a complete case analysis.

*All exposure variables were measured at the cohort baseline examination (Visit 1).

§P-values were generated by chi -square for categorical variables and t-test for continuous exposures.

¥Left Ventricular Hypertrophy was determined by electrocardiograph.

Table 24 (Supplemental results, MS1) Selected health and demographic characteristics of participants measured at the ARIC baseline examination by race group and incident heart failure status, ARIC LC-SES study.

Characteristics	Blacks			Whites		
	With HF (n=168)	Without HF (n=2516)	p-value	With HF (n= 418)	Without HF (n=8569)	p-value
Age (yrs) (mean) ± SD	54.6±5.5	52.5±5.6	<0.0001	56.5±5.3	53.7±5.6	<0.0001
Male (%)	36.3	35.5	0.8305	59.6	44.9	<0.0001
Body Mass Index (kg/m^2)						
≥25 – 30 (kg/ m^2)	29.7	39.0	<0.0001	43.8	40.1	<0.0001
≥30 (kg/ m^2)	56.6	39.7		37.1	20.5	
Type II Diabetes (%)	40.7	13.7	<0.0001	21.6	6.4	<0.0001
Hypertension (%)	67.3	50.2	<0.0001	43.2	22.8	<0.0001
Left Ventricular Hypertrophy¥ (%)	16.3	4.7	<0.0001	2.8	0.8	<0.0001
Prevalent CHD (%)	9.5	1.5	<0.0001	14.1	2.8	<0.0001
Current Smoker (%)	34.1	24.7	0.0064	32.5	21.1	<0.0001
Current Drinker (%)	25.2	30.3	0.1611	56.0	66.4	0.0002
Health Insurance (%)	65.9	77.7	<0.0001	93.8	95.9	0.0398
Center:						
Jackson City (%)	100.0	100.0	--	--	--	<0.0001
Washington County (%)	--	--		45.5	33.7	
Minneapolis Suburbs (%)	--	--		26.1	35.6	
Forsyth County (%)	100.0	100.0		28.5	30.7	

*All exposure variables were measured at the cohort baseline examination (Visit 1).
§P-values were generated by chi -square for categorical variables and t-test for continuous exposures.
¥Left Ventricular Hypertrophy was determined by electrocardiograph.

Table 25 (Supplemental results, MS1) Age-adjusted incidence rates per 1,000 person-years and 95% confidence intervals (CI) for heart failure by ethnic group and socioeconomic position (SEP), ARIC LC-SES study (1987-2004).

	Blacks (n=2684)				Whites (n=8987)			
Life Epoch	HF events	Person-years	HF incidence	95% CI	HF events	Person-years	HF incidence	95% CI
Overall	168	37,515	4.31	3.57, 5.22	418	127,231	2.96	2.61, 3.37
Childhood SEP*								
Low	145	31,869	4.36	3.69, 5.17	317	84,053	3.33	2.95, 3.78
High	23	5,646	4.04	2.68, 6.08	101	43,178	2.07	1.85, 2.74
Young-Adulthood SEP§								
Low	132	24,196	5.10	4.16, 6.26	248	70,559	3.09	2.70, 3.54
High	36	13,319	2.85	1.96, 4.13	170	56,672	2.81	2.40, 3.30
Mid-Adulthood SEP¥								
Low	145	30,320	4.52	3.70, 5.51	309	77,826	3.45	3.00, 3.96
High	23	7,195	3.45	2.14, 5.55	109	49,405	2.21	1.79, 2.73
Life-course SEP£								
Low	146	28,494	4.85	4.01, 5.86	276	70,274	3.36	2.89, 3.90
High	22	9,021	2.59	1.63, 4.13	142	56,957	2.47	2.04, 2.99

Adjusted to mean age at baseline.

*Childhood SEP was generated by summing four individual-level socioeconomic indicators pertaining to the participant's parents SEP collected retrospectively during the LC-SES study in 2001 for when the participant was 10 years of age, and dichotomized at the median.

§ Young-adulthood SEP was generated by summing four individual-level socioeconomic indicators during young-adulthood which were collected retrospectively during the LC-SES study in 2001 for when the participants were 30 years of age, and dichotomized at the median.

¥Mid-adulthood SEP was ascertained by summing four individual-level socioeconomic indicators at the time of the ARIC baseline study, and dichotomized at the median.

£Life-Course SEP was created by summing individual-level SEP in childhood, young-adulthood, and mid-adulthood, and then dichotomized at the median.

Table 26 (Supplemental results, MS1) Adjusted* hazard ratios and 95% confidence intervals (CI) for the association between individual-level socioeconomic exposures over the life-course and incident heart failure by ethnic group in the ARIC LC-SES study.

Life-Course Socioeconomic Exposures	Blacks Hazard Ratio (95% CI) (N=2503)	Whites Hazard Ratio (95% CI) (N=8519)
Childhood		
Parental Education		
≤ 8th grade	1.49 (0.92, 2.42)	1.83 (1.45, 2.30)
9-11 grade	1.02 (0.56, 1.95)	1.52 (1.13, 2.05)
≥ 12th grade	1.00	1.00
Parental Occupation		
Manual	1.15 (0.80, 1.64)	1.27 (1.04, 1.55)
Non-manual	1.00	1.00
Parental Occ. Role		
Not a Manager	2.94 (1.09, 7.93)	1.25 (1.01, 1.55)
Manager	1.00	1.00
Home Ownership		
No	0.77 (0.56, 1.06)	0.93 (0.76, 1.15)
Yes	1.00	1.00
Young Adulthood		
Education		
≤11th grade	2.00 (1.32, 3.03)	2.37 (1.82, 3.08)
HS Graduate	1.92 (1.23, 2.98)	1.28 (1.01, 1.63)
Some College or Greater	1.00	1.00
Occupation		
Manual	1.90 (1.28, 2.81)	1.19 (0.95, 1.49)
Homemaker	1.11 (0.59, 2.08)	1.01 (0.74, 1.39)
Non-manual	1.00	1.00
Occupational Role		
Not a Manager	1.69 (0.89, 3.23)	0.93 (0.73, 1.18)
Manager	1.00	1.00
Home Ownership		
No	1.39 (1.01, 1.90)	1.16 (0.95, 1.43)
Yes	1.00	1.00
Mid- Adulthood		
Income		
≤$25,000	2.70 (0.99, 7.35)	2.02 (1.54, 2.65)
$25,000-$50,000	1.70 (0.59, 4.91)	1.24 (0.95, 1.63)
≥$50,000	1.00	1.00
Occupation		
Manual	0.99 (0.71, 1.36)	1.49 (1.20, 1.84)
Homemaker§	1.43 (0.87, 2.35)	1.26 (0.87, 1.82)

Non-manual	1.00	1.00
Occupational Role		
Not a Manager	1.69 (1.07, 2.69)	1.26 (0.98, 1.62)
Managerial	1.00	1.00
Home Ownership		
No	2.00 (1.45, 2.78)	1.99 (1.49, 2.64)
Yes	1.00	1.00

*Age was adjusted for in examining the association between each individual-level childhood SES measure and incident heart failure in Blacks. Age, gender, and center were adjusted for in examining the association between individual-level SES measures in young and mid-adulthood in Blacks and Whites. §Parental socioeconomic indicators were collected from the participants retrospectively during the LC-SES study in 2001 for when the participants were 10 years of age.
¥Socioeconomic indicators during young-adulthood were collected retrospectively during the LC-SES study in 2001 for when the participants were 30 years of age.
£Socioeconomic indicators during mid-adulthood were collected during baseline of the ARIC study for the age of the participant at baseline.

Table 27 (Supplemental results, MS1) Adjusted* hazard ratios and 95% confidence intervals (CI) for the association between individual-level socioeconomic exposures over the life-course and incident heart failure by ethnic group in the ARIC LC-SES study.

Cumulative Socioeconomic Exposures	Blacks Hazard Ratio (95% CI) (N=2503)	Whites Hazard Ratio (95% CI) (N=8519)
Childhood		
Low	1.08 (0.70, 1.68)	1.48 (1.18, 1.85)
High	1.00	1.00
Young-Adulthood		
Low	1.81 (1.24, 2.62)	1.01 (0.83, 1.24)
High	1.00	1.00
Mid-Adulthood		
Low	1.31 (0.84, 2.05)	1.41 (1.13, 1.77)
High	1.00	1.00
Older-Adulhtood		
Low	1.89 (1.20, 2.96)	1.23 (1.00, 1.52)
High	1.00	1.00
z-score	0.81 (0.69, 0.95)	0.75 (0.67, 0.83)

C. Supplemental results, Manuscript 2

Table 28 (Supplemental results, MS2) Unadjusted hazard ratios and 95% confidence intervals for the association between SEP measures (low vs. high) and case fatality following an incident hospitalized heart failure event (1987-2004), ARIC study.

Blacks	**6-months**	**1year**	**5-years**	**10-years**	**15years**
Income	0.72 (0.44, 1.19)	0.75 (0.48, 1.16)	1.01 (0.74, 1.38)	1.12 (0.84, 1.49)	1.15 (0.87, 1.52)
Health Insurance	1.28 (0.78, 2.10)	1.21 (0.78, 1.87)	1.32 (0.98, 1.77)	1.25 (0.95, 1.64)	1.22 (0.94, 1.59)
Occupation	0.81 (0.49, 1.32)	0.79 (0.51, 1.22)	0.94 (0.70, 1.26)	0.93 (0.71, 1.22)	0.92 (0.71, 1.19)
Occupational Role	0.72 (0.36, 1.46)	0.63 (0.35, 1.33)	0.93 (0.58, 1.50)	0.92 (0.60, 1.41)	0.98 (0.64, 1.50)
Cumulative SEP	1.14 (0.81, 1.60)	1.08 (0.80, 1.47)	1.01 (0.81, 1.26)	1.03 (0.84, 1.25)	1.05 (0.86, 1.28)
Whites					
Income	1.11 (0.80, 1.56)	1.05 (0.78, 1.42)	1.05 (0.84, 1.30)	1.08 (0.89, 1.32)	1.12 (0.92, 1.36)
Health Insurance	0.79 (0.39, 1.61)	0.78 (0.41, 1.48)	0.87 (0.57, 1.35)	1.12 (0.79, 1.60)	1.15 (0.82, 1.62)
Occupation	0.96 (0.68, 1.37)	0.98 (0.71, 1.34)	0.84 (0.67, 1.07)	0.83 (0.67, 1.03)	0.84 (0.68, 1.03)
Occupational Role	1.67 (0.96, 2.90)	1.37 (0.87, 2.17)	1.36 (0.98, 1.89)	1.41 (1.05, 1.89)	1.41 (1.05, 1.89)
Cumulative SEP	1.12 (0.68, 1.82)	1.02 (0.66, 1.57)	1.24 (0.92, 1.66)	1.25 (0.95, 1.63)	1.23 (0.95, 1.60)

Table 29 (Supplemental results, MS2) Adjusted* hazard ratios and 95% confidence intervals for the association between SEP measures (low vs. high) and case fatality following an incident hospitalized heart failure event (1987-2004), ARIC study.

Blacks	**6-months**	**1year**	**5-years**	**10-years**	**15years**
Income	0.70 (0.43, 1.17)	0.72 (0.46, 1.12)	1.02 (0.75, 1.40)	1.14 (0.86, 1.53)	1.17 (0.89, 1.55)
Health Insurance	1.38 (0.84, 2.28)	1.28 (0.82, 1.99)	1.40 (1.03, 1.89)	1.30 (0.99, 1.71)	1.26 (0.97, 1.65)
Occupation	0.90 (0.55, 1.49)	0.86 (0.55, 1.33)	1.03 (0.76, 1.40)	1.03 (0.78, 1.36)	1.00 (0.77, 1.31)
Occupational Role	0.70 (0.35, 1.43)	0.61 (0.34, 1.10)	0.96 (0.62, 1.55)	0.97 (0.63, 1.48)	1.03 (0.67, 1.58)
Cumulative SEP	1.23 (0.74, 2.05)	1.06 (0.68, 1.67)	1.39 (1.02, 1.90)	1.40 (1.06, 1.87)	1.37 (1.04, 1.80)
Whites					
Income	1.03 (0.73, 1.47)	0.99 (0.72, 1.36)	0.98 (0.78, 1.23)	1.01 (0.82, 1.24)	1.05 (0.85, 1.28)
Health Insurance	0.80 (0.39, 1.63)	0.81 (0.43, 1.53)	0.89 (0.58, 138)	1.16 (0.82, 1.66)	1.20 (0.85, 1.70)
Occupation	1.05 (0.73, 1.51)	1.08 (0.78, 1.50)	0.95 (0.74, 1.20)	0.94 (0.75, 1.17)	0.95 (0.76, 1.17)
Occupational Role	1.54 (0.88, 2.70)	1.29 (0.81, 2.05)	1.25 (0.90, 1.73)	1.25 (0.93, 1.69)	1.25 (0.93, 1.68)
Cumulative SEP	1.14 (0.80, 1.62)	1.10 (0.81, 1.51)	1.00 (0.80, 1.26)	1.02 (0.83, 1.25)	1.05 (0.85, 1.29)

*Adjusted for age at time of HF event, gender, and center.

Table 30 (Supplemental results, MS2) Cumulative all-cause mortality following an incident hospitalized heart failure event by race, ARIC study and LC-SES survey.

	All ARIC participants		LC-SES participants	
	Blacks (n=348)	Whites (n= 775)	Blacks (n=168)	Whites (n=415)
30-days	7% (25/348)	8% (64/775)	3% (5/168)	2% (8/415)
6-month	18% (64/348)	18% (139/775)	9% (14/168)	4% (16/415)
1-year	24% (83/348)	22% (174/775)	9% (15/168)	6% (26/415)
2-years	33% (116/348)	32% (246/775)	11% (18/168)	10% (42/415)
3-years	42% (145/348)	35% (273/775)	14% (24/168)	11% (46/415)
4-years	47% (164/348)	40% (308/775)	17% (28/168)	13% (55/415)
5-years	51% (177/348)	42% (328/775)	12% (31/168)	14% (60/415)
6-years	54% (189/348)	45% (350/775)	19% (33/168)	16% (66/415)
7-years	57% (199/348)	48% (370/775)	23% (38/168)	17% (72/415)
8-years	59% (206/348)	49% (383/775)	25% (42/168)	18% (75/415)
9-years	60% (210/348)	51% (392/775)	26% (44/168)	19% (80/415)
10-years	62% (215/348)	52% (401/775)	27% (45/168)	20% (83/415)
11-years	63% (219/348)	53% (408/775)	29% (48/168)	21% (87/415)
12-years	65% (225/348)	53% (412/775)	32% (53/168)	21% (88/415)
13-years	65% (225/348)	53% (412/775)	32% (53/168)	21% (88/415)
14-years	65 %(227/348)	53% (413/775)	32% (54/168)	21% (89/415)
15-years	65% (227/348)	53% (414/775)	32% (54/168)	22% (90/415)

Table 31 (Supplemental results, MS2) The case fatality rates by race and gender for participants in the ARIC study and the LC-SES survey.

	ARIC (%)	LC-SES (%)
30days		
Black Men	12/139 (8.6)	2/61 (3.3)
Black Women	13/209 (6.2)	3/107 (2.8)
White Men	36/478 (7.5)	6/247 (2.4)
White Women	28/297 (9.4)	2/168 (1.2)
6-months		
Black Men	29/139 (20.9)	5/61 (8.2)
Black Women	35/209 (16.8)	9/107 (8.4)
White Men	85/478 (17.8)	12/247 (4.9)
White Women	54/297 (18.2)	4/168 (2.4)
1-year		
Black Men	34/139 (24.5)	6/61 (9.8)
Black Women	49/209 (23.4)	9/107 (8.4)
White Men	107/478 (22.4)	19/247 (7.7)
White Women	67/297 (22.6)	7/168 (4.2)

Table 32 (Supplemental results, MS2) Age-adjusted case fatality and 95% confidence interval from 1987-2004 by race and gender, the ARIC study and LC-SES survey.

	ARIC			LC-SES		
	30-days	***6-months***	***1-year***	***30-days***	***6-months***	***1-year***
Overall*						
Black Men	8.3 (4.7, 14.2)	20.4 (14.4, 27.9)	24.1 (32.0, 17.7)	2.9 (0.7, 11.6)	7.6 (3.1, 17.4)	9.2 (4.1,19.4)
Black Women	6.1 (3.5, 10.3)	16.6 (12.1, 22.4)	23.6 (18.2, 30.0)	2.5 (0.7, 8.2)	8.0 (4.0, 15.0)	8.0 (4.1,15.0)
White Men	7.5 (5.5, 10.3)	17.7 (21.4, 14.5)	22.4 (18.8, 26.4)	1.9 (0.7, 4.9)	3.2 (1.5, 6.8)	4.5 (2.6, 8.9)
White Women	9.3 (6.5, 13.2)	17.8 (13.8, 22.6)	22.2 (17.8, 27.4)	0.9 (0.2, 4.0)	1.5 (0.5, 4.5)	2.4 (1.0, 5.8)

*Adjusted for the average age at the time of the HF event by race and study. The average age is 67years for Whites for both the ARIC study and the LC-SES survey. The average age is 65 years for Blacks in both the ARIC study and the LC-SES study.

Table 33 (Supplemental results, MS2) The association between socioeconomic variables at exam visit 4 and case fatality in patients with incident hospitalized heart failure event between Visit 4 (1996-1998) and 2004, ARIC study.

	Blacks (n=162) HR (95% CI)	Whites (n=457) HR (95% CI)
Income* (high vs. low)		
Case fatality¥	58/141	170/452
Unadjusted	0.62 (0.36, 1.07)	1.27 (0.93, 1.72)
Age- Adjusted	0.59 (0.34, 1.03)	1.05 (0.77, 1.43)
Longest Occupation§ (non-manual vs. manual)		
Case fatality	91/151	170/456
Unadjusted	1.16 (0.64, 2.09)	0.88 (0.65, 1.19)
Age-Adjusted	1.14 (0.63, 2.05)	0.87 (0.64, 1.18)

*Income split at the median, separately for Blacks and Whites.
†The numerator is the number of fatal events and the denominator is the number of participants with an incident hospitalization for heart failure in the time period and complete exposure information.
‡Average length of follow-up from incident heart failure until death was 1.42 ± 1.64 years for Whites and 2.47 for Blacks.

Table 34 (Supplemental results, MS2) Count and percentage of participants in the ARIC study by race and coronary heart disease status at baseline.

15-year CF	CHD		Non-CHD	
	Died (n=112)	**Censored (n=56)**	**Died (n=520)**	**Censored (n=421)**
Black Men	13	5	83	36
Black Women	7	7	121	73
White Men	79	38	190	164
White Women	13	6	126	148
Total				
Blacks	20	12	204	109
Whites	92	44	316	312

Table 35(Supplemental results, MS2) Hazard ratios and 95% CI for 15-year case fatality by race and CHD status at baseline.

	CHD (n=168)	Non-CHD (n=941)
Health Insurance:		
Blacks	0.58 (0.20, 1.74)	1.32 (1.00, 1.75)
Whites	1.70 (0.85, 3.41)	1.07 (0.72, 1.59)
Income:		
Blacks	1.26 (0.49, 3.22)	1.12 (0.83, 1.50)
Whites	1.27 (0.84, 1.92)	0.96 (0.77, 1.20)
Occupation:		
Blacks	0.66 (0.22, 2.00)	0.98 (0.74, 1.30)
Whites	0.86 (0.54, 1.38)	0.99 (0.78, 1.25)
Occupational Role:		
Blacks	1.54 (0.44, 5.35)	0.94 (0.60, 1.48)
Whites	0.99 (0.49, 1.99)	1.23 (0.88, 1.71)

*Adjusted for age at time of heart failure.

Table 36 (Supplemental results, MS2) Hazard ratio and 95% Confidence interval for the association between CHD and 15-year heart failure case fatality.

Blacks	1year	5-year	10-year	15year
Prior CHD (Yes vs. No)	0.73 (0.32, 1.66)	0.75 (0.43, 1.32)	0.81 (0.50, 1.32)	0.86 (0.55, 1.37)
+Age	0.76 (0.33, 1.74)	0.79 (0.45, 1.39)	0.86 (0.53, 1.40)	0.92 (0.58, 1.45)
+Health Insurance	0.78 (0.34, 1.79)	0.81 (0.46, 1.42)	0.87 (0.53, 1.41)	0.92 (0.58, 1.46)
+ Income	0.75 (0.32, 1.71)	0.79 (0.45, 1.39)	0.87 (0.54, 1.41)	0.93 (0.58, 1.47)
+All covariates	0.37 (0.10, 1.51)	0.47 (0.22, 1.03)	0.62 (0.34, 1.15)	0.70 (0.40, 1.25)
Whites				
Prior CHD (Yes vs. No)	0.97 (0.66, 1.44)	1.29 (0.99, 1.67)	1.26 (1.00, 1.60)	1.27 (1.01, 1.61)
+Age	1.07 (0.72, 1.59)	1.42 (1.09, 1.84)	1.36 (1.07, 1.73)	1.37 (1.08, 1.73)
+Health Insurance	1.07 (0.72, 1.59)	1.42 (1.09, 1.84)	1.36 (1.08, 1.73)	1.37 (1.09, 1.73)
+Income	1.07 (0.72, 1.59)	1.42 (1.09, 1.84)	1.36 (1.07, 1.73)	1.37 (1.08, 1.73)
+All covariates	1.23 (0.79, 1.92)	1.47 (1.09, 1.98)	1.41 (1.08, 1.84)	1.44 (1.10, 1.87)

*Covariates: age at first HF event, gender, hypertension, BMI, diabetes status, drinking, smoking, marriage, and left ventricular hypertrophy.

Table 37 (Supplemental results, MS2). Unadjusted hazard ratios and 95% confidence intervals for the association between SES measures and case fatality following an incident hospitalized heart failure event (1987-2002) in blacks and whites, ARIC study.

Blacks	6-months	1year	5-years	10-years	15years
At age 50	1.00 (0.96, 1.05)	1.01 (0.97, 1.05)	1.00 (0.97, 1.03)	1.00 (0.97, 1.02)	1.00 (0.98, 1.02)
At age 60	1.00 (0.95, 1.06)	1.01 (0.96, 1.06)	0.99 (0.95, 1.02)	0.98 (0.95, 1.01)	0.99 (0.96, 1.02)
Whites					
At age 50	1.01 (0.98, 1.04)	1.01 (0.99, 1.04)	1.01 (0.99, 1.03)	1.00 (0.99, 1.02)	1.00 (0.99, 1.02)
At age 60	1.06 (0.97, 1.04)	1.01 (0.98, 1.04)	1.00 (0.98, 1.02)	0.99 (0.97, 1.02)	0.99 (0.97, 1.02)

*All exposure variables were measured at Visit 1.

Table 38 (Supplemental results, MS2). Unadjusted hazard ratios and 95% confidence intervals for the association between SES measures and case fatality following an incident hospitalized heart failure event (1987-2002) in blacks and whites, ARIC study.

Blacks	6-months	1year	5-years	10-years	15years
At age 50	1.11 (0.63, 1.95)	0.90 (0.54, 1.50)	1.06 (0.78, 1.48)	1.11 (0.82, 1.50)	1.10 (0.82, 1.48)
At age 60	1.15 (0.70, 1.90)	0.93 (0.60, 1.45)	1.11 (0.83, 1.50)	1.19 (0.91, 1.56)	1.14 (0.87, 1.48)
Whites					
At age 50	0.95 (0.68, 1.33)	0.96 (0.70, 1.31)	0.95 (0.76, 1.19)	0.98 (0.80, 1.20)	0.97 (0.79, 1.19)
At age 60	0.95 (0.68, 1.33)	0.95 (0.71, 1.29)	0.99 (0.79, 1.22)	1.00 (0.83, 1.27)	1.02 (0.84, 1.23)

*All exposure variables were measured at Visit 1.

** Neighborhood is modeled as binary (low vs. high).

Table 39 (Supplemental results, MS2) The effect of adjusting for neighborhood-level SES at ages 50 and 60 years on the association between SES measures (low vs. high) and case fatality following an incident hospitalized heart failure event (1987-2004), ARIC study.

	Blacks	Whites
Neighborhood at age 50 years		
Occupational Role		
Model 1	0.96 (0.63, 1.47)	1.40 (1.06, 1.88)
Model 2	0.99 (0.65, 1.52)	1.27 (0.95, 1.71)
Model 3	1.01 (0.66, 1.56)	1.27 (0.95, 1.71)
Insurance		
Model 1	1.22 (0.93, 1.59)	1.16 (0.82, 1.64)
Model 2	1.05 (0.70, 1.58)	1.48 (0.80, 2.74)
Model 3	1.07 (0.72, 1.61)	1.49 (0.80, 2.76)
Occupation		
Model 1	0.92 (0.70, 1.19)	0.82 (0.67, 1.01)
Model2	0.98 (0.75, 1.27)	0.93 (0.78, 1.15)
Model 3	1.00 (0.77, 1.31)	0.94 (0.76, 1.16)
Income		
Model 1	1.14 (0.86, 1.51)	1.14 (0.93, 1.39)
Model2	1.13 (0.85, 1.49)	1.05 (0.86, 1.29)
Model3	1.13 (0.85, 1.49)	1.05 (0.86, 1.29)
Neighborhood at age 60 years		
Occupational Role		
Model 1	0.95 (0.62, 1.45)	1.40 (1.05, 1.88)
Model 2	0.98 (0.64, 1.51)	1.25 (0.93, 1.68)
Model 3	1.01 (0.66, 1.55)	1.25 (0.93, 1.68)
Insurance		
Model 1	1.21 (0.93, 1.58)	1.15 (0.81, 1.62)
Model 2	1.18 (0.80, 1.76)	1.78 (1.08, 2.94)
Model 3	1.19 (0.80, 1.78)	1.78 (1.08, 2.94)
Occupation		
Model 1	0.91 (0.70, 1.18)	0.81 (0.65, 1.00)
Model2	0.97 (0.74, 1.26)	0.91 (0.74, 1.13)
Model 3	1.00 (0.76, 1.30)	0.92 (0.74, 1.14)
Income		
Model 1	1.13 (0.85, 1.49)	1.13 (0.92, 1.38)
Model2	1.13 (0.85, 1.49)	1.01 (0.83, 1.24)
Model3	1.13 (0.85, 1.49)	1.01 (0.83, 1.24)

Model 1 = individual-level SES variable + neighborhood-level SES
Model 2 = individual-level SES variable + neighborhood-level SES + age at time of heart failure
Model 3 = individual-level SES variable + neighborhood-level SES + age at time of heart failure + gender

*interaction terms with the individual-level variables were only significant at p <0.20 for insurance and Neighborhood at age 60 years in Whites, but insurance data is very homongenous, so the interaction term is not stable.