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SES, Heart Failure, and N-terminal Pro-b-type Natriuretic Peptide: The Atherosclerosis Risk in Communities Study

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Abstract

Introduction—Compared with coronary heart disease and stroke, the association between SES and the risk of heart failure is less well understood.

Methods—In 12,646 participants of the Atherosclerosis Risk in Communities Study cohort free of heart failure history at baseline (1987–1989), the association of income, educational attainment, and area deprivation index with subsequent heart failure-related hospitalization or death was examined while accounting for cardiovascular disease risk factors and healthcare access. Because SES may affect threshold of identifying heart failure and admitting for heart failure management, secondarily the association between SES and N-terminal pro-b-type natriuretic peptide (NT-proBNP) levels, a marker reflecting cardiac overload, was investigated. Analysis was conducted in 2016.

Results—During a median follow-up of 24.3 years, a total of 2,249 participants developed heart failure. In a demographically adjusted model, the lowest SES group had 2.2- to 2.5-fold higher risk of heart failure compared with the highest SES group for income, education, and area deprivation. With further adjustment for time-varying cardiovascular disease risk factors and healthcare access, these associations were attenuated but remained statistically significant (e.g., hazard ratio=1.92, 95% CI=1.69, 2.19 for the lowest versus highest income), with no racial interaction (p>0.05 for all SES measures). Similarly, compared with high SES, low SES was associated with both higher baseline level of NT-proBNP in a multivariable adjusted model (15% higher, p<0.001) and increase over time (~1% greater per year, p=0.023).

Conclusions—SES was associated with clinical heart failure as well as NT-proBNP levels inversely and independently of traditional cardiovascular disease factors and healthcare access.

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INTRODUCTION

The contribution of socioeconomic inequality to cardiovascular disease (CVD) risk poses a major public health challenge. In the U.S., substantial socioeconomic inequality in incidence and prevalence of major CVDs continue to exist.[1–3] The American Heart Association highlights the need for a better understanding of the relationship between social factors and CVD so that inequality in CVD burden can be addressed effectively.[4] In this context, the association between low SES and incidence of heart failure (HF) is less well understood.

Given that HF currently affects about 5.7 million adults and has direct healthcare costs of $21 billion/year in the U.S. alone,[5] understanding the link between socioeconomic inequality and risk of HF would be important for informing public health professionals and policy makers for strategizing health policy related to HF prevention and management. Although several studies explored the association between SES and HF, they have important caveats: limited information on SES measures, mostly focused on readmissions in HF patients, and not accounting for potential mediators, such as hypertension, as time-varying factors.[6–10] SES is a multidimensional construct, indexed not only by individual-level measures (e.g., education and income) but also by neighborhood-level measures (e.g., neighborhood deprivation).[11] Dimensions of SES beyond an individual's income and education such as area-level SES may affect the development of HF through a variety of mechanisms including accessibility of recreational facilities, neighborhood crime, and availability of healthy foods.[12–14] Thus, examining several SES measures might provide more comprehensive assessment of the association between SES and HF.

This prospective study aims to investigate the association between measures of SES, while accounting for updated CVD risk factors and factors related to healthcare access during follow-up. Because SES may affect the threshold of identifying HF and admitting for HF management,[6,15] this study also investigates the association between SES and a marker of cardiac overload (i.e., N-terminal pro-b-type natriuretic peptide [NT-proBNP], indicating higher risk or an earlier sign of HF), measured according to a research protocol but not with a clinical indication.[16]

METHODS

Study Population

Detailed description of the Atherosclerosis Risk in Communities (ARIC) study has been published earlier.[17] In brief, this is a prospective cohort study of 15,792 participants aged 45–64 years at baseline (1987–1989) sampled from four U.S. communities. The ARIC study did not exclude those with prevalent CVD (including HF) at the baseline. Physical examination and risk factors assessment were conducted at baseline, at three follow-up visits occurring approximately three years apart, and at the fifth visit from 2011 to 2013. The IRBs at each study center approved the study, and participants provided written informed consent.

Of the total 15,792 participants at Visit 1, individuals with prevalent HF (Stage 3 HF as per Gothenburg criteria or taking medications for HF in last 2 weeks[18]; n=752), prevalent coronary heart disease (n=766) and history of stroke (n=286) were excluded. In addition, participants whose race was neither African American nor white (*n*=48), African Americans from the Minneapolis and Washington County sites (*n*=55), that were missing information on income (*n*=927), education (*n*=27), and other variables of interest (*n*=601) at baseline and missing information on HF status at follow-up (*n*=287) were excluded, leaving 12,646 participants in the final study population. Analysis was conducted in 2016.

Measures

Annual household income and educational attainment, as measures of individual-level SES, and area deprivation index (ADI), as a measure of area-level SES measure, were exposures in this study. Household income was categorized into <$12,000, $12,000–$24,999, and ≥ $25,000 in 1987–1989 ($1 in 1987–1989 is about $2 in 2016).[19] In 1987, for an average household $12,000 corresponds to 150% of the federal poverty level.[20] Educational attainment was categorized as less than high school, high school or equivalent, and more than high school. ADI represents socioeconomic deprivation experienced by a neighborhood and was obtained using 17 different factors of SES from 2000 Census block group-level or the nine-digit ZIP data (Appendix).[21] In the ARIC Study, the 2000 Census data was used because currently available census tracts and block groups data from the original ADI (www.hipxchange.org/ADI) are based on 2000 Census data[23] and this ensured the use of the same set of block groups across different ARIC visits. Although original ADI was developed with data collected at the census tract level, it has been validated with data collected at more granular levels including ZIP codes and has been found to have factor loadings generally similar in magnitude and relative importance.[21] For analysis purposes, ADI was divided into quintiles, as done previously.[21]

Incident HF was the primary outcome of this study and was defined as first hospitalization or death related to HF occurring after baseline visit. HF incidence was ascertained by contacting participants annually and by active surveillance of hospitals in the ARIC communities to obtain information about interim hospitalizations and vital records.[22] HF-related hospitalizations and deaths were identified by ICD-9 code 428 or ICD-10 code I50 in any position in discharge diagnosis or death certificates, respectively. Follow-up for HF events was available through December 31, 2013.

The association of SES with levels of NT-proBNP at baseline and their changes during the follow-up period (Visit 2 through to Visit 5) was also investigated. NT-proBNP was first measured at Visit 2 (*n*=14,348) in about 94% of the participants (*n*=13,436), and thus the association between SES and NT-proBNP (continuous) was investigated in study population at Visit 2. Subsequent measurements of NT-proBNP that were performed at Visits 4 and 5 were used to assess association between SES and rate of change in NT-proBNP. After excluding participants with prevalent cases of CVD (including HF, *n*=1,501) and missing information on relevant covariates at Visit 2 (*n*=928), the analytic sample for the association between SES and NT-proBNP was 11,007. NT-proBNP was measured as previously described.[23] Because the lower limit of measurability was 5 pg/mL, a value of 2.5 pg/mL was assigned to participants with levels below the limit of measurability (*n*=421 at Visit 2, *n*=338 at Visit 4, and *n*=16 at Visit 5).[24,25]

Smoking and alcohol intake were categorized as never, former, or current. Physical activity was assessed using the Baecke questionnaire and information was modified into an index ranging from one to five.[26] Hypertension was defined as systolic blood pressure of >140 mm Hg or diastolic blood pressure of >90 mm Hg, or use of hypertension medication. Diabetes was defined as self-reported physician diagnosis, current use of glucose-lowering medications, fasting blood glucose of ≥126 mg/dL (7.0 mmol/L), or random blood glucose of ≥200 mg/dL (11.1 mmol/L). Total and high-density lipoprotein cholesterols were measured as previously described.[27] Information on health insurance status (yes/no) and frequency of visits to seek routine health care (none, less than one, or one or more visits per year) was self-reported. Information on aforementioned factors was updated during follow-up visits.

Statistical Analysis

Hazard ratios (with 95% CI) were obtained from Cox regression models (multilevel mixed-effects parametric survival models in case of ADI). The assumption of proportionality was evaluated graphically by plotting log(−log(Survival)) versus log(time) (Appendix Figure 1). Multiple models were constructed to account for potential confounders and mediators for SES–HF relationship. In Model 1, analyses were adjusted for age, sex and race-center (considered as confounders). In Model 2, smoking status, alcohol intake status, physical activity, BMI, hypertension, diabetes, total cholesterol, high-density lipoprotein cholesterol, and cholesterol lowering medication use were added to Model 1 (considered as mediators). In Model 3, health insurance status and frequency of visits to seek routine health care were added to Model 2 (considered as mediators). Whenever possible, all potential confounders and mediators were treated as time-varying covariates. If information was missing on a covariate at a follow-up visit, information from previous visit was used. The interaction between SES measures X race was tested and race/center-stratified results were presented. In primary analysis, SES measures were not adjusted for each other because this approach obscures long lasting effects of neighborhood deprivation.[28] Because proportion of whites in lowest quintile and proportion of African Americans in highest quintile of overall ADI was limited (<3% and <1%, respectively), race specific quintiles were calculated for ADI analysis.

To assess the SES–NT-proBNP association at baseline and the rate of change in NT-proBNP during follow-up, multilevel linear growth models (with random intercept and random slope) were constructed. Given the non–normal distribution (right-skewed) of NT-proBNP, values were natural log transformed.

Because a number of participants missed information on NT-proBNP at subsequent visits (n=2,238 at Visit 4 and n=5,936 at Visit 5), missing data values were imputed with 30 data replicates using multiple imputation by the chained equations method implemented by the *mi* (Multiple Imputation) program in Stata.[29]

In sensitivity analyses, first, different cut offs for household income were assessed: < $16,000, $16,000–$34,999 and ≥$35,000.[30] Second, NT-proBNP was examined as a categorical variable (≥300 pg/mL elevated and <300 pg/mL non-elevated).[31] Third, the SES–NT-proBNP association was additionally adjusted for estimated glomerular filtration rate (eGFR) because eGFR may influence NT-proBNP levels for non–HF-related reasons.[32] Fourth, given potential misclassification in assigning HF as an underlying cause of death,[33] results were confirmed after excluding such cases (*n*=85). Finally, the association of individual- and area-level SES measures with HF incidence was examined when mutually adjusting for each other. All statistical tests were 2-sided and a *p*-value of <0.05 was considered to be statistically significant. All analyses were performed using Stata/IC, version 14.0.

RESULTS

Participants in the low-income group were more often older, female, and African American (Table 1). In addition, CVD risk factor profile was generally poorer in low compared with high income groups. Similar differences in baseline characteristics were observed for educational attainment. The patterns were similar across ADI quintiles except for age and total cholesterol, which showed an inverse "U"-shaped pattern (Appendix Table 1).

A total of 2,249 participants developed incident HF over a median follow-up time of 24.3 years (25th, 75th percentiles, 17.7, 25.4, respectively). The cumulative incidence of HF followed a graded (dose–response) pattern, being highest in low income and low educational attainment groups (Figure 1; log rank test: $p<0.001$ for both SES measures).

Compared with high income, the hazard ratio for medium income was 1.68 (95% CI=1.52, 1.87) and low income was 2.47 (95% CI=1.19, 2.80). In case of educational attainment, these estimates were 1.29 (95% CI=1.16, 1.44) and 2.22 (95% CI=1.99, 2.49), respectively (Model 1 in Table 2). The trend of increasing hazard ratios of HF incidence with declining income and educational attainment remained significant after additional adjustment for updated CVD risk factors (Model 2 in Table 2) and factors related to healthcare access (Model 3 in Table 2). Likewise, incidence of HF increased across categories of area-level SES (Appendix Figure 2 and Appendix Table 2). These results were similar when data for white and African American study participants were analyzed separately (Appendix Tables 3 and 4). No statistical interaction was observed between race X any of the SES measures (*p* for interaction=0.57, 0.89 and 0.75 for income, educational attainment, and ADI, respectively, in Model 3) for the risk of incident HF.

Mean levels of NT-proBNP at each of Visits 2, 4, and 5 were generally higher in low income and low education groups compared with their higher SES counterparts (Appendix Table 5). In Model 1, medium and low income and educational attainment were associated with higher levels of NT-proBNP at baseline compared with high SES (e.g., 8% higher levels in medium and 15% higher levels in low income compared with high income). These associations remained significant in Model 2 and 3 (Table 3).

The rate of increase in NT-proBNP level (per year), although modest, was statistically significantly higher for medium and low income and educational attainment compared with their high SES counterparts (*p*-trend 0.017 and 0.012, respectively). Even in Model 2 and 3, trend for greater increases in NT-proBNP with declining SES levels remained significant (Table 3). Similar results were observed across ADI quintiles (Appendix Table 6).

Results for the association between income and incidence of HF-related hospitalization or death were essentially similar to overall results when categorizing income levels differently (Appendix Table 7) or when categorizing NT-proBNP into elevated (≥300 pg/mL) and non-elevated (<300 pg/mL; Appendix Table 8). Additional adjustment for eGFR (Appendix Tables 9 and 10) or excluding cases with HF as underlying cause of death (data not shown) also did not materially change the results. Income and education maintained association with HF in all three models when adjusted for ADI whereas ADI was only shown associated with HF in Model 1 and not in Model 2 and Model 3 (Appendix Tables 11 and 12).

DISCUSSION

SES was inversely associated with the risk of HF. Of note, similar patterns were observed for individual- and area-level measures of SES. A poorer CVD risk factor profile was seen in participants with low SES than in high SES but did not fully explain the excess risk related to SES. Inverse relationship between SES and HF persisted after additionally adjusting for factors related to heath care access. The associations were similar between whites and African Americans. Of importance, SES was also inversely associated with levels of NT-pro-BNP at baseline and their change over time.

This study has broadened understanding of SES–HF relationship in a number of aspects. First, consistent results in individual-level as well as area-level measure of SES suggest the robust contribution of SES to HF risk. Second, the SES–HF association independent of time-varying CVD risk factors, suggest that the management of these risk factors over time may not fully prevent HF in lower SES group. Third, lack of health care access in addition to CVD risk factors does not seem to adequately explain excess HF risk in low SES groups. Finally, observed SES–NT-proBNP association further support that remaining excess risk of HF in low SES groups is unlikely because of different thresholds of identifying HF or admitting for HF care by SES status.

Traditional CVD risk factors did not seem to entirely explain SES–HF association and similarly, limited access to health care only marginally attenuated the association between SES measures and HF in this study, indicating that additional factors may play a role. Other plausible factors linking SES to HF may include psychosocial and environmental factors. For instance, chronic psychological stress[34,35] and exposure to heavy metals (e.g., cadmium)[36] are known risk factors for HF and their prevalence is generally high in low SES groups. Indeed, when examining psychological stress (available at Visit 2 in this study), it was found to be generally high in low SES groups though the SES–HF association remained significant after additionally adjusting for psychological stress (Appendix Tables 13 and 14). Unfortunately, because of unavailability of data, this study could not account for environmental factors. Nonetheless, future studies would be warranted to explore other factors behind SES–HF relationship.

In this study, individual-level SES measures were observed to have stronger association with HF than area-level SES measure when mutually adjusted for each other. Similar findings have also been reported previously in HF patients.[37] This could be because of a number of reasons including the relatively less granular nature and less accurate property of area-level SES measures compared with individual-level SES measures.

Findings in this study clearly show that a wide socioeconomic gradient exists in risk for HF, and acknowledging these socioeconomic disparities would be critical for strategizing health policy related to HF prevention and management. Because CVD risk factors somewhat attenuated the SES–HF association, adequate prevention and management of CVD risk factors may reduce excess risk of HF related to SES. However, current CVD risk factors management predominantly takes place in healthcare settings where only those who seek health care are benefited. Therefore, expanding current approaches to community level efforts, in particular expanding to disadvantaged communities, may offer opportunities for greater reduction in the risk of HF. Nonetheless, results in this study suggest that addressing CVD risk factors and access to health care may reduce but are unlikely to eliminate existing inequalities. Prominent CVD risk prediction models (e.g., SCORE, Framingham 2008) do not include individual- or area-level measures of CVD as a covariate. Given the strong association between measures of SES and HF independent of traditional risk factors, findings suggest that individual-level and area-level SES should be considered when predicting HF or overall CVD risk in clinical practice. Although no interaction was observed between SES X HF in this study, the difference in distribution of whites and African Americans by SES (particularly neighborhood deprivation) may warrant race-specific assessment of SES in clinical practice.

Limitations

Definition of HF was predominantly based on HF hospitalization and potentially missed milder cases of HF managed in outpatient settings. The SES–NT-proBNP association, however, suggest that the association between SES and HF likely exist at all stages of HF. Additionally, healthcare access was assessed from health insurance status and frequency of visits to routine health care. These factors alone do not determine someone’s status of access to health care and quality of received health care. Moreover, people from low SES groups potentially seek care at healthcare facilities that provide low-quality care.[38,39] Thus, health insurance status and frequency of visits to routine health care may not necessarily account for quality of care. Finally, 2000 Census data were used to calculate ADI. Thus, there is a potential for misclassification of ADI at Visit 1 or Visit 2. However, the association of ADI at Visit 4 (i.e., 1996–1998, closest to year 2000) with HF and NT-proBNP was essentially similar to the main results (Appendix Tables 15 and 16). Strengths of this study include its prospective design, detailed information on a number of SES measures, large number of HF cases, the availability of NT-proBNP which uniquely allowed the authors to examine association of SES with earlier stages of HF, updated information on a number of relevant risk factors, and near complete follow-up regarding hospital admission (>98%).

CONCLUSIONS

In conclusion, the association between SES and risk of HF was inverse and graded. Addressing traditional CVD risk factors and limited health care access, may somewhat reduce the socioeconomic gradient in HF as well as overall burden of HF. The elimination of

SES disparities in HF risk, however, may require identifying and intervening on other modifiable factors and addressing socioeconomic inequalities.

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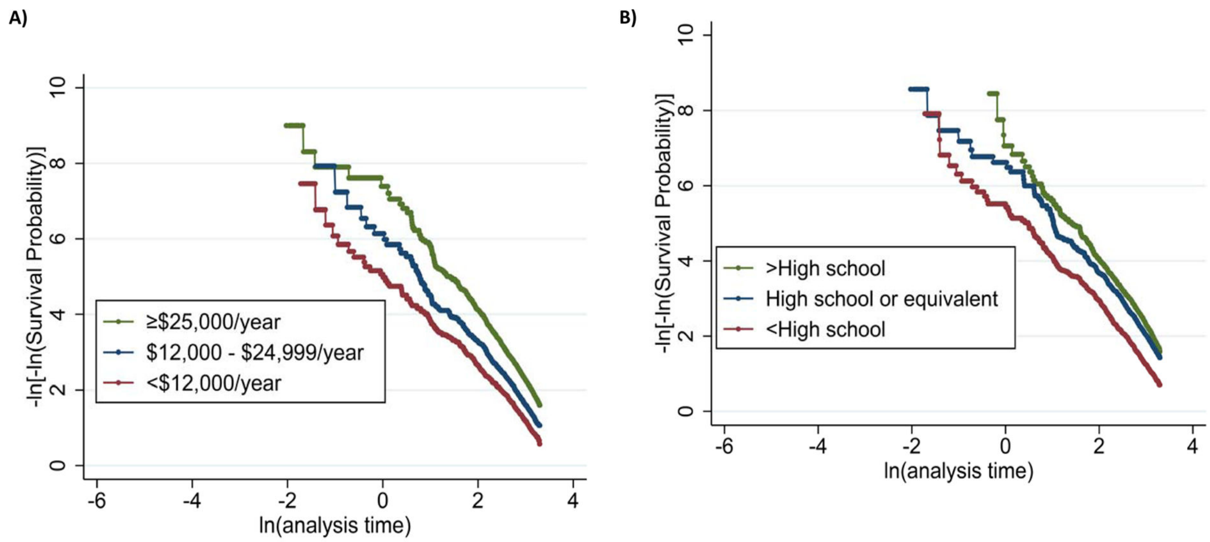
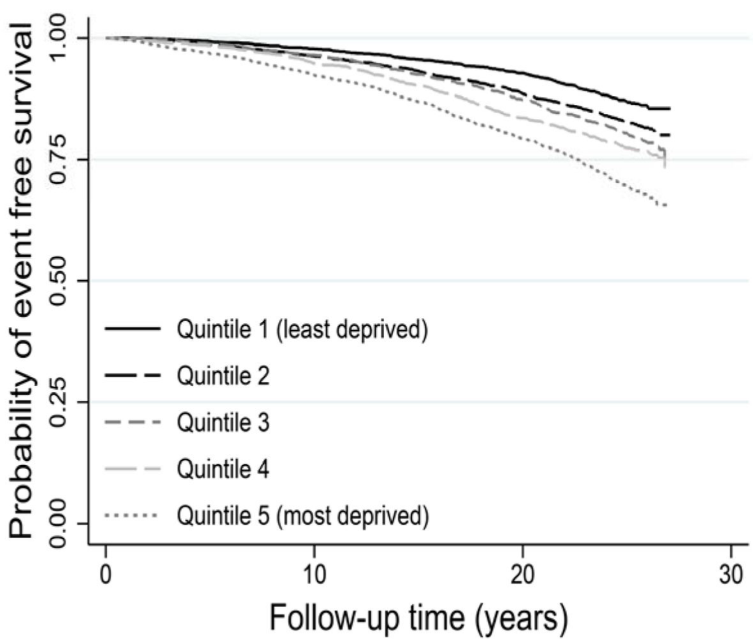
APPENDIX



Appendix Figure 1.

Log-log plot showing test for proportional-hazards assumption for A) household income and B) educational attainment



Appendix Figure 2.

Probability of survival free from heart failure-related hospitalization or death by level of Area deprivation index.

Appendix Text

List of 17 indicators of SES used to obtained Area Deprivation Index

1	Percent of the population aged ≥25 years with <9 years of education
2	Percent of the population aged ≥25 years with at least a high school diploma
3	Percent employed persons aged ≥16 years in white collar occupations
4	Median family income in U.S. dollars
5	Income disparity
6	Median home value in U.S. dollars
7	Median gross rent in U.S. dollars
8	Median monthly mortgage in U.S. dollars
9	Percent of owner-occupied housing units
10	Percent of civilian labor force population aged ≥16 years who are unemployed
11	Percent of families below federal poverty level
12	Percent of the population below 150% of the federal poverty threshold
13	Percent of single-parent households with children aged <18 years
14	Percent of households without a motor vehicle
15	Percent of households without a telephone
16	Percent of occupied housing units without complete plumbing
17	Percent of households with more than one person per room

Appendix Table 1

Baseline Characteristics of ARIC Study Population at Visit 1 (1987–1989) by Quintile of Area Deprivation Index

	Area deprivation index[a]				
Characteristics	**Quintile 1 (Least deprived)**	**Quintile 2**	**Quintile 3**	**Quintile 4**	**Quintile 5 (Most deprived)**
N	2,515	2,549	2,363	2,497	2,447
Age (years)	53.4 ± 5.7	53.8 ± 5.7	54.3 ± 5.7	54.3 ± 5.8	53.8 ± 5.7
Sex (male), % (n)	47.8 (1,201)	45.9 (1,170)	45.5 (1,076)	43.9 (1,096)	38.2 (935)
Race (African-American), % (n)	0.9 (25)	4.0 (102)	8.4 (198)	17.3 (433)	91.3 (2,234)
Smoking status, % (n)	2.0 (53)	5.4 (138)	8.9 (226)	11.8 (281)	45.3 (963)
Never	42.1 (1,058)	40.3 (1,027)	41.5 (980)	45.1 (1,126)	44.3 (1,083)
Former	36.5 (918)	35.2 (896)	31.9 (753)	30.3 (756)	24.2 (591)
Current	21.4 (539)	24.6 (626)	26.7 (630)	24.6 (615)	31.6 (773)
Alcohol intake status, % (n)					
Never	9.9 (251)	16.6 (424)	23.7 (559)	27.9 (697)	43.6 (1,066)
Former	10.7 (270)	15.3 (391)	17.9 (422)	21.1 (527)	23.9 (587)
Current	79.3 (1,994)	68.0 (1,734)	58.5 (1,382)	50.9 (1,273)	32.4 (794)
Physical activity (sports index)	2.7 ± 0.8	2.5 ± 0.8	2.5 ± 0.8	2.4 ± 0.8	2.2 ± 0.7

Characteristics	Area deprivation index[a]				
	Quintile 1 (Least deprived)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (Most deprived)
BMI (kg/m^2)	26.3 ± 4.3	26.9 ± 4.8	26.9 ± 4.8	27.7 ± 5.2	29.4 ± 6.2
Hypertension,% (n)	20.2 (507)	25.4 (648)	27.1 (641)	31.6 (788)	51.8 (1,268)
Diabetes, % (n)	5.7 (144)	9.1 (232)	8.7 (206)	10.5 (262)	17.5 (429)
Cholesterol lowering medication use, % (n)	2.3 (57)	3.4 (86)	2.4 (57)	2.5 (63)	1.6 (38)
Total cholesterol (mmol/L)	211.3 ± 40.0	213.3 ± 40.4	215.6 ± 40.4	217.5 ± 41.8	214.7 ± 45.2
High density lipoprotein (mmol/L)	53.4 ± 17.3	51.2 ± 16.7	51.3 ± 17.0	50.1 ± 16.1	54.9 ± 17.8
Health insurance (no), % (n)	1.9 (49)	4.2 (108)	4.5 (107)	8.3 (207)	26.2 (641)
Visit frequency to seek health care, % (n)					
No visit	23.2 (584)	27.4 (699)	30.2 (713)	35.2 (879)	27.0 (661)
Less than once/year	36.1 (908)	35.1 (895)	29.8 (704)	28.4 (709)	20.3 (497)
Once or more than once/year	40.7 (1,023)	37.5 (955)	40.0 (946)	36.4 (909)	52.7 (1,289)

Notes: Mean ± SD is presented for continuous variables.

[a]*p* for difference was <0.001 for all variables.

ARIC, Atherosclerosis Risk in Communities Study

Appendix Table 2

Association Between Area Deprivation Index and Incidence of Heart Failure

	Area deprivation index[a]					
	Quintile 1 (Least deprived)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (Most deprived)	
	(29.3, 96.0) (n=2,515)	(96.1, 101.7) (n=2,549)	(101.8, 107.2) (n=2,363)	(107.3, 112.5) (n=2,497)	(112.6, 127.5) (n=2,447)	*p*-trend
Events, % (n)	11.4 (287)	15.3 (389)	16.9 (399)	19.8 (495)	25.5 (623)	
Model 1, HR (95% CI)	1 (ref)	1.03 (0.83, 1.27)	1.32 (1.08, 1.62)	1.33 (1.04, 1.64)	1.83 (1.40, 2.40)	<0.001
Model 2, HR (95% CI)	1 (ref)	0.94 (0.76, 1.16)	1.15 (0.94, 1.40)	1.10 (0.88, 1.39)	1.41 (1.07, 1.87)	0.013
Model 3, HR (95% CI)	1 (ref)	0.94 (0.76, 1.16)	1.12 (0.94, 1.40)	1.13 (0.88, 1.39)	1.40 (1.07, 1.86)	0.012

Notes: *p*-trend was obtained by using Area Deprivation Index (5 quintiles) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once per year/ once or more per year).

[a]275 participants were missing information on Area Deprivation Index

HR, hazard ratio

Appendix Table 3

Association Between Household Income and Educational Attainment Level and Incidence of Heart Failure by Race[a]

	Household income			
	High ≥$25,000/year	**Medium $12,000–$24,999/year**	**Low <$12,000/year**	***p*-trend**
Whites	n=7,161	n=1,844	n=603	
Events, % (n)	13.4 (961)	21.9 (404)	27.2 (164)	
Model 1, HR (95% CI)	(ref)	1.71 (1.51, 1.92)	2.38 (2.00, 2.83)	<0.001
Model 2, HR (95% CI)	(ref)	1.51 (1.34, 1.71)	1.87 (1.57, 2.23)	<0.001
Model 3, HR (95% CI)	(ref)	1.50 (1.33, 1.69)	1.83 (1.53, 2.20)	<0.001
African Americans	n=948	n=945	n=1,145	
Events, % (n)	16.1 (153)	22.9 (217)	30.6 (350)	
Model 1, HR (95% CI)	(ref)	1.57 (1.29, 1.96)	2.50 (2.05, 3.05)	<0.001
Model 2, HR (95% CI)	(ref)	1.42 (1.15, 1.76)	2.05 (1.68, 2.52)	<0.001
Model 3, HR (95% CI)	(ref)	1.43 (1.16, 1.77)	2.05 (1.66, 2.52)	<0.001
	Educational attainment			
	High (>high school)	**Medium (high school/equivalent)**	**Low (<high school)**	***p*-trend**
Whites	n=3,696	n=4,388	n=1,524	
Events, % (n)	12.3 (453)	15.2 (666)	26.9 (410)	
Model 1, HR (95% CI)	(ref)	1.30 (1.15, 1.47)	2.33 (1.76, 2.33)	<0.001
Model 2, HR (95% CI)	(ref)	1.11 (0.98, 1.25)	1.68 (1.45, 1.95)	<0.001
Model 3, HR (95% CI)	(ref)	1.10 (0.98, 1.25)	1.65 (1.43, 1.92)	<0.001
African Americans	n=940	n=845	n=1,181	
Events, % (n)	17.3 (167)	21.0 (180)	30.6 (373)	
Model 1, HR (95% CI)	(ref)	1.32 (1.07, 1.63)	2.12 (1.77, 2.55)	<0.001

	Household income			
	High ≥\$25,000/year	**Medium \$12,000–\$24,999/year**	**Low <\$12,000/year**	***p*-trend**
Model 2, HR (95% CI)	(ref)	1.15 (0.93, 1.42)	1.74 (1.44, 2.11)	<0.001
Model 3, HR (95% CI)	(ref)	1.13 (0.91, 1.41)	1.71 (1.41, 2.08)	<0.001

Notes: p-trend was obtained by using household income and educational attainment (3 categories) as continuous variables. Model 1: Age (years), sex (male/female). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once a year/once a year or more).

[a]p for race-income interaction was 0.57 and race-education interaction was 0.89 (Model 3).

HR, hazard ratio

Appendix Table 4

Association Between Area Deprivation Index and Incidence of Heart Failure by Race[a]

	Area deprivation index[b]					
	Quintile 1 (Least deprived)	**Quintile 2**	**Quintile 3**	**Quintile 4**	**Quintile 5 (Most deprived)**	***p*-trend**
Whites	(29.3, 94.0)	(94.1, 99.3)	(99.4, 103.2)	(103.3, 108.8)	(108.9, 123.8)	
N	1,884	1,913	1,887	1,826	1,869	
Events, % (n)	11.3 (213)	13.4 (256)	16.0 (302)	17.9 (327)	20.6 (385)	
Model 1, HR (95% CI)	(ref)	1.02 (0.79, 1.31)	1.23 (0.96, 1.56)	1.32 (1.03, 1.68)	1.73 (1.30, 2.30)	<0.001
Model 2, HR (95% CI)	(ref)	0.89 (0.70, 1.14)	1.08 (0.85, 1.37)	1.04 (0.82, 1.33)	1.36 (1.02, 1.33)	0.017
Model 3, HR (95% CI)	(ref)	0.89 (0.70, 1.15)	1.07 (0.85, 1.36)	1.05 (0.82, 1.34)	1.37 (1.03, 1.83)	0.014
African Americans	(70.1, 111.5)	(111.9, 115.6)	(115.7, 117.9)	(118.1, 119.4)	(119.6, 127.5)	
N	666	587	558	596	585	
Events, % (n)	18.2 (121)	21.6 (127)	24.0 (134)	25.8 (154)	29.7 (174)	
Model 1, HR (95% CI)	(ref)	1.05 (0.69, 1.58)	1.55 (1.07, 2.24)	1.73 (1.20, 2.48)	2.01 (1.40, 2.88)	<0.001
Model 2, HR (95% CI)	(ref)	0.95 (0.63, 1.43)	1.31 (0.90, 1.90)	1.43 (1.00, 2.06)	1.71 (1.19, 2.45)	<0.001
Model 3, HR (95% CI)	(ref)	0.95 (0.63, 1.43)	1.30 (0.90, 1.89)	1.42 (0.99, 2.04)	1.70 (1.18, 2.45)	<0.001

Notes: P-trend was obtained by using Area Deprivation Index (5 quintiles) as continuous variables. Model 1: Age (years), sex (male/female). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once per year/ once or more per year)

[a]P for interaction between race and Area Deprivation Index was 0.75.

[b]275 participants were missing information on Area Deprivation Index.

HR, hazard ratio

Appendix Table 5

NT-proBNP Level in ARIC Study Population at Visit 2, 4, and 5 by Level of Household Income and Educational Attainment[a]

	Income level[b]			Educational attainment[b]		
	Low <$12,000/year	**Medium $12,000–$24,999/year**	**High ≥$25,000/year**	**Low <High school**	**Medium High school/equivalent**	**High >High school**
NT-proBNP levels (pg/ml)						
Visit 2 (Baseline) (n=11,007)	49.4 ± 3.3	49.4 ± 2.7	44.7 ± 2.7	49.4 ± 3.3	66.7 ± 3.7	44.7 ± 2.7
Visit 4 (After imputations)	81.4 ± 3.7	73.7 ± 3.7	60.3 ± 3.3	81.5 ± 4.1	73.7 ± 3.7	60.3 ± 3.3
Visit 5 (After imputations)	181.3 ± 3.7	181.3 ± 3.3	164.0 ± 3.0	200.3 ± 3.7	181.3 ± 3.3	148.4 ± 3.3

[a]For ease of interpretation log transformed values were converted back to NT-proBNP values.

[b]All comparisons had $p<0.001$.

ARIC, Atherosclerosis Risk in Communities Study, NT-proBNP, N-terminal pro-brain natriuretic peptide

Appendix Table 6

Multilevel Linear Mixed Models for the Association of Area Level SES (Area Deprivation Index Quintiles) With NT-proBNP (Log Transformed)[a]

	Area Deprivation[b]					
	Quintile 1 (Least deprived) (n=2,269)	**Quintile 2 (n=2,296)**	**Quintile 3 (n=2,182)**	**Quintile 4 (n=2,073)**	**Quintile 5 (Most deprived) (n=1,937)**	***p*-trend**
Model 1, β (95% CI)						
SES	(ref)	0.04 (−0.02, 0.09)	0.05 (−0.01, 0.10)	0.08 (0.02, 0.14)	0.22 (0.14, 0.31)	<0.001
SESXtime	(ref)	0.002 (−0.002, 0.006)	0.004 (0.00, 0.008)	0.005 (0.001, 0.009)	0.008 (0.003, 0.012)	0.001
Model 2, β (95% CI)						
SES	(ref)	0.03 (−0.03, 0.08)	0.03 (−0.03, 0.09)	0.07 (0.01, 0.13)	0.19 (0.11, 0.28)	<0.001
SESXtime	(ref)	0.002 (−0.002, 0.006)	0.004 (0.00, 0.008)	0.005 (0.001, 0.009)	0.007 (0.003, 0.011)	0.005
Model 3, β (95% CI)						
SES	(ref)	0.04 (−0.02, 0.09)	0.05 (−0.00, 0.11)	0.04 (−0.01, 0.11)	0.15 (0.06, 0.24)	0.001
SESXtime	(ref)	0.002 (−0.002, 0.006)	0.004 (0.00, 0.008)	0.005 (0.001, 0.009)	0.007 (0.003, 0.011)	0.012

Notes: The coefficient for SES X time represents the association of SES with NT-proBNP slope. P-trend was obtained by using Area Deprivation Index (5 quintiles) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3:

Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once a year/ once a year or more).

[a]The coefficient for SES represents the association of SES with NT-proBNP at baseline (e.g., in model 1, geometric mean of NT-proBNP in quintile 5 at baseline is exp(0.22)=1.25 fold higher (or 25% higher) compared to quintile 1). The coefficient for SES X time represents the association of SES with NT-proBNP slope (e.g., in model 1, per year increase in geometric mean of NT-proBNP in quintile 5 is exp(0.008)=1.01 fold higher (or 1% higher) compared to quintile 1).

[b]Additional 250 participants were missing information on area deprivation index.

NT-proBNP, N-terminal pro-brain natriuretic peptide

Appendix Table 7

Association Between Household Income Level (Redefined: <$16,000/year [Low], $16,000–$34,999/year [Medium], and ≥$35,000/year [High]) and Risk of Heart Failure

	Household income			
	High ≥$35,000/year	**Medium $16,000-$34,999/year**	**Low <$16,000/year**	**p-trend**
N	n=5,825	n=4,178	n=2,643	
Events, % (n)	12.2 (714)	19.2 (803)	27.7 (732)	
Model 1, HR (95% CI)	(ref)	1.60 (1.44, 1.77)	2.56 (2.27, 2.89)	<0.001
Model 2, HR (95% CI)	(ref)	1.37 (1.23, 1.52)	2.02 (1.78, 2.29)	<0.001
Model 3, HR (95% CI)	(ref)	1.37 (1.23, 1.52)	1.99 (1.75, 2.26)	<0.001

Notes: P-trend was obtained by using household income (3 category) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once per year/once or more per year).

HR, hazard ratio

Appendix Table 8

Results From Poisson Regression Analysis for the Association Between Household Income and Educational Attainment Level and Elevated NT-proBNP (≥300pg/ml) at Baseline

	Household income			
	High ≥$25,000/year (n=7,297)	**Medium $12,000–$24,999/year (n=2,318)**	**Low <$12,000/year (n=1,397)**	***p*-trend**
Events, % (n)	1.9 (145)	3.3 (77)	4.5 (63)	
Model 1, PR (95% CI)	(ref)	1.30 (0.97, 1.74)	1.54 (1.07, 2.21)	0.014
Model 2, PR (95% CI)	(ref)	1.22 (0.91, 1.63)	1.37 (0.95, 1.98)	0.077
Model 3, PR (95% CI)	(ref)	1.22 (0.91, 1.64)	1.36 (0.94, 1.98)	0.088
	Educational attainment			
	High (>high school) (n=4,210)	**Medium (high school/ equivalent) (n=4,663)**	**Low (<high school) (n=2,139)**	***p*-trend**
Events, % (n)	1.8 (77)	2.7 (127)	3.8 (81)	

	Household income			
	High ≥$25,000/year (n=7,297)	**Medium $12,000–$24,999/year (n=2,318)**	**Low <$12,000/year (n=1,397)**	***p*-trend**
Model 1, PR (95% CI)	(ref)	1.44 (1.09, 1.91)	1.47 (1.05, 2.06)	0.014
Model 2, PR (95% CI)	(ref)	1.32 (1.00, 1.75)	1.25 (0.88, 1.77)	0.155
Model 3, PR (95% CI)	(ref)	1.31 (0.99, 1.73)	1.23 (0.87, 1.74)	0.183

Notes: P-trend was obtained by using household income and educational attainment (3 categories) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland), estimated glomerular filtration rate (mL/min/1.73m^2). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once a year/ once a year or more).

PR, prevalence ratio, NT-proBNP, N-terminal pro-brain natriuretic peptide

Appendix Table 9

Results After Adjusting for Kidney Function in the Association of Household Income and Educational Attainment With NT-proBNP (Log Transformed) (Results From Linear Mixed Models)[a]

	Household income			
	High ≥$25,000/year (n=7,294)	**Medium $12,000–$24,999/year (n=2,317)**	**Low <$12,000/year (n=1,396)**	***p*-trend**
Model 1, β (95% CI)				
SES	(ref)	0.07 (0.03, 0.12)	0.15 (0.09, 0.22)	<0.001
SESXtime	(ref)	0.004 (0.001, 0.008)	0.006 (0.001, 0.010)	0.017
Model 2, β (95% CI)				
SES	(ref)	0.06 (0.02, 0.11)	0.14 (0.08, 0.21)	<0.001
SESXtime	(ref)	0.004 (0.001, 0.008)	0.006 (0.001, 0.010)	0.020
Model 3, β (95% CI)				
SES	(ref)	0.06 (0.02, 0.11)	0.14 (0.08, 0.20)	<0.001
SESXtime	(ref)	0.004 (0.001, 0.008)	0.006 (0.001, 0.010)	0.026
	Educational attainment			
	High (>high school) (n=4,207)	**Medium (high school/ equivalent) (n=4,663)**	**Low (<high school) (n=2,137)**	***p*-trend**
Model 1, β (95% CI)				

	Household income			
	High ≥$25,000/year (n=7,294)	Medium $12,000–$24,999/year (n=2,317)	Low <$12,000/year (n=1,396)	*p*-trend
SES	(ref)	0.03 (−0.02, 0.07)	0.07 (0.02, 0.12)	0.021
SESXtime	(ref)	0.001 (−0.002, 0.005)	0.012 (0.008, 0.016)	0.014
Model 2, β (95% CI)				
SES	(ref)	0.02 (−0.012, 0.06)	0.06 (0.01, 0.12)	0.030
SESXtime	(ref)	0.001 (−0.002, 0.005)	0.012 (0.008, 0.017)	0.023
Model 3, β (95% CI)				
SES	(ref)	0.02 (−0.02, 0.06)	0.05 (0.00, 0.11)	0.041
SESXtime	(ref)	0.001 (−0.002, 0.005)	0.012 (0.008, 0.017)	0.024

Notes: P-trend was obtained by using household income and educational attainment (3 categories) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland), estimated glomerular filtration rate (ml/min/1.73m^2). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once a year/ once a year or more).

[a]The coefficient for SES represents the association of SES with NT-proBNP at baseline (e.g., in model 1, geometric mean of NT-proBNP in low income group at baseline is exp(0.14)=1.15 fold higher (or 15% higher) compared to high income group). The coefficient for SESXtime represents the association of SES with NT-proBNP slope (e.g., in model 1, per year increase in geometric mean of NT-proBNP in low income group is exp(0.006)=1.01 fold higher (or 1% higher) compared to high income group).

β, regression coefficient, NT-proBNP, N-terminal pro-brain natriuretic peptide

Appendix Table 10

Results after adjusting for kidney function in the association between area level SES (area deprivation index quintiles) and NT-proBNP (log transformed) (results from multilevel linear mixed models)[a]

	Area deprivation index[b]					
	Quintile 1 (Least deprived) (n=2,269)	Quintile 2 (n=2,296)	Quintile 3 (n=2,182)	Quintile 4 (n=2,073)	Quintile 5 (Most deprived) (n=1,937)	*p*-trend
Model 1, β (95% CI)						
SES	(ref)	0.03 (−0.02, 0.09)	0.04 (−0.01, 0.10)	0.09 (0.03, 0.15)	0.22 (0.14, 0.31)	<0.001
SESXtime	(ref)	0.002 (−0.001, 0.006)	0.004 (0.00, 0.008)	0.005 (0.001, 0.009)	0.007 (0.003, 0.011)	0.009
Model 2, β (95% CI)						
SES	(ref)	0.03 (−0.03, 0.09)	0.03 (−0.02, 0.09)	0.08 (0.02, 0.14)	0.20 (0.12, 0.29)	<0.001
SESXtime	(ref)	0.002 (−0.002, 0.006)	0.004 (0.00, 0.008)	0.005 (0.001, 0.009)	0.006 (0.002, 0.011)	0.011

	Area deprivation index[b]					
	Quintile 1 (Least deprived) (n=2,269)	Quintile 2 (n=2,296)	Quintile 3 (n=2,182)	Quintile 4 (n=2,073)	Quintile 5 (Most deprived) (n=1,937)	*p*-trend
Model 3, β (95% CI)						
SES	(ref)	0.03 (−0.03, 0.09)	0.03 (−0.02, 0.09)	0.07 (0.01, 0.14)	0.19 (0.11, 0.28)	0.002
SESXtime	(ref)	0.002 (−0.002, 0.006)	0.004 (0.00, 0.008)	0.005 (0.001, 0.009)	0.006 (0.002, 0.011)	0.019

Notes: P-trend was obtained by using Area Deprivation Index (5 quintiles) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland), estimated glomerular filtration rate (ml/min/1.73m^2). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once a year/ once a year or more).

[a]The coefficient for SES represents the association of SES with NT-proBNP at baseline (e.g., in model 1, geometric mean of NT-proBNP in quintile 5 at baseline is exp(0.22)=1.25 fold higher (or 25% higher) compared to quintile 1). The coefficient for SES Xtime represents the association of SES with NT-proBNP slope (e.g., in model 1, per year increase in geometric mean of NT-proBNP in quintile 5 is exp(0.007)=1.01 fold higher (or 1% higher) compared to quintile 1).

[b]Additional 250 participants were missing information on area deprivation index.

β, regression coefficient, NT-proBNP, N-terminal pro-brain natriuretic peptide

Appendix Table 11

Association Between Individual Level SES Measures and Incidence of Heart Failure When Mutually Adjusted Along With ADI[a]

	Household income			
	High ≥$25,000/year	Medium $12,000–$24,999/year	Low <$12,000/year	*p*-trend
Model 1, HR (95% CI)	1 (ref)	1.26 (1.09, 1.47)	1.39 (1.14, 1.70)	<0.001
Model 2, HR (95% CI)	1 (ref)	1.23 (1.06, 1.43)	1.28 (1.05, 1.56)	0.001
Model 3, HR (95% CI)	1 (ref)	1.23 (0.82, 1.10)	1.27 (1.04, 1.55)	0.002
	Educational attainment			
	High (>high school)	Medium (high school/equivalent)	Low (<high school)	*p*-trend
Model 1, HR (95% CI)	1 (ref)	1.04 (0.90, 1.20)	1.72 (1.45, 2.03)	<0.001
Model 2, HR (95% CI)	1 (ref)	0.95 (0.82, 1.09)	1.46 (1.23, 1.73)	<0.001
Model 3, HR (95% CI)	1 (ref)	0.95 (0.82, 1.10)	1.45 (1.22, 1.72)	<0.001

Notes: P-trend was obtained by using household income and educational attainment (3 categories) as continuous variables. Model 1: Age (years), time period, sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth

County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland), household income (< $12,000, $12,000–$24,999, ≥$30,000) (in case of education model), educational attainment (<high school, high school, >high school) (in case of income model), ADI (quintile). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once a year/ once a year or more

[a]233 participants were missing information on ADI.

HR, hazard ratio, ADI, Area Deprivation Index;

Appendix Table 12

Association Between Area Deprivation Index and Incidence of Heart Failure When Adjusted for Individual Level SES Measures[a]

	Area deprivation index[a]					
	Quintile 1 (Least deprived) (29.3, 96.1)	Quintile 2 (96.2, 101.8)	Quintile 3 (101.9, 107.1)	Quintile 4 (107.2, 112.6)	Quintile 5 (Most deprived) (112.8, 127.5)	*p*-trend
Model 1, HR (95% CI)	1 (ref)	0.98 (0.79, 1.22)	1.22 (0.99, 1.49)	1.19 (0.94, 1.50)	1.42 (1.07, 1.88)	0.012
Model 2, HR (95% CI)	1 (ref)	0.93 (0.75, 1.15)	1.12 (0.91, 1.37)	1.07 (0.85, 1.36)	1.22 (0.92, 1.63)	0.164
Model 3, HR (95% CI)	1 (ref)	0.93 (0.75, 1.15)	1.12 (0.91, 1.38)	1.08 (0.86, 1.36)	1.24 (0.93, 1.65)	0.140

Notes: P-trend was obtained by using Area Deprivation Index (5 quintiles) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland), household income (<$12,000, $12,000–$24,999, ≥ $30,000), educational attainment (<high school, high school, >high school). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once per year/ once or more per year).

[a]233 participants were missing information on Area Deprivation Index.

HR= hazard ratio

Appendix Table 13

Association Between Household Income and Educational Attainment Level and Incidence of Heart Failure After Adjusting for Psychological Stress[a]

	Household income			
	High ≥$25,000/year (n=7,546)	Medium $12,000–$24,999/year (n=2,436)	Low <$12,000/year (n=1,378)	*p*-trend
VE Score	**7 (2 – 13)**	**10 (4 – 16)**	**13 (6 – 20)**	**<0.001**
Events, % (n)	13.7 (1,031)	21.6 (526)	28.7 (396)	
Model 1, HR (95% CI)	1 (ref)	1.56 (1.39, 1.75)	2.21 (1.93, 2.54)	<0.001

	Household income			
	High ≥$25,000/year (n=7,546)	**Medium $12,000–$24,999/year (n=2,436)**	**Low <$12,000/year (n=1,378)**	***p*-trend**
Model 2, HR (95% CI)	1 (ref)	1.41 (1.26, 1.58)	1.81 (1.57, 2.08)	<0.001
Model 3, HR (95% CI)	1 (ref)	1.40 (1.25, 1.57)	1.79 (1.55, 2.07)	<0.001
Model 4, HR (95% CI)	1 (ref)	1.37 (1.22, 1.53)	1.69 (1.46, 1.95)	<0.001
	Educational attainment			
	High (>high school) (n=4,344)	**Medium (high school/ equivalent) (n=4,789)**	**Low (<high school) (n=2,227)**	***p*-trend**
VE Score	**6 (2 – 12)**	**8 (4 – 15)**	**12 (6 – 20)**	**<0.001**
Events, % (n)	13.3 (576)	15.7 (754)	27.9 (623)	
Model 1, HR (95% CI)	1 (ref)	1.24 (1.11, 1.39)	2.03 (1.80, 2.30)	<0.001
Model 2, HR (95% CI)	1 (ref)	1.08 (0.96, 1.21)	1.58 (1.40, 1.79)	<0.001
Model 3, HR (95% CI)	1 (ref)	1.08 (0.96, 1.20)	1.57 (1.38, 1.78)	<0.001
Model 4, HR (95% CI)	1 (ref)	1.04 (0.93, 1.17)	1.47 (1.29, 1.67)	<0.001

Notes: P-trend was obtained by using household income and educational attainment (3 categories) as continuous variables. Model 1: Age (years), time period, sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once a year/ once a year or more. Model 4: Model 3 + depression score.

[a]Baseline is visit 2 since data on psychological stress was only available at visit 2.

VE, vital exhaustion (higher score means higher psychological stress); HR, hazard ratio

Appendix Table 14

Association Between Area Deprivation Index and Incidence of Heart Failure After Adjusting for Psychological Stress[a]

	Area deprivation index[b]					
	Quintile 1 (Least deprived)	**Quintile 2**	**Quintile 3**	**Quintile 4**	**Quintile 5 (Most deprived)**	
	(29.3 – 96.1)	**(96.2 – 101.8)**	**(101.9 – 107.1)**	**(107.2 – 112.6)**	**(112.8 – 127.5)**	***p*-trend**
	(n=2,360)	**(n=2,377)**	**(n=2,180)**	**(n=2,234)**	**(n=1,976)**	
VE Score	**6 (2 – 12)**	**7 (3 – 14)**	**8 (4 – 15)**	**8 (4 – 16)**	**10 (5 – 18)**	**<0.001**
Events, % (n)	11.2 (264)	15.0 (357)	16.4 (358)	19.6 (437)	24.9 (492)	

	Area deprivation index[b]					
	Quintile 1 (Least deprived) (29.3 – 96.1) (n=2,360)	Quintile 2 (96.2 – 101.8) (n=2,377)	Quintile 3 (101.9 – 107.1) (n=2,180)	Quintile 4 (107.2 – 112.6) (n=2,234)	Quintile 5 (Most deprived) (112.8 – 127.5) (n=1,976)	*p*-trend
Model 1, HR (95% CI)	1 (ref)	1.31 (1.12, 1.55)	1.44 (1.22, 1.70)	1.55 (1.29, 1.86)	2.18 (1.73, 2.74)	<0.001
Model 2, HR (95% CI)	1 (ref)	1.14 (0.97, 1.34)	1.22 (1.03, 1.44)	1.27 (1.06, 1.52)	1.51 (1.19, 1.90)	<0.001
Model 3, HR (95% CI)	1 (ref)	1.15 (0.99, 1.35)	1.21 (1.03, 1.43)	1.27 (1.06, 1.52)	1.50 (1.19, 1.89)	<0.001
Model 4, HR (95% CI)	1 (ref)	1.12 (0.95, 1.32)	1.18 (1.00, 1.39)	1.24 (1.03, 1.49)	1.45 (1.14, 1.83)	<0.001

Notes: P-trend was obtained by using Area Deprivation Index (5 quintiles) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once per year/ once or more per year). Model 4: Model 1 + depression score.

[a]Baseline is visit 2 since data on psychological stress was only available at visit 2

[b]233 participants were missing information on Area Deprivation Index

VE, vital exhaustion; HR, hazard ratio

Appendix Table 15

Association Between Area Deprivation Index and Incidence of Heart Failure With Visit 4 as Baseline

	Area deprivation index[a]					
	Quintile 1 (Least deprived) (81.0 – 91.5)	Quintile 2 (96.2 – 98.7)	Quintile 3 (100.7 – 102.7)	Quintile 4 (104.7 – 108.2)	Quintile 5 (Most deprived) (113.0 – 118.9)	*p*-trend
Model 1, HR (95% CI)	1 (ref)	0.87 (0.70, 1.08)	1.17 (0.96, 1.44)	1.25 (1.01, 1.53)	1.48 (1.13, 1.95)	<0.001
Model 2, HR (95% CI)	1 (ref)	0.84 (0.67, 1.04)	1.07 (0.87, 1.31)	1.08 (0.87, 1.33)	1.23 (0.93, 1.63)	0.04
Model 3, HR (95% CI)	1 (ref)	0.84 (0.68, 1.04)	1.07 (0.87, 1.31)	1.08 (0.87, 1.33)	1.23 (0.93, 1.63)	0.04

Notes: P-trend was obtained by using Area Deprivation Index (5 quintiles) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/ less than once per year/ once or more per year).

[a]275 participants were missing information on Area Deprivation Index.

HR, hazard ratio

Appendix Table 16

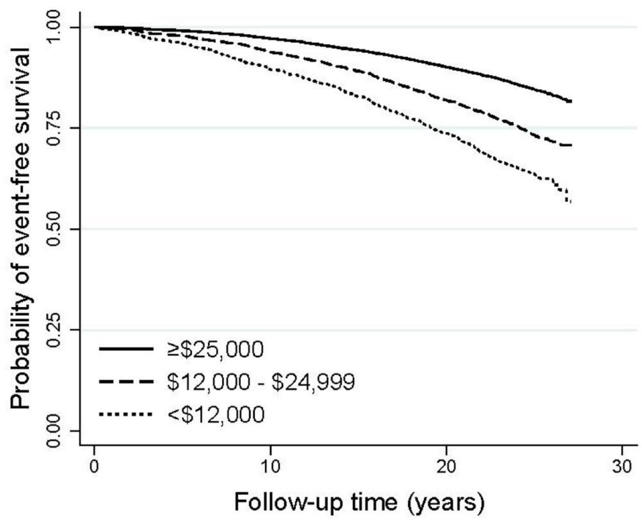
The Association Between Area Level SES (Area Deprivation Index Quintiles) and NT-proBNP (Log Transformed) (Results From Linear Regression Models) With Visit 4 as Baseline

	Area deprivation index[†]					
	Quintile 1 (Least deprived)	**Quintile 2**	**Quintile 3**	**Quintile 4**	**Quintile 5 (Most deprived)**	***p*-trend**
	(n=1,737)	**(n=1,777)**	**(n=1,689)**	**(n=1,616)**	**(n=1,509)**	
Model 1, β (95% CI)	(ref)	0.03 (−0.04, 0.10)	0.09 (0.01, 0.16)	0.09 (0.02, 0.16)	0.15 (0.04, 0.25)	<0.001
Model 2, β (95% CI)	(ref)	0.02 (−0.05, 0.08)	0.07 (0.00, 0.15)	0.07 (−0.01, 0.14)	0.13 (0.02, 0.23)	0.008
Model 3, β (95% CI)	(ref)	0.02 (−0.05, 0.09)	0.08 (0.00, 0.15)	0.07 (−0.01, 0.14)	0.12 (0.02, 0.23)	0.009

Notes: P-trend was obtained by using Area Deprivation Index (5 quintiles) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland). Model 2: Model 1 + smoking status (never/former/ current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/ less than once a year/ once a year or more).

β, regression coefficient

a



b

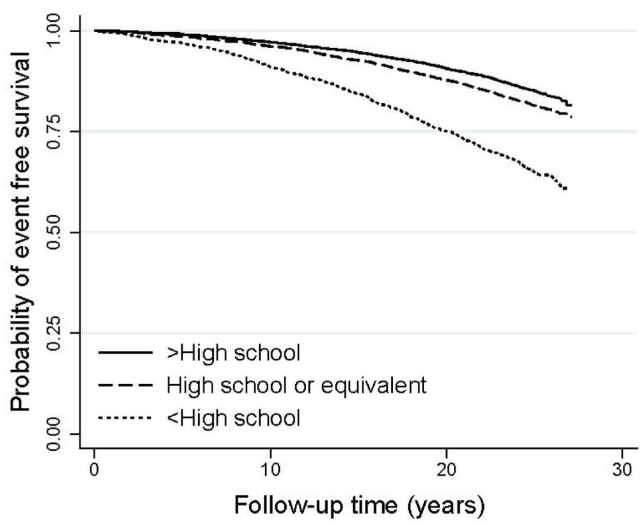


Figure 1.

Probability of survival free from heart failure-related hospitalization or death by level of (A) annual household income, and (B) educational attainment.

Table 1

Baseline Characteristics of ARIC Study Population at Visit 1 (1987–1989) by Level of Household Income and Educational Attainment[a]

Characteristics	Income level			Educational attainment		
	Low <$12,000/year	**Medium $12,000–$24,999/year**	**High ≥$25,000/year**	**Low <High school**	**Medium High school/equivalent**	**High >High school**
N	1,748	2,789	8,109	2,741	5,244	4,661
Age (years)	55.6 ± 5.9	55.2 ± 5.8	53.1 ± 5.5	55.7 ± 5.6	53.7 ± 5.6	53.1 ± 5.7
Sex (male), % (n)	27.8 (486)	38.9 (1,084)	49.7 (4,032)	44.7 (1,225)	39.1 (2,051)	49.9 (2,326)
Race (African American), % (n)	65.5 (1,145)	33.9 (945)	11.7 (948)	44.4 (1,217)	16.3 (856)	20.7 (965)
Smoking status, % (n)						
Never	42.7 (746)	44.2 (1,232)	42.0 (3,409)	36.8 (1,010)	43.3 (2,269)	45.2 (2,108)
Former	22.6 (395)	27.9 (780)	34.9 (2,828)	29.3 (803)	30.1 (1,580)	34.8 (1,620)
Current	34.7 (607)	27.9 (777)	23.1 (1,872)	20.0 (928)	26.6 (1,395)	20.0 (933)
Alcohol intake status, % (n)						
Never	39.8 (696)	33.7 (939)	17.9 (1,455)	33.8 (925)	24.5 (1,287)	18.8 (878)
Former	28.4 (497)	21.6 (602)	14.2 (1,150)	29.2 (801)	16.6 (870)	12.4 (578)
Current	31.8 (555)	44.8 (1,248)	67.9 (5,504)	37.0 (1,015)	58.9 (3,087)	68.8 (3,205)
Physical activity (sports index)	2.2 ± 0.7	2.3 ± 0.7	2.6 ± 0.8	2.2 ± 0.7	2.4 ± 0.8	2.6 ± 0.8
BMI (kg/m^2)	29.2 ± 6.5	27.9 ± 5.5	26.9 ± 4.7	28.6 ± 5.8	27.3 ± 5.2	26.9 ± 4.7
Hypertension,% (n)	50.4 (881)	27.1 (1,036)	24.8 (2,013)	43.3 (1,188)	29.4 (1,544)	25.7 (1,198)
Diabetes, % (n)	20.2 (354)	12.9 (359)	7.2 (584)	16.3 (446)	9.5 (496)	7.6 (355)
Cholesterol lowering medication use, % (n)	2.2 (38)	2.6 (71)	2.5 (203)	2.4 (66)	2.6 (136)	2.4 (110)
Total cholesterol (mmol/L)	5.7 ± 1.2	5.6 ± 1.1	5.5 ± 1.0	5.6 ± 1.1	5.6 ± 1.1	5.4 ± 1.0
High density lipoprotein (mmol/L)	1.40 ± 0.4	1.36 ± 0.4	1.33 ± 0.4	1.33 ± 0.4	1.34 ± 0.4	1.36 ± 0.4
Health insurance (no), % (n)	35.5 (620)	11.7 (327)	2.4 (194)	22.2 (608)	6.5 (341)	4.1 (192)
Visit frequency to seek health care, % (n)						
No visit	33.7 (590)	32.3 (902)	26.4 (2,138)	36.8 (1,008)	30.7 (1,609)	21.7 (1,013)
Less than once/year	19.9 (349)	23.5 (656)	34.2 (2,773)	21.2 (580)	29.6 (1,551)	35.3 (1,647)
Once or more than once/year	46.3 (809)	44.1 (1,231)	39.4 (3,198)	42.1 (1,153)	39.7 (2,084)	42.9 (2,001)

Notes: Mean ± SD is presented for continuous variables.

[a]All comparisons had p<0.001 except high density lipoprotein for education with p of 0.009, cholesterol lowering medication use for income with p of 0.69, and for education with p of 0.74.

ARIC, Atherosclerosis Risk in Communities Study

Table 2

Association Between Household Income and Educational Attainment Level and Incidence of Heart Failure

	Household income			
	High ≥$25,000/year (n=8,109)	**Medium $12,000–$24,999/year (n=2,789)**	**Low <$12,000/year (n=1,748)**	***p*-trend**
Events, % (n)	13.7 (1,114)	22.3 (621)	29.4 (514)	
Model 1, HR (95% CI)	1 (ref)	1.68 (1.52, 1.87)	2.47 (1.19, 2.80)	**<0.001**
Model 2, HR (95% CI)	1 (ref)	1.49 (1.34, 1.66)	1.95 (1.72, 2.22)	**<0.001**
Model 3, HR (95% CI)	1 (ref)	1.48 (1.34, 1.65)	1.92 (1.69, 2.19)	**<0.001**
	Educational attainment			
	High (>high school) (n=4,661)	**Medium (high school/equivalent) (n=5,244)**	**Low (<high school) (n=2,741)**	***p*-trend**
Events, % (n)	13.3 (620)	16.1 (846)	28.6 (783)	
Model 1, HR (95% CI)	1 (ref)	1.29 (1.16, 1.44)	2.22 (1.99, 2.49)	**<0.001**
Model 2, HR (95% CI)	1 (ref)	1.11 (1.00, 1.23)	1.68 (1.50, 1.89)	**<0.001**
Model 3, HR (95% CI)	1 (ref)	1.10 (0.99, 1.22)	1.65 (1.47, 1.85)	**<0.001**

Note: Boldface indicates statistical significance ($p<0.05$). P-trend was obtained by using household income and educational attainment (3 categories) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once a year/once a year or more).

HR, hazard ratio

Table 3

Linear Mixed Models for the Association of Household Income and Educational Attainment With NT-proBNP (Log Transformed)[a]

	Household income			
	High ≥$25,000/year (n=7,294)	**Medium $12,000–$24,999/year (n=2,317)**	**Low <$12,000/year (n=1,396)**	***p*-trend**
Model 1, β (95% CI)				
SES	0 (ref)	0.07 (0.02, 0.11)	0.14 (0.08, 0.21)	**<0.001**
SES X time	0 (ref)	0.004 (0.001, 0.007)	0.006 (0.001, 0.010)	**0.017**
Model 2, β (95% CI)				
SES	0 (ref)	0.06 (0.01, 0.11)	0.13 (0.07, 0.20)	**<0.001**
SES X time	0 (ref)	0.004 (0.001, 0.008)	0.006 (0.001, 0.010)	**0.019**
Model 3, β (95% CI)				
SES	0 (ref)	0.05 (0.01, 0.10)	0.13 (0.07, 0.20)	**<0.001**
SES X time	0 (ref)	0.004 (0.001, 0.008)	0.006 (0.001, 0.010)	**0.023**
	Educational attainment			
	High (>high school) (n=4,207)	**Medium (high school/equivalent) (n=4,663)**	**Low (<high school) (n=2,137)**	***p*-trend**
Model 1, β (95% CI)				
SES	0 (ref)	0.02 (−0.02, 0.06)	0.06 (0.01, 0.11)	**0.019**
SES X time	0 (ref)	0.001 (−0.002, 0.005)	0.012 (0.008, 0.016)	**0.012**
Model 2, β (95% CI)				
SES	0 (ref)	0.02 (−0.02, 0.06)	0.05 (0.00, 0.11)	**0.024**
SES X time	0 (ref)	0.001 (−0.002, 0.005)	0.012 (0.008, 0.017)	**0.017**
Model 3, β (95% CI)				
SES	0 (ref)	0.01 (−0.03, 0.05)	0.05 (0.00, 0.10)	**0.039**
SES X time	0 (ref)	0.001 (−0.002, 0.005)	0.012 (0.008, 0.017)	**0.021**

Notes: Boldface indicates statistical significance ($p<0.05$). P-trend was obtained by using household income and educational attainment (3 categories) as continuous variables. Model 1: Age (years), sex (male/female), race-center (black-Jackson, Mississippi; black and white-Forsyth County, North Carolina; white-Minneapolis, Minnesota; white-Washington County, Maryland). Model 2: Model 1 + smoking status (never/former/current), alcohol intake status (never/former/current), physical activity (sport index), BMI (kg/m^2), hypertension (yes/no), diabetes (yes/no), cholesterol lowering medication use (yes/no), total cholesterol (mmol/L), high density lipoprotein cholesterol (mmol/L). Model 3: Model 2 + health insurance status (yes/no), frequency of routine healthcare visits (never/less than once a year/ once a year or more).

[a]The coefficient for SES represents the association of SES with NT-proBNP at baseline (e.g., in model 1, geometric mean of NT-proBNP in low income group at baseline is exp(0.14)=1.15 fold higher (or 15% higher) compared to high income group). The coefficient for SES X time represents the association of SES with NT-proBNP slope (e.g., in model 1, per year increase in geometric mean of NT-proBNP in low income group is exp(0.006)=1.01 fold higher (or 1% higher) compared to high income group).

β, regression coefficient, NT-proBNP, N-terminal pro-brain natriuretic peptide