ARIC Manuscript Proposal #4153

PC Reviewed: 02/14/23	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Associations of social relationships and heart failure morbidity and mortality in the Atherosclerosis Risk in Communities (ARIC) Study and Jackson Heart Study (JHS) shared cohort

b. Abbreviated Title (Length 26 characters): Social relationships HF morbidity

2. Writing Group:

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

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3. Timeline: ~ 2 years

This work will be part of Kennedy Peter's dissertation, the timeline of which is outlined below:
Dissertation proposal: Early spring 2023
Dissertation defense: Fall 2023 or Spring 2024
Submission for publication: Fall 2023 or Spring 2024

4. Rationale:

Social relationships have been consistently associated with health outcomes, with more favorable measures of social relationships being associated with prolonged years of life, and more favorable mental and physical health outcomes.[1] Social relationships are hypothesized to affect health through behavioral processes (smoking, diet, physical activity, etc.) and psychological processes (stress management, depression, etc.), which in turn affect biological processes related to the cardiovascular, neuroendocrine, and immune systems.[2] Observational evidence suggests that poor social relationships may be related both to increased risk of incident heart failure (HF),[3] and poor prognosis after an HF diagnosis.[4-7] Additionally, social relationships measured among HF patients predicts HF-related symptoms,[8] HF self-care behaviors,[9,10] length of hospital stay,[11] and potentially even depression.[6]

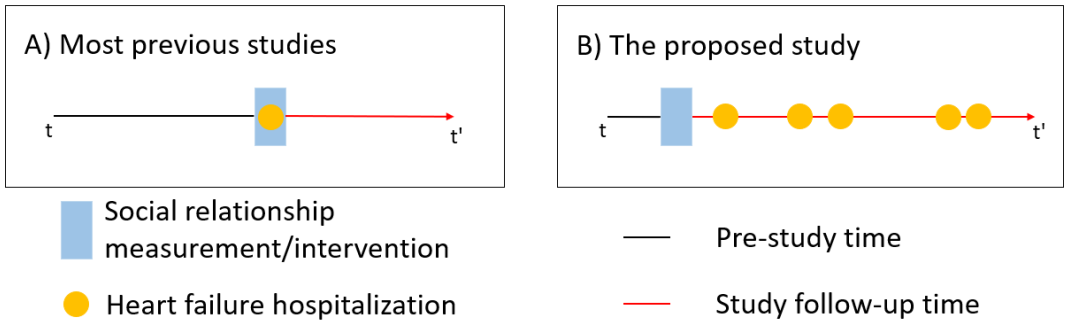
Although social relationships are alterable through interventions such as cognitive behavioral therapy,[12] experimental trials have been largely unsuccessful in changing the progression of HF by implementing social-relationship interventions among HF patients.[13,14] Reigel et al. implemented a peer support intervention among 31 heart failure patients, and found that although HF self-care management had improved in the intervention group, there was no difference in time to hospitalization between the control and intervention groups.[14] A trial using a similar intervention, reciprocal peer support, was conducted among 266 HF patients. It found that the intervention group had increased levels of social support, but that there was no difference between the control and intervention group in risk of rehospitalization or death.[13] Unlike results from observational studies that show a strong relationship between social relationships measured among HF patients and HF morbidity and mortality, these trials suggest that social relationship interventions among those with HF are not effective in altering HF morbidity and mortality. These incongruous results warrant investigation, which could lead to improved interventions.

The specific aspect of social relationships intervened on may have contributed to unsuccessful interventions. Structural (quantity of relationships, social isolation) and functional (quality of relationships, social support) aspects of social relationships may play different roles in cardiovascular disease (CVD) pathologies. Some current observational studies suggest that structural measures of social relationships measured among HF patients are related to HF morbidity and mortality,[15-19] while others did not.[20] Studies of functional measures of social relationships measured in HF patients suggest they are predictive of HF morbidity and mortality,[8,11,15,20-23] however, not all studies agree.[16-18,24] In terms of HF morbidity, social resources may determine the availability of caregivers and contacts to help access medical care, aid in performing personal care tasks and house chores, and provide emotional support, among other types of support.[25] Little work has been done to identify the specific aspects of social relationships or types of social support that are the most important for improving HF morbidity and mortality after initial hospitalization, as few studies have assessed specific types of social support rather than the overall measure.[18,20,26] Previous interventions may not have targeted the specific aspect of social relationships or specific types of social support most associated with HF morbidity and mortality, resulting in inconsistencies with observational findings. By studying multiple aspects of social relationships (structural: social isolation; functional: perceived social support) and types of social support (appraisal support, tangible support, belonging support, and self-esteem support), our research may elucidate specific aspects of social relationships most

associated with decreased morbidity and mortality due to HF, which can better inform intervention development in the future.

Additionally, experimental and observational evidence may conflict due to timing of intervention and social relationship measurement. Social relationship interventions may have been unsuccessful because intervening on social relationships after HF diagnosis is too late to change disease progression, or because social relationships later in life may not be easily altered. If true, this would point to the premorbid period as a potential time for intervention, using prevention to slow HF progression. However, little observational or experimental research has focused on the relationship between premorbid social relationships and post-HF hospitalization morbidity and mortality. Premorbid social relationships may be especially important in predicting HF morbidity and mortality since HF is a chronic condition, rather than an acute event such as a myocardial infarction or stroke. Measurement of premorbid social relationships may be more reflective of social resources available to the patient prior to HF hospitalization, as declines in health leading up to HF hospitalization may negatively affect social relationships.[12] Caregivers of HF patients report a high physical and emotional toll, regardless of the severity of the HF patient.[25] Therefore, it is important to measure the patient's social resources before they are strained by hospitalization. This proposal will avoid this issue by examining social relationships measured prior to initial HF hospitalization (Figure 1).

Figure 1. Timeline (t to t') of social relationship measurement/intervention in relation to first HF hospitalization in previous studies (panel A) and the present proposed study (panel B).



To our knowledge, only two studies have assessed the associations of premorbid social relationships with HF morbidity and mortality. Kaiser et al. assessed the associations of structural and functional aspects of social relationships with mortality, including participants of the Cardiovascular Health Study who developed HF within 2 years of the initial social relationship measurements, higher social isolation to be associated with greater mortality, but no association with premorbid social support.[27] Additionally, Krumholz et al. assessed the associations of emotional support, instrumental support, and social ties measured on average 2 years prior to initial HF hospitalization and their associations with 1-year risk of fatal or nonfatal CV events, CV death, CV readmissions, and all-cause mortality.[26] This study found only premorbid emotional social support to be associated with measures of HF morbidity and mortality.[26] Further research is needed to determine the associations of premorbid structural and functional aspects of social relationships with HF

morbidity and mortality as little evidence exists, and the results of existing studies conflict as to whether structural or functional aspects of social relationships are important to HF morbidity and mortality.

Very few studies have investigated the role of changes in social relationships and their association with HF morbidity and mortality.[28] Social relationships primarily change with life events that change social circles, such as marriage, divorce, death of a partner, moving, retirement, and declines in health.[12,29] As it is common for middle-aged populations to experience these events, and to experience declines in health due to HF, it is important to assess social relationships at multiple time points and whether changes in social relationships are associated with HF morbidity and mortality after the initial HF hospitalization.

Previous studies have primarily defined HF morbidity in terms of recurrent HF rehospitalizations.[4-7] In order to obtain a wider picture of clinical events related to the progression of HF, we will investigate the timing and number of hospitalizations, proportion of year spent in cardiovascular-related hospital stays, and risk of any cardiovascular event/all-cause mortality within the first year of incident HF hospitalization. In addition to these clinical measures of HF morbidity and mortality, we will also assess annually measured self-rated health (SRH) in the four years prior to and after incident HF hospitalization. SRH is a holistic measure of perceived health that encompasses physical, mental, and social health, and is associated with risk of CVD and mortality.[30] To our knowledge, no previous works have investigated the relationship between social relationships and SRH in the years before and following a HF hospitalization. In the ARIC cohort, it was shown that participants with HF had the lowest measures of SRH, and had the largest decreases in SRH in the four years prior to initial HF hospitalization, compared to participants who experienced other cardiovascular events such as myocardial infarction and stroke.[31] This was followed by a sharp decline in SRH following the initial HF hospitalization, and gradual downwards trajectory for the following 4 years.[31] This analysis will be able to explore whether going into a HF hospitalization with more favorable measures of social relationships, and whether changes in these relationships, are associated with higher levels of SRH both before and after HF hospitalization.

We propose to examine premorbid structural (social isolation) and functional (perceived total social support) aspects of social relationships, along with specific types of social support (appraisal support, tangible support, belonging support, and self-esteem support), at mid-life and their changes, and their associations with HF morbidity and mortality measured by clinical events and progression of SRH. Analyses will employ secondary data from the Atherosclerosis Risk in Communities (ARIC) Study, which measured social relationships in 1990-1992. Assessment of changes in social relationships will be executed among ~1,250 ARIC participants who also participated in the Jackson Heart Study (JHS), which measured social relationships in 2000-2004.

5. Main Hypothesis/Study Questions:

Aim 1: Estimate the associations of premorbid structural and functional aspects of social relationships at mid-life (ARIC) and their 10-year changes (ARIC/JHS shared cohort) with clinically recognized measures of HF morbidity and mortality.

Hypothesis: Lower premorbid social isolation and greater premorbid social support, and preservation of low social isolation and high social support, will be associated with lower morbidity and mortality due to HF in the year following initial HF hospitalization.

Aim 2: Estimate the associations of structural and functional aspects of social relationships at mid-life (ARIC) and their 10-year changes (ARIC/JHS shared cohort) with repeated measures of SRH 4 years prior to and after an initial HF hospitalization.
Hypothesis: Lower premorbid social isolation and greater premorbid social support, and preservation of low social isolation and high social support, will be associated with higher levels of SRH pre- and post-initial HF hospitalization.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

This prospective, longitudinal cohort study will include ~2,827 ARIC participants who have measures of structural and functional aspects of social relationships at Visit 2 and who had an initial HF hospitalization . Analyses that involve changes in social relationships will include all ARIC/JHS shared cohort participants with measures of social relationships at ARIC Visit 2 and JHS Visit 1 (~1200 in total and ~350 who experienced an initial HF hospitalization). Analyses will not include any JHS participants who were not also ARIC participants. All demographic characteristics and medical histories were collected at ARIC Visit 1.

Exclusions. Participants with missing social relationship data from ARIC Visit 2. Participants with a history of HF or those who experienced an incident HF hospitalization before ARIC Visit 2. Participants who did not experience an initial HF hospitalization over the course of follow-up. Non-white and non-Black participants. Participants from the ARIC/JHS shared cohort who experienced an incident HF hospitalization before the second measurement of social relationships in JHS will be excluded from analyses involving changes in social relationships.

Exposure assessment. All social relationship exposures were assessed by a single, self-administered health and life profile questionnaire at the second ARIC visit (1990-1992). In JHS, social relationships were assessed using two self-administered questionnaires at the first visit (2000-2004): one on social support and another titled Approach to Life A. Current literature often uses inconsistent language to describe measures of social relationships. Therefore, this project will classify social relationships into structural and functional measures of social relationships, as recommended by Valtorta et al.[32]

Structural measures of social relationships (social isolation). Structural measures of social relationships, a measure of the quantity of relationships, assess the number and frequency of social contacts, and involvement in social networks.[32] While there are many questionnaires designed to measure structural aspects of social relationships in different populations, the ARIC study assessed social isolation using the Lubben Social Network Scale (LSNS), a well validated[33,34] and psychometrically valid questionnaire with high internal reliability. Using 10 questions with a 0-5 rating scale, the LSNS assesses the self-reported availability of social contacts with friends, family, and peers, along with network size. Typically, total scores ranging

from 0-50 are categorized into levels of risk for social isolation: low risk (≥31), moderate risk (26-30), high risk (21-25), and socially isolated (≤20).[35]

Structural aspects of social relationships in JHS was measured by three items adapted from the Berkman Social Network Index (BSNI).[36] The BSNI is previously validated, and this version consists of three questions from it: 1) How many close friends do you have?, 2) How many close relatives to you have?, 3) How many of these friends or relatives do you see at least once a month?. Possible responses are ranges of numbers consisting of the following: none, 1 to 2, 3 to 5, 9 to 9, and 10 or more. Other papers in JHS have assigned a score of 0 to 4 to each item, computing a total ranging from 0 to 12 for all three questions, and then used the lowest tertile to represent unfavorable levels of structural aspects of social relationships.[37] Both the LSNS and BSNI primarily measure involvement in relationships, and while they do include some functional aspects of social relationships, are primarily measures of relationship structures.[32]

Functional aspects of social relationships (social support). Social support, a measure of the quality of relationships, assess the purpose of relationships and the perceived support from these relationships.[1] The functional measure of social relationships at mid-life used in the ARIC study and in the JHS is the 16-item Interpersonal Support Evaluation List (ISEL), which assesses total perceived social support using questions from 4 subscales (tangible, appraisal, belonging, and self-esteem) of the 40-item ISEL. Each question on the 16-item ISEL corresponds to a specific subtype of social support; scores for each subtype will be derived from the corresponding questions. The ISEL is highly correlated with other measures of perceived support.[38] Six-week test-retest correlation for this measure is 0.70, and the range of internal consistency is 0.88 to 0.90.[39]

Outcomes:

Clinically recognized measures of HF morbidity and mortality. Cardiovascular events were ascertained by contacting participants annually, examining hospitalizations and death records from the previous year, and by using discharge lists from local hospitals and death certificates from state vital statistics offices. These outcomes were ascertained continuously since the inception of the cohort. Patients with first HF hospitalization include adjudicated definite and probable cases by the ARIC study physician panel which began in 2005, and prior to 2005 will include ICD-9 codes 428 (428.0-428.9) in any position, as has been done in previous ARIC studies.[40] The positive predictive value of the ICD-9 code 428 in any position compared to the gold standard of physician adjudication in ARIC is 0.77, with a sensitivity of 0.95 and specificity of 0.23.[41] For comparison, the positive predictive value for ICD-9 code 428 in the primary position only is 0.97, with a sensitivity of 0.36 and specificity of 0.97.[41] Clinically recognized measures of HF morbidity and mortality are described in Table 1, and will each be assessed separately. These definitions will be used both in aims that include the full ARIC cohort, and in those that include only ARIC/JHS co-participants.

Table 1. Clinically recognized measures of HF morbidity and mortality, their definitions, and measurement.

HF progression outcome	Definition	Measurement/identification	Estimand of interest

Any cause hospitalization: time to first hospitalization	Date of first hospitalization from any cause	ICD-9/ICD-10 codes	Time to event (hazard ratio)
Any cause hospitalization: number of hospitalizations within first year	Number of hospitalizations within a year of the incident cardiovascular event	ICD-9/ICD-10 codes	Counts
Proportion of first year spent in cardiovascular-related hospital stays	1. Length of hospital stay due to stroke and heart failure 2. Length of hospital stay due to coronary heart disease	1. ICD-9 code: 428, ICD-10 code: 150, in any position 2. Validated events by ARIC reviewer classification	Beta
1-year risk of any cardiovascular event or all-cause mortality	1. Death from stroke or heart failure 2. Death from coronary heart disease 3. Death due to any cause, not restricted to cardiovascular deaths 4. Hospitalized fatal or non-fatal stroke, myocardial infarction, heart failure 5. Hospitalized fatal or non-fatal coronary heart disease 6. Hospitalized fatal or non-fatal other cardiovascular events	1. State vital statistics office and death certificates 2. Validated death by ARIC reviewer classification 3. State vital statistics office and death certificates 4. ICD-9 code: 428, ICD-10 code: 150, in any position 5. Validated events by ARIC reviewer classification 6. Other relevant ICD-9/ICD-10 codes	Probability (risk ratio)
Long-term survival	See above	See above	Time to event (hazard ratio)

Repeated Measures of Self-Rated Health. Annual phone interviews in both the ARIC and JHS cohorts have measured self-rated health since the first study visit. For participants who have remained in the study, there are up to 30 annual measurements of self-rated health. The self-rated health question in ARIC asks participants to rate their own health compared to others who are the same age: "Over the past year, compared to other people your age, would you say that your health has been excellent, good, fair or poor?" We will interpret this measure as year-specific perceived health status, rather than a proxy for clinical measures of disease due to its placement before other health related questions on the annual follow-up form.[42] We will analyze the progression of SRH in the four years prior to and following first HF hospitalization.

We will assign the following values to SRH categories based on the recommendations by Diehr et al.[43] and that have been previously used in longitudinal analyses of SRH in the ARIC cohort[31]: excellent = 95, good = 80, fair = 30, poor = 15, death = 0. These values represent the probability of being health 2 years from the initial SRH measurement, conditional on the initial value of SRH.[44]

Covariates of Interest.

1. Visit 1 (1987-1989)
    a. Sex
    b. Education
    c. Race
    d. Physical activity
2. Visit 2 (1990-1992)
    a. Age
    b. Occupational status
    c. Family income
    d. Marital status
    e. Living arrangement
    f. Hypertension
    g. High cholesterol
    h. Diabetes
    i. BMI
    j. Dietary intake
    k. Multivitamin use
    l. Frequency of physical examinations
    m. Alcohol use
    n. Smoking status
    o. Vital exhaustion
    p. Depression/anxiety medications
3. Visit 3
    a. Change in occupation/retirement
4. Annual follow-up form
    a. Marital status

Variables to be considered as confounders include biologic sex, education, self-reported race, age, occupational status, changes in occupational status, family income, changes in marital status, living arrangement, hypertension, high cholesterol, diabetes, and BMI. Both health behaviors (dietary intake, physical activity, multivitamin use, frequency of physical examinations [healthcare utilization], alcohol use, and smoking status) and mental health markers (vital exhaustion and depression/anxiety related medications) will be considered mediators of the exposure-outcome relationship. If changes in occupation between Visit 1 and 3 occur before the initial HF hospitalization, these will be accounted for, along with changes in marital status that occur before the initial HF hospitalization. Time-varying variables measured again at JHS Visit 1 may also be used in analyses involving measures of social support from JHS.

Statistical Evaluation. Social isolation (LSNS) will be analyzed as a categorical variable, with established scores corresponding to different levels of risk for social isolation.[35] Established cut-points for social support measures derived from the ISEL do not exist, therefore we will first categorize these scores by tertile (low, medium, and high social support). Perceived social support will be assessed using the conglomerate measure, and by each specific type of social support in exploratory analyses.[45]

Change in social relationships will be assessed as a continuous numeric change, which can be categorized into tertiles, and as a change between categories of change from one time point to the next. These categories may include labels such as “high to high”, “high to medium”, “high to low”, “low to high”, and so on, depending on how many categories are defined. We will evaluate different methods of comparing the LSNS and the BSNI. Questions from the BSNI and LSNS will be matched as closely as possible, and will be scored according to the following table, for a total score ranging from 0-9:

LSNS Questions		BSNI Questions	
Question	Response (Scoring)	Question	Response (Scoring)
1.How many relatives do you feel close to? That is, how many of them do you feel at ease with, can talk to about private matters, or can call on for help?	Zero (0) One (1) Two (1) Three or Four (2) Five to Eight (3) Nine or more (3)	1.How many relatives do you have that you feel close to?	None (0) 1 or 2 (1) 3 to 5 (2) 6 to 9 (3) 10 or more (3)
2.Do you have any close friends? That is, do you have any friends with whom you feel at ease, can talk to about private matters, or can call on for help? If so, how many?	Zero (0) One (1) Two (1) Three or Four (2) Five to Eight (3) Nine or more (3)	2.How many close friends do you have (people you feel at ease with, can talk to about private matters, and can call on for help)?	None (0) 1 or 2 (1) 3 to 5 (2) 6 to 9 (3) 10 or more (3)
3a.How many relatives do you see or hear from at least once a month?	Zero (0) One (1) Two (2) Three or Four (3.5) Five to Eight (6.5)	3.How many of these friends or relatives do you see at least once per month?	None (0) 1 or 2 (1) 3 to 5 (2) 6 to 9 (3) 10 or more (3)

	Nine or more (9)		
3b.How many of these friends do you see or hear from at least once a month?	Zero (0) One (1) Two (2) Three or Four (3.5) Five to Eight (6.5) Nine or more (9)		
3.Scores from these two questions will be summed together, and the grouped according to the following categories for a final summary score of how many relatives and friends are seen each month: 0 = 0 1-2 = 1 3-4 = 2 > 5 = 3			

If distributions show a large proportion of participants reporting 9+ or 10+ friends/family, this will instead be scored on a scale of 0-4, with a total possible score ranging from 0-12. Based on distributions of these scores, we will create categories that represent low, moderate, and high social isolation. Change in social isolation will be assessed by changing from one category to another. Continuous changes in scores of structural aspects of social relationships will not be assessed as it may imply a higher level of precision than we actually have.

We will also conduct a sensitivity analysis using dichotomous scoring of each question (0 = 1-2 friends/family, 1 = >2 friends/family), summing for a total potential score of 0-3 points. These 4 potential scores will be assessed as a categorical variable, and 10-year changes will be assessed as changes between these 4 categories.

We will start with directed acyclic graphs (DAGs) to assess confounders, and will use these in combination with model selection techniques including for example 10% change in estimate to determine an adjustment set that maximizes parsimony. Descriptive statistics of social relationships, demographic, and clinical measures will be examined in both the full ARIC cohort and the smaller ARIC/JHS shared cohort. Additionally, for those that experience an incident HF hospitalization, we will examine descriptive statistics of measures of CV health progression, demographic, and clinical characteristics stratified by levels of social relationships in the full ARIC cohort. These will be repeated in the ARIC/JHS shared cohort, but stratified by categories of change in social relationships instead.

The associations of social relationships measured at mid-life (ARIC measurement only) with clinical and subjective measures of HF progression following initial HF hospitalization will be investigated both in the full ARIC cohort, and in the ARIC/JHS shared cohort. Analyses involving 10-year changes in social relationships will only be conducted among the ARIC/JHS shared cohort.

Associations of social relationships at mid-life and their 10-year changes with clinical measures of HF morbidity and mortality will be assessed using appropriate models such as Cox proportional hazard models, Poisson models, and linear and log binomial regressions.

Associations of social relationship measures at mid-life and their 10-year changes with SRH in the 4 years before and after incident HF hospitalization will be assessed using linear mixed effects models that account for repeated measures of SRH among participants who experienced an incident HF hospitalization. Varying times between social relationship measurements and incident HF hospitalization will be adjusted for in the analysis.

We are not expecting loss to follow-up after incident HF hospitalization to be a large issue, although this will be investigated. However, loss to follow-up and death that occurs over time may cause selection bias into the analysis sample. Participants whose annual telephone calls were answered by a proxy will have missing data on SRH, which will be imputed using prior measurements of SRH along with other relevant health information collected on the annual follow-up call. This will be investigated and accounted for in the analysis using methods such as multiple imputation by chained equations (MICE). The additional variables used in imputation models will not be used as adjustment variables in main models.

We will explore whether the association between social support and HF progression is modified by social isolation, as social support is generally determined by structural aspects of social relationships. This will elucidate whether it is important to have high levels of social interactions for health outcomes, even if the person perceives high levels of available social support. Effect measure modification by gender, race, and marital status may be explored, but will likely be underpowered and will serve only as exploratory analyses.

Sensitivity analyses categorizing social support measures and changes in social relationships by other quantiles (quartiles, quintiles, deciles, etc.) will be conducted. Additionally, to explore the impact of defining incident HF hospitalization as a combination of adjudicated cases of HF starting in 2005 and ICD-9 identified cases before adjudication started in 2005, we will conduct three sensitivity analyses: one that will define HF hospitalization only using ICD-9 code 428 in any position, another that define HF hospitalization as and ICD-9 code of 428 in the primary position only, and another restricting analyses only to adjudicated HF hospitalizations that occurred after 2005. As patients tend to be prescribed medications after an initial HF hospitalization and HF progression may not worsen until years (5-10) later, all analyses will be repeated using second HF hospitalization as time 0 rather than the initial HF hospitalization, as a sensitivity analysis. A further sensitivity analysis will restrict the analysis sample only to participants who developed HF within 5 years of the social relationship measures, to investigate the impact of time between exposure measurement and initial HF hospitalization.

Limitations. The ARIC study and JHS used different measures of structural social relationships, which will make the assessment of changes in structural social relationships more difficult. The varying times between social relationship measurement and initial HF hospitalization are a limitation but will be addressed in analyses and sensitivity analyses. Another limitation is the racial distribution of participants by study site, as mostly Black participants are located at the Jackson, MS site. This makes study center and race highly correlated, and requires the use of the covariate race-center. Additionally, this means that the assessment of changes in social relationship can only be conducted among Black participants at the Jackson, MS site, as no white participants were a part of the ARIC/JHS shared cohort. Social relationships were only measured

twice among the ARIC/JHS shared cohort, which will reduce power in these analyses, and also limit the generalizability of portions of this analysis. Outpatient HF events were not ascertained, and therefore we are only limited to investigating the disease once it is severe enough to warrant hospitalization, and not the initial diagnosis of HF. Additionally, the definition of HF hospitalization is limited in that outcomes were only adjudicated starting in 2005, resulting in a definition of HF that combines adjudicated HF and code-identified HF. However, the impacts of this definition will be investigated using three sensitivity analyses. We are also limited by excluding any HF hospitalizations that occurred between the two social relationship measurements for analyses of changes in social relationships. If the number of exclusions due to HF between the two social relationship measurements is large, we will characterize this group of people and consider accounting for this exclusion in analyses.

7.a. Will the data be used for non-ARIC analysis or by a for-profit organization in this manuscript? ____ Yes __X__ No

b. If Yes, is the author aware that the current derived consent file ICTDER05 must be used to exclude persons with a value RES_OTH and/or RES_DNA = "ARIC only" and/or "Not for Profit" ? ____ Yes ____ No
(The file ICTDER has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript? ____ Yes __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the current derived consent file ICTDER05 must be used to exclude those with value RES_DNA = "No use/storage DNA"? ____ Yes ____ No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status.
ARIC Investigators have access to the publications lists under the Study Members Area of the web site at: http://www.cscc.unc.edu/aricproposals/dtSearch.html

_____ Yes _____ No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

Published papers:
Garg et al (2020): Associations of anger, vital exhaustion, anti-depressant use, and poor social ties with incident atrial fibrillation: The Atherosclerosis Risk in Communities Study
Kats et al (2016): Social support and cognition in a community-based cohort: the Atherosclerosis Risk in Communities (ARIC) Study
Wattanakit (2005): Association of anger proneness, depression, and low social support with peripheral arterial disease: the Atherosclerosis Risk in Communities Study

Cene (2012): Social isolation, vital exhaustion, and incident heart failure: findings from the Atherosclerosis Risk in Communities Study

Manuscript proposals:
Liu: Social isolation, social support, and the risk of incident dementia and MCI: the Atherosclerosis Risk in Communities (ARIC) Study
Liu: Social Isolation, social support, and cognitive decline: the Atherosclerosis Risk in Communities Study
Nagayoshi: Social isolation, social support, and risk of incident stroke: the Atherosclerosis Risk in Communities Study
Mosely: Dimensions of social support and risk of CHD events, carotid arterial wall thickness, and mortality
Mosely: The moderating effects of social support on the association between negative emotions and CHD events, carotid arterial wall thickness, and mortality
Kornegay: The effect of social support on the relationship between hostility and seated blood pressure
McGovern: The relationship of social support to incident myocardial infarction and ischemic stroke
Hagan: Individual and neighborhood SES and its association with measures of social support
Foraker: Neighborhood and Individual Socioeconomic Status and Heart Failure Rehospitalization: ARIC Cohort
Thai: Predictors of discharge to outpatient rehabilitation and physical therapy services among hospitalized heart failure patients: The Atherosclerosis Risk in Communities Study
Caughey: Hospital readmissions for patients hospitalized with acute decompensated heart failure and preserved vs. reduced ejection fraction
Sueta-Dupree: Outcomes and healthcare utilization of heart failure stages in the ARIC cohort
Kucharska-Newton: Patterns of healthcare utilization following an initial diagnosis of heart failure. The Atherosclerosis Risk in Communities (ARIC) Study
Kucharska-Newton: Patterns of healthcare utilization preceding an initial heart failure hospitalization. The Atherosclerosis Risk in Communities (ARIC) Study
Foraker: Socioeconomic status (SES) and case-fatality among participants with incident heart failure

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

11.b. If yes, is the proposal

___ A. primarily the result of an ancillary study (list number* _____)
___ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* _____ _____ _____)

*ancillary studies are listed by number https://sites.cscc.unc.edu/aric/approved-ancillary-studies

12a. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is **your responsibility to upload manuscripts to PubMed Central** whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

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