ARIC Manuscript Proposal #3638

PC Reviewed: 6/9/20	**Status: _____**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Life-course trajectories of neighborhood socioeconomic conditions and cardiovascular outcomes in the Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 26 characters): neighborhood SES and CVD

2. Writing Group:

Writing group members: Qian Xiao, Eric Whitsel, Anna Kucharska-Newton, Gerardo Heiss, Ganga Bey, Shelly-Ann Love

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

First author: **Xiao, Qian**
Address: 1200 Pressler St. Houston, TX 77030
Phone: 713-500-9233 Fax: 713-500-0900
E-mail: qian.xiao@uth.tmc.edu

ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).

Name: **Eric A. Whitsel**
Address: 123 West Franklin Street
Suite 410, Room 4226
Chapel Hill, NC 27516-8050
Phone: 919-966-3168 Fax: 919-966-9800
E-mail: eric_whitsel@med.unc.edu

3. Timeline:

May 2020-July 2020	Obtain DUA and arrange for dataset transfer
Aug 2020-Oct 2020	Data analysis
Oct 2020-Feb 2021	Prepare for abstract and manuscript
Feb 2021-Apr 2021	Internal review
Apr 2021	Manuscript submission

In addition, we anticipate to start planning for future studies and possible grant applications after we have obtained analytic results from this analysis in fall 2020.

4. Rationale:

Neighborhood socioeconomic environment has been increasingly recognized as an important determinant of health [1,2]. A growing body of literature has shown that people living in neighborhoods with more severe socioeconomic deprivation have higher risks for a variety of

adverse health conditions, including cardiovascular diseases (CVD) [3] and CVD mortality [4]. However, most previous studies only examined neighborhood socioeconomic factors at one point in time, and it is unclear whether changing the neighborhood environment can influence health outcomes. Answering this question may provide evidence supporting the need for designing interventions that focus on moving people to a better neighborhood environment or bringing changes to disadvantaged neighborhoods.

Several earlier studies examined the effects of changing neighborhood environment on health outcomes. For example, the consequences of moving have been studied by randomizing people to receive relocation vouchers as in the landmark Moving to Opportunity study, which reported that moving to less disadvantaged neighborhoods may have a positive impact on obesity and diabetes risk, as well as mental health in girls. [5,6] In observational studies, increase in neighborhood poverty was associated with higher risk of preterm birth, [7] improvement in neighborhood safety was linked to decrease in body-mass index (BMI), [8] and loss of neighborhood supermarkets were related to worsening glycemic control. [9] In an earlier study in a large US cohort, the NIH-AARP Diet and Health Study, Xiao et al. examined 10-year change in neighborhood socioeconomic status (nSES) in relation to total and cause-specific mortality. [10] The study found that among participants who lived in the same neighborhood between 1995 and 2000, improvement in neighborhood socioeconomic status was associated with lower mortality rate, while deterioration was associated with higher mortality rate, and the associations were most pronounced for CVD mortality. Here we propose to expand our earlier study in the ARIC study by 1) studying nSES trajectories for a longer period (1987-2013) 2) examining nSES in earlier adulthood and childhood to assess life-course nSES conditions; 3) including both movers and non-movers to study whether moving status modifies the relationship between nSES trajectories and CVD outcomes. We expect our study to contribute to the growing literature examining the role of nSES in health disparities.

5. Main Hypothesis/Study Questions:

We hypothesize that life-course nSES trajectories are associated with CVD outcomes. Specifically, we expect that stable high and upward trajectories of nSES are associated with lower CVD incidence and mortality, while stable low and downward trajectories of nSES are associated with higher CVD incidence and mortality.

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).

Inclusion/exclusion

We will initially include all participants with at least one nSES measure between V1 and V5 and had no history of CVD (see *CVD outcomes* for details) at V1. We will subsequently exclude any participant with sparse nSES measurements over time and assess the impact of the exclusion on the results. We will also use multiple imputation and inverse probability weighting (see *Assessment of nSES trajectories* for details) to handle missingness.

For analyses that examine earlier adulthood and childhood nSES, we will base exclusion on availability of nSES measures at these time points. We also will base exclusion on availability of key confounders, particularly individual-level SES indicators such as education and income.

Assessment of nSES trajectories

We will use latent class growth analysis to derive nSES trajectories between V1 and V5. The derivation will rely on the U.S. Census tract-level nSES summary z score previously computed and linked to V1-V5 addresses. Similar methods also will be used to derive life course nSES trajectories including childhood and earlier adulthood nSES.

Although latent class growth models are generally flexible in handling partially missing measurements, the likelihood of misclassification increases with higher number of missing nSES data points. Moreover, missingness in nSES measurements may be influenced by many factors such as baseline nSES, individual-level SES and health status, and thus missingness may introduce bias to the analysis. We will use several methods to address this problem: 1) we will conduct a series of analysis by excluding people with a certain number of missing values (i.e. one through four) to evaluate the impact of exclusion on both sample size and results; 2) we will use inverse probability weighting to adjust for the likelihood of exclusion due to missingness; and 3) we will use multiple imputation by chain equations to impute missing data points.

CVD outcomes

We will evaluate incident heart failure (HF), coronary heart disease (CHD), stroke, and CVD death. Incident HF will include the first occurrence of either a hospitalization with an ICD-9 discharge diagnosis code 428 or a death certificate with any listing of ICD-9 428 or ICD-10 I50 code. Incident CHD will include the first occurrence of hospitalized definite or probable myocardial infarction (MI) based on chest pain symptoms, electrocardiograms, and cardiac biomarkers from hospitalizations; definite fatal CHD based on chest pain, CHD history, underlying cause of death from the death certificate, and other information from hospitalizations, medical histories, and ARIC visits; or silent MI based on Minnesota-coded serial ECG changes over ARIC visits. Incident stroke will include the first occurrence of definite or probable stroke based on signs, symptoms, neuroimaging, and other diagnostic reports according to National Survey of Stroke criteria. We will both evaluate the three outcomes separately, and combine them to examine total CVD events. Participants lost to follow-up will be censored at the date of last contact.

Statistical analysis

We will consider several modeling strategies for the analyses. First, to examine the temporal relationship between nSES and CVD outcomes, we will use Cox proportional hazards regression models including nSES as a time-varying variable. Second, we will use logistic regression to estimate the odds ratio for CVD outcomes comparing each nSES trajectory group with the reference group (high stable trajectory, which represents consistently high nSES). Third, we will use Cox regression to model the relationship between nSES in childhood and earlier adulthood as a time-invariant variable in relation to CVD outcomes that occurred after baseline and over follow-up. For all models that include both neighborhood and individual factors, we will use multilevel models to address the hierarchical structure of variables.

We will consider several factors as confounders, including age, sex, race, education, income and center. We will also consider several lifestyle factors that may act as both confounders and mediators of the relationship, including smoking, alcohol, sleep, physical activity, sedentary behavior, body mass index, and medical history. Finally, we will perform subgroup analysis by sex, race and education to assess whether and how the relationship between nSES and CVD outcomes differ by individual sociodemographic factors.

Methodologic limitations

We will be mindful in selecting trajectory groups to allow for the formation of distinct trajectories without overfitting. We will also consider the non-random probabilities of experiencing certain neighborhood trajectories (which can be influenced by factors that also impact CVD outcomes) in sensitivity analyses using propensity scores. Moreover, we will conduct additional sensitivity analyses knowing that the tract-level nSES summary z score was based on the ARIC population. Characterizing change is therefore challenging because all changes are relative to other neighborhoods such that improvements in z score may either be due to actual improvement in neighborhood environment or to decline (or less improvement) in other neighborhoods. To assess how much this may impact our results, we will conduct sensitivity analyses using % of families below the U.S. poverty line as an alternative indicator for nSES.

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/aric/mantrack/maintain/search/dtSearch.html

__X___ Yes _____ No

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

We have identified the following three proposals that are the most related to our proposed analysis:

1114 An evaluation of area-level measures of SES: CVD health outcomes in the ARIC study communities

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

3259 SES and Incident Cardiovascular Disease Among Individuals with Obesity and Diabetes

The main difference between our study and these studies is that while all the previous proposals focused on nSES at a single time point using measures from the Census 2000, our study will examine long-term trajectories of nSES.

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

11.b. If yes, is the proposal

___ A. primarily the result of an ancillary study (list number* _____)

_X_ B. primarily based on ARIC data with ancillary data playing a minor role (usually control variables; list number(s)* AS1998.02 Lifecourse SES)

*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.

References

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