ARIC Manuscript Proposal #2838

PC Reviewed: 09/13/16 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Neighborhood and individual socioeconomic characteristics and progression to hypertension at older age in the Atherosclerosis Risk in Communities Study

b. Abbreviated Title (Length 26 characters): Neighborhood SES and late life hypertension

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

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3. Timeline:
Data for this project is readily available, thus we intend to conduct analysis and manuscript preparation in 6-7 months from approval.

4. Rationale:

Hypertension is a common condition and a major risk factor of cardiovascular disease and stroke.[1] Approximately 1 in 3 U.S. adults are currently diagnosed with hypertension, with another 17% remaining undiagnosed. [1] The prevalence of hypertension is projected to increase as a result of age-related changes in the vascular system.[2,3] This association between age and blood

pressure is marked by a progressive increase in systolic blood pressure in every decade of life. In contrast, while diastolic blood pressure also increases with age it plateaus or slightly declines from mid- to late life.[2–4] Increases in pulse pressure, the difference between systolic and diastolic pressure, has been associated with a variety of adverse cardiovascular outcomes, such as coronary heart disease, heart failure, and mortality. [5–7] Furthermore, results from the Framingham study estimated that adults aged 55-65 years without hypertension have an estimated 90 percent lifetime risk of developing hypertension.[8] Thus, timely identification of key risk factors associated with progression to hypertension represents an important public health priority.

Although dietary and lifestyle changes are proven to lower blood pressure, contextual risk factors, such as one's demographic profile and area-level factors can also impact blood pressure levels. Extant research has suggested that the role of area-level variables (e.g. neighborhood poverty, income inequality, housing, or social resources) often impact the risk for a variety of poor health outcomes in addition to individual-level characteristics (e.g. gender, age, or individual education status and income).[9,10] Neighborhood socioeconomic status (SES), defined as any factors broadly representing community economic, educational or occupational status[9] have been associated with cardiovascular outcomes such as coronary heart disease,[11] subclinical atherosclerosis,[12] and mortality.[13] Neighborhood SES may affect health through a variety of mechanisms including: availability of social and economic resources, accessibility of recreational facilities, neighborhood crime, cost and availability of healthy foods.[14–16] These characteristics contextualize an individual's social and economic environment [9,17,18] and are important for understanding disparities in epidemiologic studies.[17]

In a previous ARIC investigation, Diez-Roux et al. have shown that SES measures (individual and area level) are associated with hypertension incidence and blood pressure changes in midlife.[19] The investigators reported an inverse association between hypertension incidence and SES indicators. This relationship was more apparent among whites in lower SES than higher SES groups as well as a decline of diastolic blood pressure among those age 50+. Another ARIC study examining employment status as a dimension of SES and the association with hypertension in middle-aged women found an inverse association between both incident and prevalent hypertension.[20] However, the relationship of SES to late life blood pressure changes and hypertension control are less well studied. The prospective follow-up of the ARIC cohort to late life provides a unique opportunity to extend the existing research to older age and compare changes in late life to those in mid-life.

5. Main Hypothesis/Study Questions:

Research Aim: Examine the longitudinal association between neighborhood and individual SES in late life and the change in blood pressure, pulse pressure, and risk of hypertension and its poor control in late life.

Hypotheses:

H1: Neighborhood and individual disadvantage will be associated with a higher risk of hypertension (self-report, use of antihypertensive medications, or measured at visits) in late life.

H2: At older age (70+ years at visit 5) neighborhood and individual disadvantage will be associated with higher pulse pressure adjusted for the number of antihypertensive medications.

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).

Study Design

Prospective longitudinal cohort for hypothesis 1. The initial analysis will define the baseline at study visit 4. We will also compare the post-visit 4 associations in later life to the associations with earlier hypertension incidence between visits 1 and 4 (following the earlier publication by Diez Roux). Hypothesis 2 will be addressed cross-sectionally at visit 5.

Inclusion/exclusion criteria

Participants with geocoded neighborhood data at visit 4 will be included. Participants with hypertension at baseline (defined as blood pressure ≥140/90 mmHg, self-reported diagnosis, or use of anti-hypertensive medication) will be excluded. We will also exclude participants with missing information on blood pressure at baseline, or the key exposure-- neighborhood SES.

Exposure(s)

Similar to previous analyses,[17] we will use neighborhood SES defined as a z-score that sums six indicators of neighborhood characteristics at the census-tract level, based on the geocoded address at the baseline visit of each participant. The six indicators represent various dimensions of SES including income/wealth, education, and occupation at the census-tract level (see Table 1). A z-score will be estimated for each indicator by subtracting the overall mean and dividing by the standard deviation. The six indicators will be summed to create a summary score. We will then categorize the neighborhood SES variable into high, medium, or low based on the z-score distribution. We will stratify neighborhood SES by race as there is overlap between the lowest tertile for Whites and the highest tertile for Blacks.

Table 1. Neighborhood SES components

Indicator	**Definition**
Income/Wealth	
Household income	log of median household income
Housing value	log median housing value
Household rental income	percent of household with interest or rental income
Education	
High school education	proportion of adults >25 years old with high school education

College education	proportion of adults >25 years old with college education
Occupation	
Professionally employed	proportion of adults > 16 years old with executive, managerial or professional occupations.

Outcome

Hypothesis 1: Incident hypertension (defined as self-reported diagnosis or reported use of antihypertensive medications available from AFU telephone questionnaires; or blood pressure ≥140/90 mmHg which is measured and only available at visits). Participants will be followed through December 31, 2013. Participants will be censored in the event of death or loss-to-follow-up at visit. Sensitivity analyses can examine the validity of self-reported hypertension among the subset (n~2000) of participants who attended the CARMRI visit during 2004-2006.
Hypothesis 2: Pulse pressure (defined as the difference between systolic and diastolic pressure measured at visit 5).

Data analysis

For *hypothesis 1,* race-stratified and age-stratified (< 65 and ≥65) cox proportional hazards regression models will be used to obtain hazard ratios and 95% confidence intervals to assess differences in risk of incident hypertension by neighborhood SES (using low neighborhood SES as the referent). Models will examine progressive adjustment for covariates and key risk factors for hypertension: age, individual SES (education & income), BMI, age, race-center, total cholesterol, HDL-c, alcohol consumption, physical activity, and smoking status. Baseline blood pressure is a powerful risk factor and models will be examined before and after its inclusion in the model since adjustment for baseline levels measured with error can bias inferences about change. If the adjustment makes a large impact on inferences, we will consider additional modeling strategies which will formally incorporate the measurement error or blood pressure which can be estimated from multiple measures at ARIC visit 4 as well as measures at previous visits (e.g. visit 3). Time since baseline will be calculated to examine aging-related changes. Kaplan-Meier curves will be used to examine absolute risk and visual assess proportionality of relative hazards over time in addition to more formal testing.

To address *hypothesis 2,* we will construct linear regression models to examine the continuous association between pulse pressure and SES measures (neighborhood and individual measures) after adjustment for number of antihypertensive medications and key risk factors as mentioned above. We focus on pulse pressure as the primary outcomes since earlier work in ARIC suggested lower SES is associated with a greater rise in SBP and a greater fall in DBP (particularly at older age) leading to higher pulse pressure (PP) which is known to be a marker of arterial stiffness and a strong risk factor for subsequent CVD. We will also look at SBP and DBP separately as well as conduct analyses stratified by self-reported use of medications for hypertension.

We will explore alternative model specifications including Poisson to account for the discrete outcome (visit-based hypertension) and a multi-level framework to examine the neighborhood level effect.

Additionally, we will conduct several sensitivity analyses: 1) examine the association of the 6 components of neighborhood SES with progression to hypertension, separately; 2) compare the neighborhood SES of those who attended visits to those who did not attend to examine if mortality, CVD, and loss to follow-up are related to neighborhood SES to place the findings in context and assess the potential for bias; and 3) examine blood pressure as a continuous variable to determine if the relationship between neighborhood SES and incident hypertension reflects a continuous/incremental relationship rather than a threshold effect. The evaluation of neighborhood SES with BP at visit 5 is also useful as a first step to look at cardiac function by echocardiography and subclinical measures of cardiac disease to complement individual level analyses that are ongoing for the latter (proposal by Vart et al.).

Limitations

The definition of neighborhoods at the census tract level may not correspond to the actual geographic boundaries of a neighborhood as defined by the participants. Furthermore, census tracts were originally designed to be homogenous in SES characteristics, thus it is possible that defining neighborhood SES at the census tract level could obscure variation within tracts. Selection bias of those who survived to or participated in visit 5 are potential limitations specific to hypothesis 2. There could be a potential temporal mismatch between data on the neighborhood environment and blood pressure—blood pressure could be influenced by neighborhood characteristics prior to the baseline exam at visit 4. The long interval between visit 4 and 5 without visits (1999 to 2011) makes us have to rely on self-reported hypertension for the analysis of hypothesis 1.

References

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7.a. Will the data be used for non-CVD analysis in this manuscript? ____ Yes __X__ No

b. If Yes, is the author aware that the file ICTDER03 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used? ____ Yes ____ No
(This file 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 file ICTDER03 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/search.php

____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)?

a. Neighborhood socioenvironmental characteristics, race, and incidence of hypertension in the ARIC cohort (#456).
   - The paper in 2002 was limited to data by visit 4. The current proposal extends the follow-up to self-reported hypertension and visit 5 measures.

b. Women's Employment Status: Associations with Prevalent and Incident Hypertension
   - This proposal was limited by data to visit 2, only examined one component of SES—employment status, and limited the analyses to women. The current proposal extends follow-up to visit 5, includes all adults, and includes multiple measures of SES.

c. The relationship of neighborhood characteristics to trends over time in cardiovascular risk factors in the ARIC cohort (#455)
   - This proposal was limited by data to visit 4 and focused on risk factors. The current proposal extends the follow-up to self-reported hypertension and visit 5 measures.

d. The relationship of neighborhood characteristics to incidence of cardiovascular disease in the ARIC cohort (#454)
   - This paper followed participants through visit 3 and focused on CHD and stroke outcomes. Our proposal examines hypertension outcomes through visit 5.

e. Neighborhood socioeconomic characteristics and cardiovascular disease (#180)
   - This paper used a cross-sectional analysis with visit 1 data. Whereas our proposal uses both cross-sectional and prospective analysis through visit 5.

f. The association of socioeconomic status with elevation of N-terminal pro-B-type natriuretic peptide and subsequent risk of cardiovascular disease and mortality. (#2655)
   - This proposal focuses on association between individual SES characteristics, BNP, and CVD. Our proposal will look at area level SES.

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 at http://www.cscc.unc.edu/aric/forms/

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.

13. Per Data Use Agreement Addendum, approved manuscripts using CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to

publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript ____ Yes ____ No.