ARIC Manuscript Proposal #2146

PC Reviewed: 5/14/11 **Status: A** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Systolic blood pressure trajectories and incident cardiovascular disease

b. Abbreviated Title (Length 26 characters): **SBP trajectories and CVD**

2. Writing Group:

Writing group members: Daichi Shimbo, Paul Muntner, Christy Avery, Andrea L. C. Schneider, David Couper; Others welcome

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

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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).

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3. Timeline: Analyses can start immediately following proposal approval. We will aim to prioritize the publication of the resulting manuscript by December 2013.

4. Rationale:

The association of systolic and diastolic blood pressure (BP) with cardiovascular events is well documented. Most studies examining those associations have assessed blood pressure as single point measurements or as change in blood pressure over a specified time interval. Few studies have examined patterns of blood pressure change over time and attempted to evaluate the impact of distinct blood pressure patterns with cardiovascular outcomes. Although elevated blood pressure will be adversely associated with cardiovascular events, it is the elevated blood pressure sustained over time which will have a greater negative impact on cardiovascular health.

A prior study has demonstrated that in midlife, most people have a slow rise in BP, but there is also a group of people who exhibit a more marked increase [1]. This latter group was shown to be at increased risk for angina. BP trajectory is influenced by antihypertensive medication, with those whose BP rises more steeply more likely to be prescribed BP-lowering medication . However, there is also likely a group whose BP rises slowly because of BP-lowering medication. One study demonstrated that treatment intensification, but not necessarily adherence, among

patients with coronary artery disease affects BP trajectories, and better BP trajectories are associated with lower rates of myocardial infarction and revascularization [2].

In this study we propose to take advantage of the longitudinal aspect of the ARIC cohort to describe distinct trajectories of blood pressure change over the four ARIC examinations (Visit 1 to Visit 4) and to evaluate the association of identified categories of blood pressure trajectories with incident coronary heart disease, heart failure and stroke occurring in follow-up through 2010.

5. Main Hypothesis/Study Questions:

Study Aim 1: To identify and characterize distinct systolic blood pressure (SBP) and diastolic blood pressure (DBP) trajectories over the four ARIC visits.

Study Aim 2: To evaluate the association of distinct SBP (DBP) trajectories with the incidence of heart failure, coronary heart disease and stroke in follow-up from the date of the Visit 4 examination through December 31, 2010.

Study Aim 3: To evaluate the association of distinct SBP (DBP) trajectories with mortality in follow-up from the date of the Visit 4 examination through December 31, 2010.

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 population: All ARIC cohort participants free of coronary heart disease, heart failure and history of stroke at baseline (visit 1) and through visit 4. We will exclude from analyses ARIC cohort participants with missing blood pressure measurements at any of the four ARIC Visits. We will also exclude participants who are missing covariates included in our model, participants who self identify as non-white or non-black race, participants who self-identify as black at the Washington County, MD or Minneapolis, MN field centers.

We recognize that this proposed study design will constitute a limitation as a proportion of CVD events will have occurred prior to visit 4. As part of sensitivity analyses, aimed at estimating this potential bias, we will limit trajectories of SBP to the initial two and three ARIC visits, recognizing that two- and three-point trajectories constitute a limitation in their own way.

Analytical approach:

We will use the PROC TRAJ SAS program to identify distinct trajectories of change in systolic and diastolic blood pressure levels across the four ARIC cohort examinations. Although blood pressure measurements may reflect the effect of blood pressure medication, we are interested in the effective levels of blood pressure and will therefore not consider medication use in the main analyses of the effect of the identified trajectories on clinical outcomes. We will consider secondary analyses stratified by antihypertensive treatment status.

We will use Cox proportional hazard models to evaluate the association of the identified blood pressure trajectories with incident coronary heart disease, incident heart failure, incident stroke, mortality. We will evaluate the use of the following covariates in the proposed models: age, sex, field center, race, smoking, education, BMI and diabetes status. All covariates will be defined at baseline (visit 1).

We will evaluate effect measure modification of the observed associations by race/study center and sex. If present, we will stratify analyses by the variable (race/study center or sex) for which the interaction term will be statistically significant ($p<0.10$).

Missing information on systolic and diastolic blood pressure at ARIC visits 1-4 may introduce bias into the estimation of blood pressure trajectories. However, the estimated number of study participants missing information on systolic and diastolic blood pressure at any of the visits is small (less than 15), therefore we do not anticipate that data missingness will significantly impact trajectory assessment. Nevertheless, in an effort to detect potential bias, we will compare salient characteristics of study participants with and without blood pressure data at individual visits. If significant differences are found, we will impute missing data.

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)?

Ms # 114 Nieto et al., Blood Pressure Distributions

Ms# 733 Marsh et al., Blood Pressure and Risk of Myocardial Infarction in Washington County, MD

MS # 734 Alves de Moraes et al."Blood pressure over time and changes in cognitive function"

Ms # 1412 Ehret et al., GWAS for longitudinal blood pressure levels

Ms # 1852 Rodriguez et al., Systolic Blood Pressure Control and incident Heart Failure : TheAtherosclerosis Risk in Communities Study

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.

References

1. Wills, A.K., et al., *Population heterogeneity in trajectories of midlife blood pressure.* Epidemiology. **23**(2): p. 203-11.

2. Maddox, T.M., et al., *Blood pressure trajectories and associations with treatment intensification, medication adherence, and outcomes among newly diagnosed coronary artery disease patients.* Circ Cardiovasc Qual Outcomes. **3**(4): p. 347-57.