ARIC Manuscript Proposal # 1961

PC Reviewed: 10/9/12	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Non sitting BP recordings and the impact on CHD, stroke, and heart failure risk prediction in the ARIC study

b. Abbreviated Title (Length 26 characters): BP variation impact on outcomes

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

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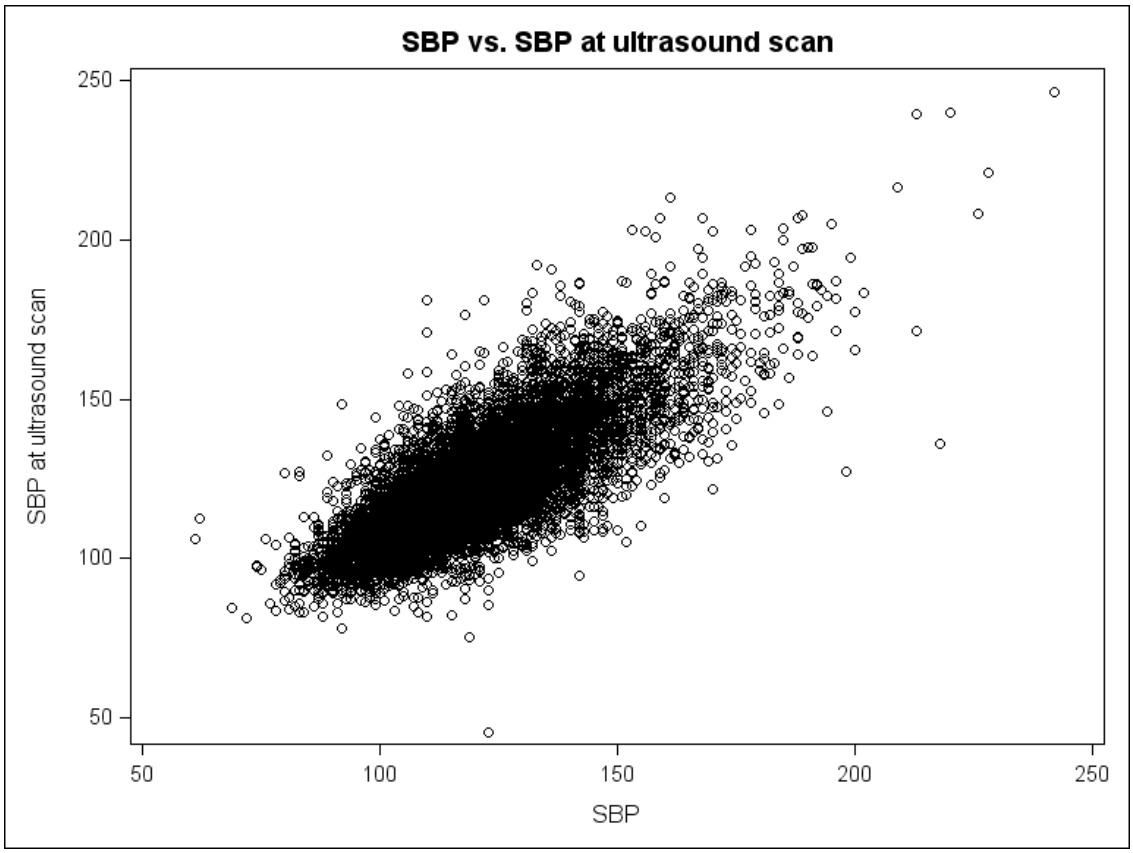
3. Timeline: Analysis to start as soon as approval is obtained. Manuscript is to be prepared as soon as analyses are completed. Analysis and manuscript preparation will take place within 1 year from approval of the proposal.

4. Rationale: Blood pressure (BP) is used in all coronary heart disease (CHD) heart failure and stroke risk prediction models. The association of BP with stroke is stronger than its association with CHD (R. Collins et all 1994). Often the BP used in risk prediction models is a sitting BP (the gold standard) reading obtained at a clinical exam.

BP values change throughout the day in response to position and other factors (Parati G et al., 1998). These may have an impact on risk prediction scores. How BP measured under other postural cardiovascular risk estimation - has not been adequately described or considered.

In ARIC visit 1 and 2, BP measurements were available for most subjects at three time points: (1) a sitting measurement using a random zero mercury manometer, (2) BP measurements performed during ultrasound imaging in the recumbent position, and (3) measurement of BP in the standing position. The measurements performed while lying down and standing were in the same arm using a Dinamap system. Additionally, at each of these time points, several BP recordings were performed (thrice when sitting, once every 5 minutes during the ultrasound imaging, and every 20 seconds when standing). As part of the analysis for MS1461, we examined differences between BP readings during a participant's visit and during the ultrasound scan and noted that these were highly correlated, with a mean difference of only 3.2 mmHg. However, substantial within-individual variation was noted (see Figure).



While some differences may be due to measurement error, most may represent changes during the day in response to position or other factors. Irrespective of whether these were measurement errors or true differences, knowledge of how they impact risk prediction scores will be important as clinical decisions may be made on the basis of the estimated risk.

Although efforts have been made in ARIC to look at orthostatic hypotension and 1) CHD (Nardo C et al *Hypertension.* 1999;33:1123-1129) 2) heart failure (Jones CD et al hypertension. *2012;59:913-918)* 3) mortality (Rose KM Circulation. 2006 Aug 15;114(7):630-6), and 4) stroke (Stroke. 2000 Oct;31(10):2307-13.) so far, no study has evaluated the impact of differences in BP measurements on risk prediction scores. We aim to study the relationship between the different BP recordings and estimated risk prediction scores.

5. Main Hypothesis/Study Questions:

Hypothesis:

We will test the following hypotheses

1. Determine if standing and recumbent BP measurements alter risk score prediction when compared to the currently used reference,-sitting blood pressure.

2. Determine if standing and recumbent BP measurements when added individually to CHD, heart failure and stroke risk prediction scores will result in reclassification of individuals to different risk groups.

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 methodological limitations or challenges if present).

After standard ARIC exclusions, all individuals with prevalent CHD, Heart failure and stroke, as well as individuals with missing covariate data (i.e. covariates required to estimate the ARIC or Framingham risk scores) will be excluded. Individuals who do not have recumbent or standing BP measurements will also be excluded.

6. Analysis plan:

The following analyses involve only exposure variables from visit 1.

1. Identify all clinically relevant variables necessary for the estimation of the ARIC Coronary Heart Disease Risk Score (ACRS), the Framingham Risk Score, the ARIC Stroke Risk Score, and the ARIC Heart Failure Risk Score

2. Examine for any outliers among BP measurements from all three assessments (sitting, standing, and recumbent) and exclude values which are physiologically improbable.

3. Complete a descriptive analysis of the SBP readings in the different positions –sitting, standing and recumbent.

4. Using Cox proportional hazards models, describe the estimated CHD risk using the ACRS and FRS (separately) with the sitting BP first, then with the recumbent BP, and then the standing BP.

5. Show a reclassification table for each pair of BP readings: i.e. number and percentage of individuals whose risk group changed and the maximum change in estimated risk in the study subjects. Calculate the net reclassification index (NRI)

6. Repeat above for incident ischemic stroke as the outcome and the ARIC stroke risk score and similarly incident heart failure as the outcome.

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 ICTDER02 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 ICTDER02 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 ICTDER02 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

10What 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)? MP #1821: Relation of Different blood pressure indices with risk of different cardiovascular events in the community.
MS 768: Year, 2001: Postural Blood Pressure Change and Incident Stroke, Coronary Heart Disease, and All-cause Mortality: Marsha L. Eigenbrodt (Lead)
MS1104: Year 2005: Orthostatic Hypotension and Cognitive Function: the ARIC Study: Kathryn Rose (Lead)
MS1332: Year 2008: Orthostatic hypotension and incident chronic kidney disease: the Atherosclerosis in Communities study: Nora Franceschini (Lead).
MS 1334: Year 2008: Does Orthostatic Hypotension Predict Diabetes: The ARIC Study: Kathryn Rose (Lead)
MS 1352: The association of orthostatic hypotension with incident heart failure: Laura Loehr (Lead)
MS 1560: Postural changes in blood pressure and incidence of ischemic stroke subtype in the ARIC study: Hiroshi Yatsuya (Lead)
Christopher J. Nardo et al:'Descriptive Epidemiology of Blood Pressure Response to Change in Body Position: The ARIC Study'.
Christine D. Jones et al: 'Orthostatic Hypotension as a Risk Factor for Incident Heart Failure: The Atherosclerosis Risk in Communities Study'

Rose KM et al: 'Orthostatic hypotension predicts mortality in middle-aged adults: the Atherosclerosis Risk In Communities (ARIC) 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/

12. 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.