ARIC Manuscript Proposal # 2864

PC Reviewed: 10/11/16 **Status: _____** **Priority: 2**
SC Reviewed: _____ **Status: _____** **Priority: ____**

1.a. Full Title: Statistical methods for the association of visit-to-visit blood pressure variability with cardiovascular disease

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

2. Writing Group:
Writing group members: Jessica Barrett, Raphael Huille, Angela Wood

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __JKB___ **[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: We will aim to submit a manuscript to the ARIC publications committee within one year.

4. Rationale:
The association of visit-to-visit variability of systolic blood pressure (SBP) with cardiovascular disease has received a lot of attention in the literature. But visit-to-visit variability is typically

measured with error based on a limited number of SBP measurements, leading to bias in the estimated effect size.

5. Main Hypothesis/Study Questions:
Statistical methods using longitudinal modelling of SBP measurements can reduce the measurement error bias in the association of SBP variability with CVD events.

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: Statistical methodology study using prospective cohort data
Inclusion/exclusion: Exclude all those with a history of cardiovascular disease at baseline
Outcome: Time to first non-fatal or fatal cardiovascular event
Other variables: All repeat measurements of systolic blood pressure, total cholesterol and HDL cholesterol and measurement times. Baseline age, sex, smoking status and history of diabetes.
Data analysis: Comparison of statistical methods to estimate SBP variability: (1) the SD of the SBP measurements for each individual, (2) using longitudinal mixed models with a random intercept and slope and an additional random effect on the residual variance to allow SBP variability to differ between individuals, (3) modelling repeated SBP measurements (as in (2)) and cardiovascular events jointly. For survival analysis we will use Cox proportional hazards models with SBP and SBP variability as exposures, estimated using methods (1) – (3) above, and adjusted for baseline risk factors including total cholesterol, HDL cholesterol, baseline age, sex, smoking status and history of diabetes.

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

_____ Yes ____x___ 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)?

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 _x___ No.