

## ARIC Manuscript Proposal #1984

PC Reviewed: 8/14/12  
SC Reviewed: \_\_\_\_\_

Status: A  
Status: \_\_\_\_\_

Priority: 2  
Priority: \_\_\_\_\_

**1.a. Full Title:** Impact of shifting population distributions of blood pressure on rates of coronary heart disease, heart failure and stroke: the Atherosclerosis Risk in Communities Study

**b. Abbreviated Title (Length 26 characters):** Shifting CVD risk factors

### 2. Writing Group:

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

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### 3. Timeline:

Analyses will begin once the manuscript proposal is approved.

#### 4. Rationale:

Rates of numerous cardiovascular diseases (CVD) including cerebral vascular disease, renal failure, heart failure (HF), and coronary heart disease (CHD), increase progressively as blood pressure rises.<sup>1-6</sup> Among blood pressure related deaths, estimates suggest that approximately one third of the excess CHD and all-cause mortality can be attributed to systolic blood pressure designated as non-hypertensive.<sup>7, 8</sup> Research also has consistently demonstrated that the association between blood pressure and vascular events is linear on a semi-log scale and shows no evidence of a threshold, indicating that benefits achieved from decreases in blood pressure are not limited to individuals with clinical hypertension.<sup>9-13</sup> Together, these studies support a population wide blood pressure reduction approach to decreasing the burden of chronic vascular diseases.

Several authors have estimated the theoretical effects of shifting the distribution of blood pressure, either through reducing the population mean or by decreasing the proportion of the population in the highest risk categories.<sup>9, 13-16</sup> For example, Framingham Heart Study investigators found that a 2-mmHg reduction in the population average of diastolic blood pressure would result in an estimated 17% decrease in the prevalence of hypertension, and a 6% reduction in the risk of coronary heart disease.<sup>14</sup> However, many of studies investigating the influence of population shifts of blood pressure on CVD examined CHD and stroke events, largely in only populations of European descent.<sup>9, 11, 14</sup> The degree to which modest decrements in blood pressure may affect the incidence of heart failure remains unknown. Additionally, few reports have examined the effects of blood pressure shifts in African American populations, who shoulder a higher burden of hypertension and experience high rates of CHD and heart failure.<sup>9, 11, 14, 17</sup>

#### 5. Main Hypothesis/Study Questions:

We propose to estimate the number of incident heart failure events observed in the ARIC population that may be prevented by 2 mm Hg reductions in systolic blood pressure (SBP), consistent with what could theoretically be achieved through population level lifestyle interventions.

- 1) Estimate the predicted reductions of incident heart failure from counterfactual distributions of SBP, by race and sex.

We propose to estimate the number of incident myocardial infarction observed in the ARIC population that may be prevented by reductions of 2 mm Hg in SBP, consistent with what could theoretically be achieved through population level lifestyle interventions.

- 2) Estimate the predicted reductions of incident myocardial infarction from counterfactual distributions of SBP, by race and sex.

We propose to estimate the number of incident stroke observed in the ARIC population that may be prevented by reductions of 2 mm Hg in SBP, consistent with what could theoretically be achieved through population level lifestyle interventions.

- 3) Estimate the predicted reductions of incident myocardial infarction from counterfactual distributions of SBP, by race and sex.

**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 methodological limitations or challenges if present).**

**ARIC COHORT:**

Exclusions: For heart failure, participants with prevalent HF at baseline will be excluded (i.e. those who self-reported having medications for treatment of HF, those with stage 3 HF defined by the Gothenburg criteria, and those hospitalized for heart failure between visits 1 and 2). For CHD, individuals who at baseline had a positive history or missing data for prevalent CHD will be excluded. Participants with a self-reported prior stroke at baseline will be excluded for the stroke analysis. We will also exclude participants with self-reported race other than Caucasian or African American.

Outcome definition: Incident hospitalized HF will be identified by the first occurrence of hospital discharge diagnosis codes 428.X. Definite or probable incident CHD and stroke will be defined according to the ARIC event classification criteria. Follow-up time for each event begins on the date of the baseline examination.

Main exposures: First, we will examine the effect of shifting the population distribution of blood pressure, as measured continuously and previously described.<sup>14</sup> Specifically, we will calculate incidence rate differences by race and sex for 2 mmHg decrements in blood pressure. If differences by race and/or sex are not observed, we will collapse across categories.

Covariates: Age, sex, race, and medication use.

**STATISTICAL METHODS**

First, the race- and sex-specific incidence rates of incident HF, CHD, and stroke will be calculated in 10-year age categories. Next, a method based on a weighted least-squares regression approach that uses a robust standard error estimator<sup>18</sup> will be used to estimate incidence rate differences (IRD) for incident stroke, CHD, and HF associated with continuous and categorical shifts in SBP and hypertension, respectively. For example, the effect of reducing the population distribution of SBP on incident CHD will be calculated by estimating a 2 mmHg incidence rate difference (i.e. the beta estimate for SBP will be multiplied by 2).

**7.a. Will the data be used for non-CVD analysis in this manuscript?**     Yes     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 ICTDER03 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.csc.unc.edu/ARIC/search.php>

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)?**

This manuscript is related to #1570 (Avery, The heart failure population burden due to acquired risk factors: the Atherosclerosis Risk in Communities study). This paper is now in press at *JACC*.

This manuscript is also related to #1475 (Rodriguez, Hypertension, left ventricular hypertrophy, and risk of incident hospitalized heart failure: The ARIC study). Drs. Chang, Loehr, and Folsom are members of the writing group and have approved of this proposal.

**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.csc.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.**

## REFERENCES

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