ARIC MANUSCRIPT PROPOSAL #865
February 7, 2002

PC Reviewed: 02/13/02 **Status: __D__** **Priority: _____**
SC Reviewed: 02/14/02 **Status: __D__** **Priority: _____**

1.a. Full Title

High Normal Blood Pressure and the Risk of Cardiovascular Disease

b. Abbreviated Title

High Normal BP & CVD

2. Writing Group

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3. Time Line

Obtain data set:	March 2002
Begin statistical analysis:	March 2002
Complete statistical analysis:	June 2002
Complete manuscript:	October 2002

4. Rationale/Background

There is compelling evidence of a strong, continuous, positive association of systolic and diastolic blood pressure with cardiovascular disease (1-5).

As a matter of health (public) policy, U.S. and International organizations have categorized blood pressure into levels (6,7). The goals of this classification have been to identify those individuals at greatest risk for CVD and to set thresholds for initiation of therapy. Clinical practice patterns reflect this classification scheme. Therapy directed at lowering blood pressure in the general population occurs when the systolic blood pressure rises above 140 mm Hg and/or diastolic blood pressure rises above 90 mm Hg (8).

High normal blood pressure is defined as a SBP 130-139 mm Hg or a DBP 85-89 mm Hg (6). Individuals with high normal blood pressure are likely to have a higher risk of cardiovascular disease than individuals with normal (or optimal blood pressure) given the continuous relationship of blood pressure and CVD. There is a scant data quantifying the risk for individuals with high normal blood pressure.

Most recently, Vasan et al. (9) quantified the risk for CVD among individuals with high normal blood pressure from the Framingham Study (10). Having high normal blood pressure increased the risk of fatal & nonfatal CVD 2.5 fold among women and 1.6 fold among men compared to individuals with optimal levels of blood pressure. This increased risk held despite adjusting for most obvious covariates.

While the study by Vasan adds important information, it has some limitations that may be obviated by examining similar data from the ARIC cohort. Methodologically, the study was not able to adjust for insulin resistance, markers of systemic inflammation (fibrinogen, white blood cell count) (11,12), or for markers of endothelial dysfunction (von Willebrand Factor) (13). Because the investigators used a one-time blood pressure reading, the analysis was not able to adjust for regression dilution bias (1,14). Thus the true effect of high normal blood pressure may have been underestimated. Finally, the Framingham cohort included few minority participants.

5. Main Hypothesis

High normal blood pressure, as defined in the rationale, is associated with an elevated risk of fatal and nonfatal cardiovascular disease than individuals with normal or optimal blood pressure.

6. Data (variables, time window, source, inclusions/exclusions):

ARIC cohort visit 1 (and visit 2 for use in regression dilution analyses) blood pressure, age, race, gender, prevalence of hypertension, prevalence of CHD, medication use variables, insulin, glucose, cholesterol, LDL, HDL, triglycerides, von Willebrand Factor, fibrinogen, white blood cell count, BMI, diabetic status, smoking status, physical activity level, education level, incident CHD indicator, event date, and follow-up time.

Exclusions: hypertension, race other than black or white, prevalent CHD disease

Analysis summary: First of all, tests for the homogeneity of baseline characteristics among each comparison groups will be performed. The Kaplan-Meier estimates will be used to compute the cumulative incidence of CVD. Separate curves will be studied according to gender, race, and blood pressure category. In addition, the linearity of hazard over time will be also examined for each group. Multivariate Cox proportional hazards model will be constructed to evaluate the association between blood pressure and the risk of fatal and nonfatal CVD, adjusting other risk factors. Blood pressures available at two time points (visit 1 and visit 2) will be used to examine the effects of within-subject variability (regression dilution). In the model, the data measured over time will be incorporated as time-varying covariates and various potential effect modifications will also be tested. Hazard ratios of CVD for each group, compared to subjects with optimal level of blood pressure, will be calculated along with 95% confidence intervals.

All analyses will be done with SAS software (SAS Institute, Cary, N.C.). Two sided p-values will be used as criteria to assess statistical significance.

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://bios.unc.edu/units/cscc/ARIC/stdy/studymem.html

___X___ Yes _____ No

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