ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #505A

1. Title (26 length):
Weight loss-hypertension
Full Title: Associations between weight loss and the remission of hypertension in a biethnic cohort: The Atherosclerosis Risk in Communities Study

2. Writing Group (list individual with lead responsibility first):
Lead: Juhaeri
Address: CB#7400 McGavran-Greenberg Hall
Department of Epidemiology, School of Public Health
University of North Carolina Chapel Hill
Chapel Hill, NC 27599-7400
Phone: (919) 966-0117 Fax: (919) 962-3265
Email: juhaeri.juhaeri@sph.unc.edu
June Stevens, LE Chambless, Daniel Jones, Moyses Szklo, FJ Nieto, Pam Schreiner

3. Timeline:
Much of the work for this manuscript was doen as part of MS #505. The analyses will be completed in one month. The manuscript will be completed in two additional months.

4. Rationale:
Both cross-sectional (1-3) and prospective (4-7) studies have shown that obesity is associated with hypertension. Clinical trials indicate that weight loss is associated with decreased blood pressure (8-10). These clinical trials have several weaknesses. First, participants were limited to highly selected overweight subjects, and thus the generalizability is limited. Second, all the populations studied were white, and results may not be applicable to other groups. Third, weight reduction programs were used, and these programs may have effects independent of weight loss they produce. Finally, the studies were conducted over relatively short time periods (<3 year) and the long-term effects (that is, effects over a period of nine years) could not be evaluated.

To the best of our knowledge, associations between weight loss and the remission of hypertension have been compared in African Americans and whites only in a cohort from Evans County, GA initially examined between 1960 and 1962 and followed for seven years. Using data from this cohort, tyroler et al. showed that weight loss on the remission of hypertension were greater in whites than in African-Americans (11). The study, however, did not include SBP and blood pressure medication into their criteria of hypertension. Also, other potential confounding factors such as baseline SBP, DBP, age, diet intake, and pre-existing diseases were not included into their models. The purpose of this study was to examine the associations between weight loss and the remission of

hypertension in African American and white men and women in the ARIC Study. The roles of ethnicity, gender, and blood pressure medication on the associations between weight loss and the remission of hypertension were also examined.

5. Hypothesis:
1. Weight loss is associated with an increased remission of hypertension.
2. The associations between weight loss and the remission of hypertension are different in participants who report taking blood pressure medication and in those who do not.
3. The associations are different across ethnicity-gender groups.

6. Design:
The study will be conducted among participants who were hypertensive at visit 1. Weight loss will be calculated as the difference in weight from visit 1 to visit 2, from visit 1 to visit 3, and from visit 1 to visit 4. Remissions of hypertension will be assessed at visits 2, 3, and 4. Only the first occurrence of remissions will be included in the analyses. For participants with antihypertensive medication, they will be classified as having remissions of hypertension if they have all the following three conditions. First, they did not report taking antihypertensive drugs or other drugs with antihypertensive effect within two weeks preceding a visit (visit 2, 3 or 4). Second, their DBP is less than 90 mmHg. And third, their SBP is less than 140 mmHg. For participants who reported taking no blood pressure medication, the criteria of hypertension are as above and a decrease in DBP of at least 3.5 mmHg and a decrease in SBP of at least 7.0 will be chosen because they represent approximately one standard deviation of changes in the respective variables within visits 1-4. Within visits 1-4, the root mean square error of the linear regression between SBP and date of visit within visits 1-4 was 6.9 mmHg. The corresponding value for DBP was 3.6 mmHg.

Unadjusted and adjusted associations between annual weight loss and the remission of hypertension will be calculated across ethnicity-gender groups. Several covariates will be selected for incluson in all models a priori: baseline age, study center, SBP, DBP, BMI, height, WHR, smoking status, educatonal level, total caloric intake, percent calories from fat, and physical activity. Effect modifications by baseline age, BMI, and prevalence of CVD, cancer, and diabetes will be examined by testing interaction terms in the models.

We will correct for the measurement error in blood pressures by replacing the baseline blood pressures with the Stein estimates of the true values of these baseline blood pressures (12). We will use these Stein estimates for baseline SBP and DBP in the models as covariates. In these corrections for measurement error, we will use reliability coefficients of 0.75 and 0.62 for baseline SBP and DBP, respectively. These values were from a sample of 363 ARIC participants with repeat measurements 1-2 weeks apart during ARIC visit 3.

Cox Proportional Hazard Models with time-dependent weight loss will be used to examine the associations between weight loss and the remission of hypertension across ethnicity-gender groups (13). Effect modifications by gender and ethnicity will be

examined by testing the interaction term in the combined model. Analyses will be performed using SAS (PROC PHREG) (14).

7. Data Requirement:
We will use data from the ARIC visits 1-4.

Identification information:
- Participant identification number
- Visit date
- ARIC field center

Demographics:
- Ethnicity
- Gender
- Date of Birth
- Age

Anthropometrics:
- Weight
- Height
- Waist circumference
- Hip circumference

Blood Pressure/Hypertension:
- Systolic blood pressure
- Diastolic blood pressure
- Blood pressure medication

Others (baseline only):
- Smoking
- Physical activity
- Education
- Dieting status
- Type of dieting
- Dietary intakes
- History of CVD
- History of diabetes
- History of non-skin cancer

8. Manuscript Requests with Overlap:
Proposal #505 "The Relationship of weight change and weight cycling with hypertension" that examines the associations of weight change in blood pressure changes, the incidence of hypertension (among normotensive people), and the remission of hypertension (among hypertensive people).

This proposed manuscript is a subset of manuscript #505. It will examine the associations between weight loss and the remission of hypertension in hypertensive subjects. Studies of the incidence versus the remission of hypertension examine two different groups of participants (normotensive versus hypertensive). The associations between weight loss and the remission of hypertension in hypertensives are very important and we think it is appropriate to examine the associations in a separate manuscript.

REFERENCES

1. Croft J, Strogatz D, Keenan N, James S, Malarcher A, Garrett J. The independent effects of obesity and body fat distribution on blood pressure in black adults: the Pitt County study. Int J Obesity 1993; 17:391-7.

2. Stamler R, Stamler J, Riedlinger W, Algera A, Roberts R. Weight and blood pressure: findings in hypertension screening of 1 million Americans. JAMA 1978; 240:1607-12.

3. Harris M, Stevens J, Thomas N, Schreiner P, Folsom A. Associations of fat distribution and obesity with hypertension in a bi-ethnic population. in progress 1999.

4. Ascherio A, Rimm E, Giovannucci E, et al. A prospective study of nutritional factors and hypertension among US men. Circulaton 1992; 86:1475-84.

5. Kannel W, Brand N, Skinner J, Dawber T, McNamara P. The relation of adiposity to blood pressure and development of hypertension. Ann Intern Med 1967; 67: 48-59.

6. Cassano P, Segal M, Vokonas P, Weiss S. Body fat distribution, blood pressure, and hypertension: A prospective cohort study of men in the Normative Aging Study. Ann Epidemiol 1990; 1:33-48.

7. Huang Z, Willett W, Manson J, et al. Body weight, weight change, and risk of hypertension in women. Ann Intern Med 1998; 128:81-8.

8. MacMahon S, Cutler J, Brittain E, Higgins M. Obesity and hypertension: epidemiological and clinical issues. Eur Heart J 1987; 8(Suppl B):57-70.

9. He J, Whelton P, Appel L, Charleston J, Klag M. Long-term effects of weight loss and dietary sodium reduction on incident of hypertension. Hypertension 2000; 35:544-9.

10. Hunt S, Cook N, Oberman A, et al. Angiotensin genotype, sodium reduction, weight loss, and prevention of hypertension: trials of Hypertension Prevention, Phase II. Hypertension 1998; 32:393-401.

11. Tyroler H, Heyden S, Hames C. Weight and hypertension: Evans County studies of blacks and whites. In: O P, ed. Epidemiology and Control of Hypertension. New York: Stratton Intercontinental Medical Book Corp., 1975:177-204.

12. Chambless L, Roeback J. Methods for assessing difference between groups in change when initial measurement is subject to intra-individual variation. Statistician Medicine 1993; 12:1213-37.

13. Kalbfleisch J, Prentice R. The statistical analysis of failure time data. New York, NY: Joh Wiley and Sons, 1980.

14. SAS Institute I. SAS/STAT User's Guide. Cary, NC: SAS Institute Inc., 1997.