ARIC Manuscript Proposal # 1469

PC Reviewed: 2/10/09	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: Impact of body mass index on incident hypertension in young-adult and middle-aged Chinese Asians, American Whites, and American Blacks: The People's Republic of China Study, the Atherosclerosis Risk in Communities Study and the Coronary Artery Risk Development in Young Adults Study

b. Abbreviated Title (Length 26 characters): BMI and incident hypertension

2. Writing Group:

Eva Katz, MPH, RD, June Stevens, MS, PhD, Jianwen Cai, PhD, Linda Adair, PhD, Kari North, PhD, Kimberly Truesdale, PhD, Lyn Steffen, PhD, MPH

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

First author: **Eva Katz**
Address: The Department of Nutrition,
Gillings School of Global Public Health, CB 7461,
University of North Carolina at Chapel Hill
Chapel Hill, NC 27599-7461

Phone: 919-259-3374 Fax: 919-966-7215
E-mail: ekatz@unc.edu

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).

Name: **June Stevens**
Address: The Department of Nutrition,
Gillings School of Global Public Health, CB 7461,
University of North Carolina at Chapel Hill
Chapel Hill, NC 27599-7461

Phone: 919-966-7218 Fax: 919-966-7216
E-mail: June_Stevens@unc.edu

3. Timeline:

December 2008: Apply for CARDIA proposal approval (Approved 1/09 by CARDIA committee)
January 2009: Apply for ARIC proposal approval; apply for CARDIA & ARIC data access
February 2009: Obtain datasets and begin data cleaning
March/April 2009: Begin exploratory work
May/June 2009: Begin preliminary analysis
July/August 2009: Continue analyses and begin draft of manuscript
Sept/Oct 2009: Complete draft of manuscript
Nov/Dec 2009: Revise manuscript and submit draft to CARDIA committee

4. Rationale:

Numerous studies have shown an increase in hypertension and other metabolic risk factors with increasing body mass index (BMI), and the level of risk at a specific level of obesity often varies by ethnicity. Epidemiologic studies on Chinese populations have shown an increase in metabolic risk factors at a BMI of 21-24 kg/m^2; values considered normal by the World Health Organizations (WHO) standards ($\geq$18.5 and <25 kg/m^2). [1,2,3,4] Based on this literature a BMI of 23 or 24 kg/m$^{2.}$ is commonly suggested to be a more appropriate cutpoint to define overweight within China. The WHO's most recent consensus statement, issued in 2004, suggested a range of plausible BMI cutpoints for overweight and obese exist for Asians, depending on the outcome of interest.[5] Based on the existing scientific evidence and expert consensus, China responded by establishing country specific standards to define overweight (24 kg/m2<BMI<28 kg/m^2) and obesity (BMI>28 kg/m^2).

Much of the research cited in support of lower BMI cutpoints, examines disease prevalence rather than incidence and lacks a Caucasian or non-Asian comparison group. ROC curves, driven by the underlying population distribution of BMI, and odds ratio estimates from cross-sectional studies are the two most common methods used to support the need for lower BMI cutpoints in China.

These approaches have important flaws that may lead to incorrect conclusions.[6] To our knowledge, our research group published the only study[7] directly comparing differences in the *incidence* of hypertension by BMI among Chinese Asians, American Whites and American Blacks. The American Whites and American Blacks were from the Atherosclerosis Risk in Communities Study (ARIC) and the Chinese Asians were from the People's Republic of China Study (PRC). Our results supported a stronger influence of BMI on incident hypertension among Chinese Asians compared to American Whites. However, subjects were 45-64 years old at baseline and within this age range the adjusted prevalence of hypertension among Chinese Asians, American Whites and American Blacks was 29.6, 22.5 and 44.2%, respectively. The high and differential prevalence of cases at baseline may limit studies of the relationship of BMI to incident hypertension. The very high prevalence in African Americans may mean that the participants remaining in an incidence study were resistance to hypertension. Therefore, to further explore the effect of BMI on incident hypertension, we propose to examine the relationship in a younger adult population in whom the prevalence of hypertension will be lower. We will compare the ethnic specific relationship to that which is observed in an older adult population of the same ethnic groups.

We will use population-based samples of American White, American Black and Chinese Asian men and women from three longitudinal cohorts to examine associations of adiposity with hypertension. Chinese Asians will be from the People's Republic of China Study (PRC), American White and American Black young-adults will be from the Coronary Artery Risk Development in Young Adults (CARDIA) study and American White and American Black middle-aged adults will be from the Atherosclerosis Risk in Communities Study (ARIC). No new data collection is proposed.

Cohorts:

In addition to the **The ARIC Study** - *American White and American Black mature adults,* we will use data from:

The CARDIA Study - *American White and American Black young adults*

The CARDIA Study, funded by the NHLBI, is an on-going, prospective, multi-site investigation examining the etiology of heart disease in young adults. In 1986, baseline data were collected from 5,115 Black and White American men and women aged 18-30 years. Participants were from four U.S. sites (Birmingham, AL; Chicago, IL; Minneapolis, MN; and Oakland, CA) to provide approximately equal numbers within subgroups of race, gender, education (high school or less and more than high school) and age (18-24 and 25-30). Follow-up examinations occurred during 1987-1988 (Year 2), 1990-1991 (Year 5), 1992-1993 (Year 7), 1995-1996 (Year 10), 2000-2001 (Year 15), and 2005-2006 (Year 20). The retention rate at each follow-up visit is 90% (Year 2), 86% (Year 5), 81% (Year 7), 79% (Year 10), 74% (Year 15), and 72% (Year 20), respectively.

The PRC Study *Chinese Asian Adults*

The PRC Study is a prospective, observational study of cardiovascular disease in China. This was a joint research program sponsored by the NIH involving the People's Republic of China and the United States of America under the USA-PRC Cooperation in Science and Technology to conduct prospective studies on CVD and its risk factors. In 1983–1984, baseline data were collected from 13,210 Chinese men and women aged 24 – 84 years. Participants were from urban and rural regions of Beijing (Northern China) and Guangzhou (Southern China). Follow-up examinations were in 1987-88 and 1993-94. There were 1,848 between the ages of 24-35 (n=1,077 CF & n=771 CM) and 6,575 subjects were between the ages of 45 to 64 at baseline (n= 3,286 CF & n=3,289 M).

There are many similarities in the design and data collection among the three cohorts. The Collaborative Studies Coordinating Center (CSCC) at the University of North Carolina, Chapel Hill served as the coordinating center for both the PRC and ARIC studies. They provided training manuals and protocols for data collection and were responsible for data processing and review for both studies. Informed consent was obtained from each participant at each examination. Many of the data collection methods were similar among the PRC, ARIC and CARDIA studies.

5. Main Hypothesis/Study Questions:

Determine and compare the relationship of BMI with hypertension in American White, American Black and Chinese Asian adults in early and middle adulthood.

a. Determine the ethnic specific relationship of BMI with *prevalent* hypertension among American White, American Black and Chinese Asian adults in early (24-35 year olds) and middle (45-64 year olds) adulthood.

*We hypothesize the measure of effect associated with the BMI – **prevalen**t hypertension relationship will vary by ethnicity during early and middle adulthood. Specifically, during early adulthood, the association will be steepest in Black Americans and least steep in Chinese Asians. During middle adulthood, the association will be steepest in Black Americans and least steep in White Americans.*

b. Determine the ethnic specific relationship of BMI with *incident* hypertension among American White, American Black and Chinese Asian adults in (24-35 year olds) and middle (45-64 year olds) adulthood.

*We hypothesize the effect associated with the BMI – **incident** hypertension relationship will vary by ethnicity during early and middle adulthood. Specifically, during early adulthood, the association will be steepest in Black Americans and least steep in White Americans. During middle adulthood, the association will be steepest in Chinese Asians and least steep in White Americans.*

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).

We propose to use data from each cohort during the bolded visit years listed in Table 1. below. This will facilitate the best match of calendar year and age.

Table 1. Cohort exam years

	Cohort Exam Years		
Visit #	**PRC**	**CARDIA**	**ARIC**
1	**1983-84**	1985-86	**1987-89**
2	**1987-88**	1987-88	**1990-92**
3	**1993-94**	**1990-91**	1993-95
4		1992-93	**1996-98**
5		**1995-96**	
6		**2000-01**	
7		2005-06	

Overview of Analytic Plan:

Outcome, exposure and covariates

The primary outcome for this manuscript will be hypertension. We will also examine the outcome pre-hypertension in the young adult population. Participants will be classified as hypertensive if they present with 1) systolic blood pressure greater than or equal to 140 mm Hg, 2) diastolic blood pressure greater than or equal to 90 mm Hg or 3) self-report of current antihypertensive medication use. Participants will be classified as pre-hypertensive if they present with 1) systolic blood pressure of 120 to 139 mm Hg or 2) diastolic blood pressure of 80 to 89 mm Hg.

All models will use the same exposure variable, BMI, calculated from measured weight and height. BMI will be treated as a continuous variable unless a quadratic term is deemed appropriate. Models will be stratified by race within each age group. Covariates will include age, gender, field center, smoking, alcohol use and education.

Measure of effect:

We will calculate prevalence and cumulative incidence. Comparisons of the effect of obesity between ethnic populations are susceptible to spurious conclusions depending on the use of multiplicative or additive risk estimates. As demonstrated by Stevens,[8] conclusions regarding

the relative effect of obesity in Black vs. White adults were contradictory when employing risk ratio vs. risk difference measures. This was attributed to differences in the rate at the reference level of adiposity between ethnic groups and the impact of these differences when using a multiplicative as opposed to an additive risk assessment.[9,10] This is one of the main reasons epidemiologists encourage the use of risk difference measures to estimate risk.[11] Therefore, for each aim, we will calculate the risk difference to estimate risk.

Limitations

There are limitations in the proposed work. Namely, several factors that influence blood pressure are hard to measure (physchosocial factors); some of the variables are not equivalent across ethnic groups (education level); potential bias may be introduced by variable treatment rates across ethnic groups; the overlay of ethnicity and social factors, geography and nationality cannot be separated; populations studies are from different countries; and lastly we do not have adequate measures of diet or physical activity measures across ethnic groups.

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 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

8.c. If yes, is the author aware that the participants with RES_DNA = 'not for profit' restriction must be excluded if the data are used by a for profit group?
____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

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)?

June Stevens past work with the ARIC cohort has been most similar to this analysis. She will be involved in the current project.

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.

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[1] Bei-Fan, Z. (2002). "Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults: study on optimal cut-off points of body mass index and waist circumference in Chinese adults." Asia Pac J Clin Nutr 11 Suppl 8: S685-93.

[2] Hu, F. B., B. Wang, et al. (2000). "Body mass index and cardiovascular risk factors in a rural Chinese population." Am J Epidemiol 151(1): 88-97.

[3] Weng, X., Y. Liu, et al. (2006). "Use of body mass index to identify obesity-related metabolic disorders in the Chinese population." Eur J Clin Nutr 60(8): 931-7.

[4] Zhou, B. F. (2002). "Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases--report for meta-analysis of prospective studies open optimal cut-off points of body mass index in Chinese adults." Biomed Environ Sci 15(3): 245-52.

[5] WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004 Jan 10;363(9403):157-63. Review. Erratum in: Lancet. 2004 Mar 13;363(9412):902.

[6] Stevens J, Juhaeri, Cai J, Jones D. The effect of decision rules on the choice of a body mass index cutoff for obesity: examples from African American and white women. Am J Clin Nutr 2002; 75: 986–992.

[7] Stevens J, Truesdale KP, Katz EG, Cai J. Impact of body mass index on incident hypertension and diabetes in Chinese Asians, American Whites, and American Blacks: the People's Republic of China Study and the Atherosclerosis Risk in Communities Study. Am J Epidemiol. 2008 Jun 1;167(11):1365-74.

[8] Stevens J.Ethnic-specific revisions of body mass index cutoffs to define overweight and obesity in Asians are not warranted. Int J Obes Relat Metab Disord. 2003 Nov;27(11):1297-9.

[9] Stevens J, Juhaeri, Cai J, Jones D. The effect of decision rules on the choice of a body mass index cutoff for obesity: examples from African American and white women. Am J Clin Nutr 2002; 75: 986–992.

[10] Stevens J. Impact of age on associations between weight and mortality. Nutr Rev 2000; 58: 129–137.

[11] Spiegelman D, Hertzmark E.Easy SAS calculations for risk or prevalence ratios and differences. Am J Epidemiol. 2005 Aug 1;162(3):199-200.