ARIC Manuscript Proposal # 2393

PC Reviewed: 7/8/14	**Status: A**	**Priority: 2**
SC Reviewed: _____	**Status: _____**	**Priority: ____**

1.a. Full Title: CVD risk in adults recommended for weight loss treatment by the US clinical guidelines

b. Abbreviated Title (Length 26 characters): CVD and weight loss guidelines

2. Writing Group:

Writing group members: June Stevens
Jianwen Cai
Eva Erber
Zhaohui Cui
David Wormser
Emanuele Di Angelantonio

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

F**irst author**: **June Stevens**
Address: CB 7461
University of North Carolina, Chapel Hill

Phone: 919 966 7348 Fax: 919 966 7216
E-mail: June_Stevens@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: CB 7461
University of North Carolina, Chapel Hill

Phone: 919 966 7348 Fax: n/a
E-mail: June_Stevens@unc.edu

3. Timeline:

We plan to submit a manuscript within one year of the approval of this proposal.

4. Rationale:

The 1998 "*Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*" sponsored by the National Heart, Lung and Blood Institute (NHLBI) had far-reaching impact on the definition and treatment of excess body weight. The report established body mass index (BMI) cutoffs to define underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2) and obesity ($\geq$30kg/m^2). Waist circumference (WC) cutoffs designated to indicate increased cardiovascular risk were >88 cm in women and >102 cm in men. In November 2013, an updated report sponsored by NHLBI was released under the auspices of The American Heart Association, The American College of Cardiology and The Obesity Society entitled *"Guideline for the Management of Overweight and Obesity in Adults"*. In both reports BMI, WC and cardiovascular disease (CVD) risk factors were used in algorithms to identify patients who may be at increased risk for CVD or other obesity-related conditions and who are candidates for weight loss treatments. There are multiple differences in the 1998 and 2013 algorithms related to the choice, definitions and number of risk factors used to determine groups to be recommended for weight loss.

Construction of the 1998 and the 2013 algorithms for weight loss treatment relied heavily on opinions of expert panels. Although relevant literature was cited and reviewed in both reports, there was no direct line drawn between each element used to determine patients in need of treatment and supporting evidence. Neither report, nor any other publication known to us, has presented CVD risk estimates for each of the categories of patients specified to be treated or untreated according to either algorithm.

5. Main Hypothesis/Study Questions:

The purpose of this study was to examine first-onset CVD risk in the subsets of adults designated to be untreated versus treated by the two guidelines using data from the ARIC study.

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).

Our outcome of interest is first incident CVD event, which includes incident CHD events and incident ischemic strokes. Incident CHD events include CHD death and myocardial infarction. CHD death is defined as death lacking a probable non-CHD cause and with a recent myocardial infarction, chest pain within 72 hours of death, or a history of CHD. We will conduct analyses with and without additional inclusion of silent infarction identified by ECG, coronary artery bypass surgery, and coronary angioplasty.

Ischemic stroke uses abstractor recorded signs and symptoms and CT, MRI and other diagnostic reports if the discharge diagnoses included a cerebrovascular disease code (ICD, 9^{th} revision, codes 430 to 438), if a cerebrovascular condition or procedure was mentioned in the discharge summary, or if a cerebrovascular finding was noted on a CT or MRI report. Criteria adapted from the National Survey of Stroke are used and qualifying strokes are further classified as definite or probable ischemic or hemorrhagic stroke on the basis of neuroimaging studies and autopsy, when available. A stroke is classified as ischemic if a brain CT or MRI revealed acute infarction or showed no evidence of hemorrhage.

The maximum follow-up period available in ARIC for our outcomes of interest will be used (through 2011)

The main study exposures are the categories of individuals described to be treated or untreated for weight loss according to published algorithms. Variables used in the algorithms include baseline age, gender, height, weight, waist circumference, smoking hypertension, diabetes, plasma glucose, LDL, HDL and family history of CVD.

The 1998 guidelines[1] recommended treatment for adults with the following characteristics: (1) obese (BMI ≥30 kg/m^2); (2) overweight (BMI 25.0-29.9 kg/m^2) plus ≥2 CVD risk factors; or (3) high WC (women: >88 cm, men: >102 cm) plus ≥2 CVD risk factors. Risk factors included age (men: ≥45 years; women ≥55 years), smoking, hypertension (≥140/90 mmHg or antihypertensive medication), LDL-cholesterol ≥160 mg/dl, HDL-cholesterol <35 mg/dl, fasting glucose ≥110 mg/dl or history of diabetes, and family history of premature coronary heart disease (definite myocardial infarction (MI) or sudden death ≤55 years of age in father or other male first-degree relative, or ≤65 years of age in mother or other female first-degree relative). Because this detailed information on family history is not available to us, we use family history of MI in our analyses.
The 2013 guidelines[2] recommended weight loss for adults who are: (1) obese; or (2) overweight plus have ≥1 CVD risk factor(s) or other obesity-related comorbidities. We did not include other obesity-related comorbidities because no clear definition was provided in the 2013 guidelines. CVD risk factors included: type 2 diabetes mellitus (here defined as self-reported diabetes or fasting glucose ≥126 mg/dl), prediabetes (here defined as fasting glucose: 100 to <126 mg/dl), hypertension (≥140/90 mmHg or antihypertensive medication), dyslipidemia (LDL-cholesterol ≥160 mg/dl[10] or HDL-cholesterol < 40 mg/dl or lipids-lowering medication), and high WC (NHLBI cutpoints: >102 cm for men and >88 cm for women).[2]

We cannot clearly separate intentional and unintentional weight change in the ARIC data. This manuscript is about CVD risk levels in the groups recommended for treatment, by the guidelines and does not investigate the effects of weight change or weight over time. We have published a paper using ARIC data that illustrates the complexity of the timing of weight change and CVD events.[3]

The major exclusions will be for missing data.

Cox proportional hazards regression models will be used.

We will examine effect modification by race, gender and smoking. We will also examine analyses within race and gender groups.

1. NIH. National Heart Lung and Blood Institute. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. the evidence reports. *Obes Res*. 1998;6:53S.

2. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: A report of the american college of Cardiology/American heart association task force on practice guidelines and the obesity society. *Circulation*. 2013. doi: 10.1161/01.cir.0000437739.71477.ee.

3. Stevens J, Erber E, Truesdale KP, Wang CH, Cai J. Long- and short-term weight change and incident coronary heart disease and ischemic stroke: The atherosclerosis risk in communities study. *Am J Epidemiol*. 2013;178(2):239-248. doi: 10.1093/aje/kws461; 10.1093/aje/kws461.

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 __X__ 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

__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)?

Stevens J, Erber E, Truesdale KP, Wang C-H, Cai J. **Long- and short-term weight change and incident coronary heart disease and ischemic stroke: the Atherosclerosis Risk in Communities Study.** Am J Epidemiol. 2013 ;178(2):239-48.

Bradshaw PT, Monda KL, Stevens J. **Metabolic syndrome in healthy obese, overweight, and normal weight individuals: the Atherosclerosis Risk in Communities Study.** Obesity (Silver Spring). 2013 ;21(1):203-9.

Stevens J, Truesdale KP, Wang C-H, Cai J, Erber E. **Body mass index at age 25 and all-cause mortality in whites and African Americans: the Atherosclerosis Risk in Communities study.** J Adolesc Health. 2012 ;50(3):221-7.

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.