ARIC Manuscript Proposal #3023

PC Reviewed: 8/8/17  Status: ____  Priority: 2
SC Reviewed: _______  Status: ____  Priority: ___

1.a. Full Title: Body Mass Index in Early Adulthood, Cardiometabolic Health and Outcomes

b. Abbreviated Title (Length 26 characters): Early adult BMI and outcomes

2. Writing Group:
   Writing group members: Sara B. Seidelmann, Brian Claggett, Amil Shah, [OTHERS WELCOME], Chiadi Ndumele, Christy Avery, June Stevens, Scott D. Solomon, Susan Cheng

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

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3. **Timeline:** Analysis will begin following proposal approval with the aim of completing the analysis and associated manuscript(s) within 1 year of data availability.

4. **Rationale:**
   Body mass index (BMI) in middle age is a well-known risk factor for cardiovascular diseases (including coronary artery disease, stroke, and heart failure) and type 2 diabetes (T2DM), however, less is known about the impact of BMI in early adult life. The prevalence of overweight and obesity has grown in recent decades, and are increasingly affecting younger individuals, resulting in a growing concern for the long-term health consequences of increased exposure to elevated body weight from early adult life, which may heighten the risks of cardiovascular diseases and T2DM in later life.\(^1,^2\)

5. **Main Hypothesis/Study Questions:**
   1) We hypothesize that elevated BMI in early adulthood is associated with the risk for the development of obesity, cardiovascular diseases and diabetes in middle and advanced age.

   2) In addition to BMI measured in middle age, we hypothesize that elevated BMI in early adulthood is an independent predictor of the risk for the development of cardiovascular diseases and diabetes in middle and advanced age.

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).**

   **Exposures:**
   Self reported weight at age 25, ascertained by questionnaire at Visit 1 will be utilized. Height at Visit 1 will be used to estimate BMI at 25 years of age.

   **Outcomes:**
   **Primary Outcomes**—The outcomes studied will be death and cardiovascular events since the first visit, as well as prevalence of obesity, diabetes and hypertension at V1-V5. We will evaluate all cause mortality, stroke (fatal or non-fatal), CHD (fatal or non-fatal MI or CHD death), HF (including both systolic heart failure and heart failure with preserved ejection fraction) and atrial fibrillation since the first visit to the latest adjudication (currently 2014) among subjects who were free of these outcomes at the beginning of visit one.

   **Secondary Outcomes**— Cardiac structure and function at Visit 3 and 5 by echocardiography including measures of ventricular volumes, atrial volumes, systolic function (ejection fraction and strain), Doppler measures of diastolic function. Blood Pressure - systolic and diastolic blood pressure measured at visits 1-5. Diabetic and metabolic related phenotypes-- Total cholesterol, high density
lipoprotein cholesterol, low density lipoprotein cholesterol, triglycerides, HbA1C, BMI, waist-to-hip ratio, percent body fat, fat mass, lean body mass, fasting glucose, insulin levels and oral glucose tolerance test will be assessed.

Confounders:
Age, gender, race, education, income level, physical activity, and cigarette smoking.

Analysis plan:

Descriptive statistics: Descriptive statistics of the study sample will be presented by body weight categories (underweight, normal weight, overweight and obese). Categorical data will be displayed as percent frequencies and compared by χ² or Fisher exact tests. Continuous data will be displayed as means (±SD) for normally distributed variables and medians (interquartile range) for variables with skewed distributions and compared between groups via Wilcoxon rank sum test or nonparametric trend tests as appropriate. We will utilize univariable and multivariable linear regression models for the analysis to examine the cross-sectional associations for BMI classes and quantitative characteristics. Basic, age- and gender-adjusted, as well as covariate adjusted hazard ratios will be used to test the association between BMI class and the risk of death, cardiovascular outcomes and heart failure using Cox proportional hazards regression.

Limitations: weight at 25 years is self-reported and not measured.

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)?

Avery (3016), Stevens (2625, 2471), and Ndumele (2352)

Past (inactive) proposals:

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.

13. Per Data Use Agreement Addendum for the Use of Linked ARIC CMS Data, approved manuscripts using linked ARIC CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication. Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript ___ Yes ___x__ No.
References