ARIC Manuscript Proposal #2625

PC Reviewed: 9/8/15  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. **Full Title**: Risk Factors for Weight Gain Trajectories Across Sex, Race and Socioeconomic Status: The Atherosclerosis Risk in Communities Study

b. **Abbreviated Title (Length 26 characters)**: Weight trajectories in ARIC

2. **Writing Group**:

   Writing group members: Emmanuel Quaye, Dr. Elizabeth Selvin, Dr. Karen Bandeen-Roche, Dr. Kunihiro Matsushita, Dr. June Stevens, Dr. Priya Palta, and Dr. Josef Coresh; others welcome

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

   First author: **Emmanuel Quaye**
   Address: 2024 E. Monument Street, Room B-314, Baltimore, MD 21287

   Phone: (973) 738 – 0897  Fax: N/A
   E-mail: equaye1@jhu.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: **Dr. Josef Coresh**
   Address: 2024 E. Monument Street, Room 2-635, Baltimore, MD 21287

   Phone: 410-955-0495  Fax: (410) 955 – 0476
   E-mail: coresh@jhu.edu
3. **Timeline:**

- Exploratory and preliminary data analysis will be completed by September 30, 2015.
- Main data analysis will begin and be completed by November 30, 2015.
- Interim report of research progress for the diversity research supplement will be submitted to the NHLBI for renewal by December 15, 2015.
- Drafting of manuscript will begin on December 1, 2016 and will be revised and completed by January 1, 2016.
- Submission to the ARIC committee for review by January 15, 2016.

4. **Rationale:**

Knowledge of the biological consequences and careful analysis of the obesity epidemic, which occurred primarily after 1980, is critical in our understanding of the epidemiology of obesity and cardiovascular disease and has important social implications. In the United States, approximately two-thirds of adults are overweight or obese. The prevalence of obesity has increased from 14% in 1974 to 34.9% in 2012. However, recent studies suggest that the prevalence of obesity does not appear to be continuing at the same rate and seems to be leveling off. Previous literature shows that the prevalence of obesity increased by 8 – 9% in men and women between 1980 and 1994, by 7 – 8% in men and women between 1994 and 2000 and by 2 – 5% from 2000 to 2008.

This rising trend in obesity has been associated with an increased risk of cardiovascular risk factors, such as hypertension. Hypertension is a major and potentially modifiable risk factor for the development of cardiovascular disease and has been strongly associated with renal disease, stroke, myocardial infarction, heart failure and mortality. Conversely, associations of socioeconomic status (SES) and hypertension are less understood. In addition, there is mounting evidence of several biological pathways linking an increase in adiposity with higher blood pressure levels.

The obesity epidemic has also altered disparities among individuals of different racial and ethnic backgrounds and socioeconomic status. For example, the prevalence of obesity is greater in African Americans compared to non-Hispanic Whites. Although there has been a reduction in the disparity in obesity over the past three decades across different socioeconomic groups; lower SES is still associated with an increased prevalence of overweight and obesity.

Much of the literature examining racial and socioeconomic differences in weight patterns across the lifespan have been cross-sectional. Longitudinal data with repeated measures are important in the analysis of weight trajectories because individual variation in body build may influence health beyond the static weight at any one point in time and also allows for the identification of important periods of increased susceptibility that may be advantageous for intervention. Furthermore, very few longitudinal studies have examined the trends in the prevalence of obesity and hypertension in middle-aged and older adults across age, sex, race, birth cohort, and socioeconomic status in a well-
characterized cohort, which are needed to adequately address differences in weight trajectories in regard to socio-demographic and other cardiovascular risk factors.

ARIC has published two papers regarding weight patterns across age and birth cohort and the risk of hypertension and weight gain [(1) Juhaeri J, Stevens J, Jones DW, Arnett D. Associations of aging and birth cohort with body mass index in a biethnic cohort. *Obes Res.* 2003; 11(3): 426-433] [(2) Juhaeri J, Stevens J, Chambless LE, Tyroler HA, Nieto FJ, Schreiner P, Jones DW, Arnett D. Associations between weight gain and incident hypertension in a bi-ethnic cohort – the ARIC study. *International Journal of Obesity*. 2002; 26, 58-64.]. This paper will extend the trajectory work by looking at categories of SES and expanding the follow-up to older ages (including visit 5).

5. Main Hypothesis/Study Questions:

**Hypothesis**

Weight gain in the most recent birth cohorts started earlier and was more pronounced in African Americans and individuals of lower socioeconomic status with consequent higher risk of hypertension among other cardiovascular risk factors (e.g. diabetes).

**Study Question 1:** Are there differences in weight trajectories over follow-up in ARIC across age, sex, race and birth cohort?

**Study Question 2:** Are there differences in weight trajectories over follow-up in ARIC across categories of socioeconomic status? The primary focus will be on education level within whites and African-Americans.

**Study Question 3:** What is the risk of hypertension as a function of different weight trajectories across sex, race and socioeconomic status in ARIC?

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).

**Study Design:**

The Atherosclerosis Risk in Communities (ARIC) study is a prospective cohort study conducted in 4 communities in the United States (Washington County, Maryland, Forsyth, North Carolina, Minneapolis, Minnesota and Jackson, Mississippi). Individuals were recruited by population-based sampling methods and the baseline visit occurred in 1987 through 1989. Subsequent visits from baseline were conducted every 3 years with the exception of the fifth visit, which occurred approximately 15 years after the fourth visit.
**Exposures:** The primary exposures for addressing study questions 1 and 2 will be age, sex, race, birth cohort, and socioeconomic status (SES).

SES will be defined primarily by categories of educational level. Other indicators of SES, such as family income, occupational status and health payment type (e.g. health insurance, Medicare, Medicaid, etc.) may also be analyzed. A systematic review of cross-sectional studies examining the association between SES and adiposity revealed that educational level tended to show more consistent associations with adiposity than family income or occupational status, which tend to be more variable by nature.\(^\text{10}\)

The primary exposure for answering study question 3 will be BMI categories depicting weight gain stratified by sex, race and SES. May also use the exposure obese-years, which comprises the degree and duration of obesity. The obese-years exposure has been shown to be more predictive of cardiovascular risk factors, such as diabetes, than either duration of obesity or degree of obesity.\(^\text{17}\)

**Outcome:** The central outcome for addressing study questions 1 and 2 will be body mass index (BMI), which is clinically defined as the weight in kilograms (kg) divided by height in square-meters (m\(^2\)). BMI is a commonly used measure of overweight and obesity and will be examined as a continuous variable and in categories that define overweight (25 – 29.9 kg/m\(^2\)) and obesity (≥ 30kg/m\(^2\)). Examining BMI over the life-course is important, and as such, this study will take advantage of the available self-reported BMI at age 25 and subsequently measured anthropometry at each ARIC visit. Although BMI is advantageous because of its widespread use in research and clinical settings and its strong associations with many cardiovascular risk factors, it has its limitations. BMI is an imperfect measure of adiposity because weight, a component of BMI, reflects the mass of all tissues and does not account for differences in body composition. A sensitivity analysis will be performed to analyze patterns of central adiposity using waist circumference and waist-to-hip ratio.

The primary outcome for addressing study question 3 will be hypertension status. Hypertension will be defined by a systolic blood pressure of ≥140 mmHg, or a diastolic blood pressure of ≥ 90 mmHg and/or self-reported antihypertensive medication use from clinical examinations during study visits or from annual follow-up (AFU) telephone calls.

**Inclusion/Exclusion:** The majority of participants in ARIC will be included in order to maximize generalizability, however, individuals will be excluded if they do not self-identify as White or African American, if they are African American from Washington County and Minnesota field centers, and if they are missing vital anthropometric or socioeconomic information at all visits.\(^\text{11}\)

**Statistical Analysis Plan:** Taking a stepwise approach with increasing complexity, initial exploratory data analysis will focus on characterizing BMI from visits 1 – 5 in ARIC. BMI and BMI change will be characterized using means, standard deviations and percentiles. Histograms, scatterplots, kernel density plots and lowess curves will be created to assess normality and linearity of BMI at each visit. Correlations of BMI with
BMI change between consecutive visits (e.g. BMI at visit 2 – BMI at visit 1) will also be assessed.

Longitudinal data analysis will first focus on changes in BMI (secondary analyses will examine waist circumference and waist to hip ratio) between consecutive visits. Changes in BMI between visit 4 and visit 5 will also be examined, however studies have shown that individuals have attained their maximum weight during middle age, and as such, the primary focus will be on both weight gain and weight loss.\(^2,1^1\) Each change can be used as the dependent variable in descriptive analyses and regressions with the main predictors (race and SES) adjusted for covariates (with supplementary stratified analyses, e.g. by sex). Further analyses will explore interactions, primarily between race and socioeconomic status. Finally, a longitudinal random (mixed) effects model will be used to examine the full weight trajectories within and across individuals using code and approaches developed in the ARIC Neurocognitive study (limitations note concerns about informative censoring).

Survival analysis methods, such as Kaplan-Meier curves and complimentary log-log regression, will be used to model the risk of hypertension (measured using self-report and AFU questionnaires) as a function of different weight trajectories (stable, increasing, or decreasing), while adjusting for baseline age, BMI, waist-to-hip-ratio, alcohol consumption, diet, physical activity, systolic and diastolic blood pressure and smoking status.\(^12,1^4\)

**Methodologic Challenges:**

Longitudinal analyses require participants to attend multiple follow-up visits. A substantial number of participants did not attend the fifth visit, and thus, informative censoring may bias future results. In order to correct for the potential bias, a sensitivity analysis using inverse probability of attrition weights (IPAW) or multiple imputation methods may need to be employed.

Other methodological challenges will include defining categories of socioeconomic status. For example, education level and income are commonly used measures of socioeconomic position, but do not reflect SES equally across ethnic groups. Also, there is a bi-directionality of using these factors as a proxy for SES because obesity may affect an individual’s education, and opportunities for employment. On the contrary, an individual’s education, and opportunities for employment and other factors may foster an obesogenic environment.\(^4\)

**References:**


7.a. Will the data be used for non-CVD analysis in this manuscript?  ____ Yes  ____ 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 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  ____ 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.cscn.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)?


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.