Jackson Heart Study Manuscript Proposal Form

Submission Date: 2/15/2017 Proposal ID: P0859

I. TITLE

I. Title Information

A. Proposal Title:

Age-related variations in obesity and diabetes correlates in the Jackson Heart Study

B. Abbreviated Title:

Age-related variations in obesity and diabetes

C. Suggested Keywords

Obesity, Diabetes, Age, Gender, JHS and African Americans

II. AUTHOR INFORMATION & CONTRIBUTIONS

Lead Author:

LaVonne Brown ☐ Senior Author ☐ Corresponding Author

a. Responsibilities:

Literature Review,Draft/Review

Is this manuscript proposal for a student/trainee research project?

Yes

Type of student/trainee:	Doctoral Student
Other student/trainee:	
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Mentor assurance? ☑

Mentor assurance letter: Uploaded

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Co-author(s) Agreement: Uploaded

III. MANUSCRIPT PROPOSAL OUTLINE

F. Is this manuscript proposal based on an Ancillary Study? No

If yes, please provide the ASC#:

A. Brief Overview

Provide a brief overview of the proposal including the nature of the problem to be addressed, scientific relevance, objectives/aims, research question/hypotheses, and methods/analytical plan (<250 words):

Nationwide, the prevalence of obesity increased among women from 2005 through 2014. Furthermore, the prevalence of obesity increased between the age groups of 25-39 and 40-59 years among men and women and then declined for those = 60 years, except for African American women, among the prevalence of obesity did not decrease in this group. Possible reasons for these trends are not clear. One challenge in analysis of variations in prevalence of obesity is that BMI does not distinguish between phenotypes, body composition. To address this challenge, several alternate measures that correlate better with upper body adiposity are proposed: waist circumference and waist-to-height ratio. Whether recently observed variations in obesity with age are evident for African Americans when obesity is defined by measures of central adiposity is unclear. Analyses of obesity prevalence using measures of central adiposity are insightful as such measures tend to correlate better than BMI with biomarkers associated with risk of diabetes, namely high-sensitivity C-reactive protein (hsCRP), insulin resistance, and blood glucose levels (FPG and hemoglobin A1c). Whether changes in prevalence of central adiposity with age correlate better with changes in levels of these biomarkers than changes in prevalence of obesity defined by BMI among African Americans is unclear. We aim to examine age-related variations in: (1) prevalence of obesity among Jackson Heart Study participants using BMI and measures of central obesity; and (2) levels of hsCRP, insulin resistance, and blood glucose measures in relation to obesity.

B. Background/Rationale

(Please include discussion on relevance of African Americans to the proposed topic) (< 1000 words):

Obesity (i.e., body mass index (BMI) = 30 kg/m2) is a major global health challenge given its associated health risks and increased prevalence worldwide (1). Analyses of changes in prevalence of obesity over the period from 2005 through 2014 in the United States using NHANES data showed significant increasing linear trends among women

for overall obesity and for class 3 obesity (BMI = 40 kg/m2) but not among men (2). Furthermore, the prevalence of overall obesity (BMI = 30 kg/m2) increased between the age groups of 25-39 and 40-59 years among men and women and then declined in the age group of = 60 years, except for African American women, among whom the prevalence of obesity did not decrease in the oldest age group. Possible reasons for these trends and age-related variations in obesity are not clear but are important to elucidate as such variations in obesity prevalence may provide insights into variation in underlying potential drivers (e.g., physical activity, diet, cigarette smoking, menopause status) and future changes in outcomes (e.g., diabetes, hypertension, heart failure). One challenge in analysis of variations in prevalence of obesity based on BMI is that BMI does not distinguish between phenotypes that differ in body composition (i.e., in distribution and amount of adipose tissue) (3). Changes in prevalence of obesity as defined by BMI may reflect changes in fat-free mass (i.e., muscle, bone), fat mass (visceral and subcutaneous adipose tissue), as well as changes in size and composition of upper and lower body compartments (e.g., abdomen, thighs) and decrease in height with age. To address this challenge, several alternate measures that correlate better with upper body adiposity have been proposed, including: waist circumference, waist-to-hip ratio, and waist-to-height ratio. Whether recently observed trends in prevalence of obesity with age in the United States (1) are also evident for obesity as defined by measures of central adiposity among African Americans is unclear. Analyses of variations in obesity prevalence using measures of central adiposity may be less subject to artifacts than using BMI as the former are likely to be influenced less by age-and sex-related variations in fat-free muscle mass than BMI. Measures of central adiposity correlate better than BMI with biomarkers associated with risk of diabetes (4, 5, 6), namely high-sensitivity C-reactive protein (hsCRP), insulin resistance, and blood glucose levels (i.e., fasting plasma glucose [FPG]) and hemoglobin A1c [A1c]). However, whether changes in prevalence of central adiposity with age correlate better with changes in levels of these biomarkers than changes in prevalence of obesity defined by BMI among African Americans is unclear. The prevalence of obesity as defined by BMI is reported to be higher among African Americans than among other race/ethnicity groups in the United States (2). However, JHS participants with a higher prevalence of BMI-defined obesity than Framingham Study participants are noted to have lower levels of visceral adiposity (7, 8), suggesting that BMI may not be a reliable measure of unhealthy obesity among African Americans. As obesity is a major public health problem for African Americans given the high prevalence of obesity and burden of cardiometabolic risk in this population (8, 9), it is important to identify practical and reliable measures of obesity with which to monitor prevalence of central obesity among African Americans. This study aims to show that measures of obesity based on waist circumference are better than BMI for evaluating and monitoring age-related variations in obesity and in levels of biomarkers of risk for diabetes among African Americans in Jackson, MS.

C. Research Hypothesis

1. The prevalence of obesity as defined by the BMI increases with age up to about 60 years and then declines. 2. The prevalence of obesity as defined by measures of waist circumference adjusted for height shows less variation with age and gender than the prevalence of obesity defined by BMI. 3. Levels of biomarkers associated with diabetes correlate better with measures of central obesity than with measures of overall obesity defined by BMI.

C. Study Design

Cohort

Other (specify):

D. Inclusions

D. Exclusions

Exclusions will consist of participants with missing data for the proposed cross-sectional analyses.

☑ **Received TRANS data package**

E. Data

Location of Statistical Analysis:

GTEC

Working Group: ▼

☐ Vanguard Center: ▼

☐ Other:

Will data be requested from JHSCC: Yes
Requested data: Uploaded

E. Brief Statistical Analysis Plan and Methods:

(Including power calculations, if necessary.)

We will conduct separate cross-sectional analyses of measures of obesity with age and diabetes correlates with data from Exam 1. Data to be requested Variable Exam 1 Age x Gender x BMI x Waist circumference x Waist to height ratio x hsCRP x HOMA-IR x Fasting plasma glucose x Hemoglobin A1c x Menopause status x Pre-diabetes x Diabetes x Diabetes medications x Smoking status x Physical activity category x Definitions General obesity: Overall obesity: BMI = 30 kg/m2 Overweight: 25 kg/m2 = BMI < 30 kg/m2 Reference: < 25 kg/m2 Class 3 obesity vs. ref (< 25 kg/m2): Class 3 obesity: BMI = 40 kg/m2 Central obesity: quartiles of waist circumference and waist to height ratio will be compared with bottom quartile Age categories: 20 – 39 years, 40-59 years, = 60 years Analysis plan 1. Prevalence of obesity as defined by the BMI increases with age up to about 60 years and then declines. a. Plots of obesity prevalence (y-axis) vs. age (x-axis, continuous), stratified by gender b. Plots of BMI (continuous) (y-axis) vs. age (x-axis, continuous), stratified by gender c. Tables of prevalence of obesity by age (groups) and gender d. Multinomial regression for 3 categories of obesity and age (continuous), adjusted for smoking and physical activity, stratified by gender e. Logistic regression for class 3 obesity (vs. reference) and age (continuous), adjusted for smoking and physical activity, stratified by gender 2. The prevalence of obesity as defined by measures of central obesity shows a smaller variation with age than with measures of general obesity defined by BMI. a. Scatter plots of each measure of central obesity with age (continuous), stratified by gender b. Tables of quartiles of each measure of central obesity with age (groups), stratified by gender c. Multinomial logistic regression of quartiles of each measure of central obesity with age (continuous), adjusted for smoking and physical activity, stratified by gender 3. Levels of biomarkers associated with risk for diabetes correlate better with measures of central obesity than with measures of general obesity defined by BMI. a. Separate scatter plots of each biomarker (ln transformed if distribution skewed) with each measure of central obesity (continuous, standardized), stratified by gender. b. Linear regression of each biomarker (ln transformed if distribution skewed) with quartiles of each measure of central obesity, adjusted for age (continuous), smoking and physical activity, stratified by gender We will also consider possible effect modification of age related variations in obesity and diabetes correlates by menopause and diabetes medication status.

Table Shell: No File Uploaded

F. References:

(Maximum 15)

1. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384:766-81. 2. Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD and Ogden CL. Trends in Obesity Among Adults in the United States, 2005 to 2014. JAMA. 2016;315:2284-91. 3. Dulloo AG, Jacquet J, Solinas G, Montani JP and Schutz Y. Body composition phenotypes in pathways to obesity and the metabolic syndrome. Int J Obes (Lond). 2010;34 Suppl 2:S4-17. 4. Despres JP and Lemieux I. Abdominal obesity and metabolic syndrome. Nature. 2006;444:881-7. 5. Fox ER, Benjamin EJ, Sarpong DF, Nagarajarao H, Taylor JK, Steffes MW, Salahudeen AK, Flessner MF, Akylbekova EL, Fox CS, Garrison RJ and Taylor HA, Jr. The relation of C--reactive protein to chronic kidney disease in African Americans: the Jackson Heart Study. BMC Nephrol. 2010;11:1. 6. Kahn HS and Bullard KM. Beyond Body Mass Index: Advantages of Abdominal Measurements for Recognizing Cardiometabolic Disorders. Am J Med. 2016;129:74-81 e2. 7. Liu J, Coady S, Carr JJ, Hoffmann U, Taylor HA and Fox CS. Differential associations of abdominal visceral, subcutaneous adipose tissue with cardiometabolic risk factors between African and European Americans. Obesity (Silver Spring). 2014;22:811-8. 8. Liu J, Fox CS, Hickson DA, May WD, Hairston KG, Carr JJ and Taylor HA. Impact of abdominal visceral and subcutaneous adipose tissue on cardiometabolic risk factors: the Jackson Heart Study. J Clin Endocrinol Metab. 2010;95:5419-26. 9. Taylor HA, Jr., Coady SA, Levy D, Walker ER, Vasan RS, Liu J, Akylbekova EL, Garrison RJ and Fox C. Relationships of BMI to cardiovascular risk factors differ by ethnicity. Obesity (Silver Spring). 2010;18:1638-45.

IV. JHS MANUSCRIPT OVERLAP

Manuscript Overlap

The Lead Author has reviewed all existing JHS manuscripts / manuscript proposals and found: Found similarities

Maniscript/Proposal List (1)

PID: P#0535

Title:	"Comparison of the Association of Measures of Body Habitus and Cardiovascular Disease Risk Factors: The Jackson Heart Study"
Author:	Ronnie Bell
Comments:	Proposal P#0535 aims to compare associations of BMI and waist circumference measures with several CVD risk factors in an effort to show that measures of central adiposity are better correlates of CVD risk than BMI for use in risk management in clinical settings. The current proposal differs from P#0535 in that it will compare variations in prevalence of obesity as measured by BMI and measures of central adiposity with respect to age and gender in the JHS in an effort to: (1) identify possible reasons for recent trends in prevalence of obesity among African Americans in the US; and (2) identify more reliable measures of obesity for monitoring trends in obesity and diabetes among African Americans at the population level.

V. ADDITIONAL INFORMATION

H. Genetic Information:

1. Do you propose use of data from a participant's DNA? No
2. If yes, for a primary aim or secondary aim of JHS? (check one or both)

- ☐ Primary Aim (heart, vascular disease)
- ☐ Secondary Aim (other conditions)

I. Conflict of Interest

1. Are these analyses to involve a for-profit corporation? No

If yes, please describe the nature of conflict of interest:

Name of corporation:

2. Do you or any member of your Writing Group intend to patent any process, aspect of outcome of these analyses? No

Describe plans for such patents:

J. Manuscript Completion

Note: It is expected that the manuscript will be completed within <u>two years</u>. The manuscript proposal will expire if no manuscript is submitted for JHS review after two years from the date of approval.