1.a. Full Title:  Black/white differences in the relationship of the MetSyn components to insulin resistance

b. Abbreviated Title (Length 26 characters): MetSyn and insulin resistance

2. Writing Group:
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3. Timeline:

Begin Analyses -- April 2007
Manuscript completed – January 2008
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4. Rationale:

The metabolic syndrome (MetSyn), variously termed insulin resistance syndrome, multiple metabolic syndrome, syndrome X, and deadly quartet, is defined as a clustering of cardiovascular disease (CVD) risk factors, including high blood pressure levels, low high-density lipoprotein levels, central adiposity, high blood glucose and high triglyceride (TG) levels. It is estimated that the MetSyn affects approximately 22.8% men and 22.6% women in the United States, indicating no significant differences by gender (1). However, significant racial/ethnic differences exist in the prevalence of this syndrome. Recent estimates from NHANES-III (as determined by the ATP-III criteria) indicate that Mexican-American women (27.2%) and white men (24.3%) had the highest prevalences of the MetSyn, followed by white women (22.9%), black women (20.9%), and black men (13.9%) (1). In the ARIC cohort, McNeill and colleagues (using the ATP III criteria) observed the highest prevalence of the MetSyn among black women (38.4%), followed by white men (30.6%), white women (28.2%), and black men (25.6%) (2). Using the WHO criteria, McNeill and colleagues reported a prevalence of 39.7% among black women, 29.2% among white men, 19.6% among white women, and 32.1% among black men (2).

Insulin resistance has been implicated as the disorder underlying the MetSyn (3). There is evidence that insulin resistance differs by race/ethnicity. The origin of insulin resistance is thought to be different for blacks and whites, being primarily vascular in blacks and visceral in whites. Blacks compared to whites have more microvascular disease, such as lacunar stroke (4), white matter lesions (5), retinopathy (6), and retinal arteriolar narrowing (7). The role of microvascular dysfunction in insulin resistance has been widely documented in basic science research (8). Additionally, retinal arteriolar narrowing, an independent risk factor for diabetes, is more predictive of diabetes in blacks than in whites (7). Further, compared to whites, blacks have been found to have less adiponectin, an adipocyte-derived secretory protein that has a protective effect on the arteries and a protective effect in diabetes development (9).

For reasons that are not well understood, blacks are more insulin resistant than whites (10-12), despite similar levels of obesity and a more positive TG/HDL ratio (13). Haffner and colleagues (10) reported that, compared to whites, nondiabetic blacks had higher fasting and 2-hour insulin levels, higher first-phase insulin secretion, and lower insulin sensitivity even after adjustment for body fat distribution and overall obesity. Carnethon and colleagues (11) reported that among black and white women of similar body weight, blacks had higher fasting insulin levels; moreover, at each level of BMI, blacks showed greater insulin resistance. Similarly, Grower and colleagues (12) reported that, between prepubertal black and white children, blacks had higher fasting and postchallenge insulin levels despite similar levels of total body fat, subcutaneous abdominal adipose tissue and intra-abdominal adipose tissue.

In addition, there is evidence to suggest that the markers for insulin resistance in blacks and whites are different, but those differences have not been well studied. Among whites, TG and HDL-C levels are strongly associated with insulin resistance (13), but only weakly so in blacks (14). Plasma TG concentrations in the most insulin resistant blacks and white have
been reported as different, being significantly lower in blacks than in whites (15, 16). Recently, Sumner and colleagues (15) reported that TG levels and TG-HDL ratio were not significant predictors of insulin resistance in blacks, thereby indicating that the lipid component of the MetSyn is not a reliable marker for insulin resistance in blacks. These findings suggest that different components of the MetSyn contribute differently to insulin resistance in blacks and in whites. The purpose of the proposed analysis is to determine whether there are black-white differences in the MetSyn components that are associated with insulin resistance. Black-white differences in the configuration of MetSyn components associated with insulin resistance may account for racial/ethnic differences in the ability of current MetSyn criteria to predict adverse events associated with the metabolic syndrome, such as diabetes and cardiovascular disease.

5. Main Hypothesis/Study Questions:

1) Of the MetSyn components, which are significantly associated with insulin resistance in blacks and in whites? The homeostasis model assessment (HOMA-IR) method will be used to define insulin resistance (17). The MetSyn will be defined in terms of the ATP III and the WHO criteria.

5a. Statistical Analyses

The study question will be answered using multivariable linear regression. Insulin resistance will be regressed on components of the MetSyn, controlling for age and gender. If HOMA-IR is not normally distributed, it will be log-transformed for the linear regression analyses. Separate models will be conducted for blacks and for whites. The p-value of each MetSyn component will be inspected for its relationship to insulin resistance. Statistical significance will be set at an alpha level of 0.05.

6. Data (variables, time window, source, inclusions/exclusions):

Visit 1 Variables: fasting insulin, fasting serum glucose, systolic blood pressure, diastolic blood pressure, triglycerides, HDL-C, waist circumference, waist-to-hip ratio, BMI, age, race/ethnicity, gender.

Excluded will be participants with:
1) a racial/ethnic identity other than black or white.
2) a fasting time < 8 hours.

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 ICTDER02 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 ICTDER02 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 ICTDER02 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)?

Metabolic syndrome, diabetes and decline in cognitive function, McNeill A: #1066

Empirical validation of the metabolic syndrome components and cutpoints through the prediction of CHD and diabetes using partitioning methods, McNeill A: #1031

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.

References


15. Sumner AE, Finley KB, Genovese DJ, Criqui MH, Boston RC. Fasting triglyceride and the triglyceride-HDL cholesterol ratio are not markers of insulin.
