ABSTRACT

Title of Document: IS THE CURRENT DEFINITION OF THE METABOLIC SYNDROME A USEFUL TOOL FOR THE DETECTION OF CARDIOVASCULAR DISEASE IN NON-HISPANIC BLACKS?

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Blacks in the country suffer from higher prevalences of obesity, diabetes, hypertension and cardiovascular disease compared to whites. Paradoxically, they have the lowest prevalence of the Metabolic Syndrome (MS) compared to whites and Mexican Americans. This is likely due to the fact that blacks tend to have lower triglycerides (TG) and higher high density cholesterol (HDL) levels. We challenged the current lipid criteria established by the Adult Treatment Panel III for the detection of the MS and set out to find more appropriate TG and HDL cutoffs to detect the MS in blacks. Using data from the National Health and Nutrition Examination Survey from 1999-2006, we identified that a more appropriate TG cutoff for blacks to detect the MS is 110 mg/dL but were not able to identify more suitable HDL cutoffs. Our results confirm that race/ethnic-specific criteria should be established for the detection of the MS across racial/ethnic groups.

IS THE CURRENT DEFINITION OF THE METABOLIC SYNDROME A USEFUL TOOL FOR THE DETECTION OF CARDIOVASCULAR DISEASE IN NON-HISPANIC BLACKS?

By

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Dedication

I dedicate this work to the Lord, my God and savior, Jesus Christ. To Him be all the glory forever.

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List of Abbreviations

1. AHA = American Heart Association
2. Apo B = apolipoprotein B
3. ASCVD = atherosclerotic cardiovascular disease
4. ATP III = Adult Treatment Panel III
5. BMI = body mass index
6. BP = blood pressure
7. CDC = Centers for Disease Control and Prevention
8. CHD = coronary heart disease
9. CLRD = chronic lower respiratory diseases
10. CRP = C-reactive protein
11. CVD = cardiovascular disease
12. EGIR = European Group for the Study of Insulin Resistance
13. FHS = Framingham Heart Study
14. FN = false negatives
15. FP = false positives
16. FPG = fasting plasma glucose
17. HL = hepatic lipase
18. HDL = high density lipoprotein cholesterol
19. HERITAGE = The Health, Risk Factors, Exercise Training, and Genetics Family Study
20. HT = hypertension

21. IDF = International Diabetes Federation

22. LDL = low density lipoprotein cholesterol

23. LPL = lipoprotein lipase

24. MA = Mexican American

25. MCC = Matthew Correlation Coefficient

26. MS = Metabolic Syndrome

27. NCEP = National Cholesterol Education Program

28. NCHS = National Center for Health Statistics

29. NIH = National Institutes of Health

30. NHANES = National Health and Nutrition Examination Survey

31. NHB = non-Hispanic black

32. NHLBI = National Heart, Lung, and Blood Institute

33. NHW = non-Hispanic white

34. NIH = National Institutes of Health

35. PIR = poverty income ratio

36. PSU = primary sampling unit

37. PPS = probability proportional to a measure of size

38. ROC = receiver operating characteristic curve

39. SE = standard error

40. TA = Total Accuracy

41. TARA = The Triglyceride and Cardiovascular Risk in African Americans Study

42. TC = total cholesterol

43. TG = triglycerides

44. TG:HDL = triglyceride to high density lipoprotein cholesterol ratio

45. TN = true negatives

46. TP = true positives

47. WHO = World Health Organization

48. WC = waist circumference

Chapter 1: Introduction

Cardiovascular Disease

An estimated 80,000,000 American adults have one or more types of cardiovascular disease (CVD), the number one killer of men and women in the United States (U.S.). It refers to a class of diseases that involve the heart and/or blood vessels and includes any of the following systemic abnormalities: coronary heart disease, stroke, high blood pressure (BP), acute coronary syndrome (acute myocardial infarctions and unstable angina), angina pectoris, congenital cardiovascular defects, heart failure, and peripheral arterial disease[1].

According to the American Heart Association (AHA) one in three adults in the in the country has some form of CVD. Each day nearly 2,400 Americans die of CVD, at an average of one death every 36 seconds. CVD claims more lives yearly than cancer, chronic lower respiratory diseases, accidents and diabetes mellitus combined[2].

The Metabolic Syndrome

In 1988, Dr. Gerald M. Reaven revealed that insulin resistance and its related compensatory hyperinsulinemia were central to the etiology of type 2 diabetes, hypertension (HT), and CVD, particularly coronary artery disease. In his investigations Reaven identified the co-occurrence of several metabolic abnormalities such as resistance to insulin-stimulated glucose uptake, glucose intolerance, hyperinsulinemia, increased plasma triglyceride (TG), decreased high density

lipoprotein cholesterol (HDL), and elevated BP. At the time, he called this clustering of abnormalities 'Syndrome X' due to the fact that it was largely not understood. Presently it is more commonly known as the Metabolic Syndrome (MS), but because more recent evidence points out that the underlying abnormality that leads to these changes is resistance to glucose-mediated disposal, it is not difficult to see why it has also been aptly termed the 'Insulin Resistance Syndrome'[3, 4].

In order to more effectively detect the presence of the MS, and in light of the fact that its prevalence has reached epidemic proportions worldwide, several major health organizations have proposed sets of defining criteria for the syndrome. These organizations include the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH), the World Health Organization (WHO), the International Diabetes Federation (IDF), and the European Group for the Study of Insulin Resistance (EGIR).

Nationally, the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, Adult Treatment Panel III (NCEP, ATP III), instituted by the NHLBI, defines the MS as having three or more of the following abnormalities: a waist circumference (WC) of 102 cm (40 inches) or greater in men and 88 cm (35 inches) or greater in women, a blood TG concentration of 150 mg/dL or higher, HDL cholesterol levels of less than 40 mg/dL in men and less than 50 mg/dL in women, a BP of 130/85 mm Hg or higher or drug treatment for HT, and fasting plasma glucose (FPG) level of 100 mg/dL or higher. This combination of metabolic risk factors has been observed to be

strongly associated with type 2 diabetes mellitus and its risk as well as with CVD morbidity and mortality[5].

In the U.S. an estimated 76 million people have the MS. The age-adjusted prevalence among adults is 34 percent, with men having slightly higher prevalence (35.1%) than women (32.6%)[6]. According to the AHA Heart Disease and Stroke Statistics 2008 report, Mexican Americans (MA) have the highest age-adjusted prevalence of the MS in the country with 31.9 percent of MA's suffering from the syndrome. Whites follow MA's with a prevalence of 23.8 percent. Blacks have the second to lowest MS prevalence of 21.6 percent. People reporting "other" race or ethnicities have the lowest prevalence at 20.3 percent[2].

As we can see, statistics show that the prevalence of the MS is lower overall among black men and women as compared to other racial and ethnic groups. However, this seems paradoxical due to the fact that blacks have one of the highest CVD rates both nationally and worldwide[7-9]. What is more, blacks have higher rates of overall obesity and central obesity, diabetes, hyperglycemia, HT, and insulin resistance as compared to whites. They also tend to have higher CVD mortality, even in the absence of diabetes, than whites [8, 10].

It has been observed that for genetic and anatomical reasons blacks have lower plasma TG levels and higher HDL levels, even in the presence of diabetes and insulin resistance, and at similar levels of obesity as whites. Because of these differences in lipid and lipoprotein concentrations many blacks do not meet the criteria the MS proposes. In light of this, several research groups question the utility of the MS to detect CVD and type 2 diabetes risk in blacks and propose that

race/ethnic-specific definitions be designed and instituted. Some attempts have been made to find more suitable lipid and lipoprotein cutoffs among this population, but unfortunately such studies have been conducted in small samples not representative of the U.S. population[11].

Purpose of the Study

The purpose of this study was to help reveal that lipid and lipoprotein parameter distributions are different across racial/ethnic groups and that using single TG and HDL cutoffs for detecting the presence of the MS is not equally helpful across all racial/ethnic groups. With this in mind, we set out to find more suitable TG and HDL cutoffs for blacks to adequately predict the MS utilizing a sample representative of the current U.S. population. We also sought to add support to the idea that the currently established lipid and lipoprotein parameter cutoffs might not be sufficient to predict diabetes and CVD risk among all racial/ethnic populations, particularly blacks.

Research Hypothesis

We hypothesized that a TG cutoff point that is lower than the currently established 150 mg/dL by NCEP's ATP III criteria would be a more precise and accurate predictor of the MS in blacks. Also, we expected that cutoffs for HDL levels greater than 40 mg/dL for men and 50 mg/dL for women would be necessary to stave off MS risk in this racial group.

Chapter 2: Research Objectives

This study was designed to answer the following questions:

1. What is the prevalence of MS and CVD among non-Hispanic whites (NHW), non-Hispanic blacks (NHB) and Mexican Americans (MA) in NHANES 1999 to 2006, a nationally representative sample of the U.S. population? How are these prevalences different between males and females and between racial/ethnic groups?

2. What is the prevalence of MS and CVD risk factors: overweight and obese body mass index (BMI), elevated WC, elevated total cholesterol, elevated LDL, low HDL, elevated TG, elevated FPG, HT, and diabetes among NHW's, NHB's and MA' in NHANES 1999 to 2006? How are these prevalences different between racial/ethnic groups?

3. What is the relationship between the predictor variables of interest, TG and HDL, and MS while controlling for age, race/ethnicity, BMI, WC, LDL cholesterol, blood glucose, systolic BP, diastolic BP, socioeconomic (education, income, health insurance coverage) and lifestyle factors (physical activity, smoking, drinking), and the inflammatory factor C-reactive protein (CRP)?

4. Are the currently proposed cutoffs for TG and HDL accurate and precise predictors of MS for non-Hispanic blacks? If not, what are more accurate and precise cutoffs?

5. What is the prevalence of MS in NHB's using the newly proposed cutoffs?

Chapter 3: Literature Review

Cardiovascular Disease

CVD is the number one killer of men and women in the U.S. It refers to a class of diseases that involve the heart and blood vessels and includes any of the following systemic abnormalities: coronary heart disease (CHD), stroke (cerebrovascular disease), high BP or HT, acute coronary syndrome (acute myocardial infarctions and unstable angina), heart failure, and peripheral arterial disease. CHD is comprised of acute MI, other acute ischemic (coronary) heart disease, angina pectoris, atherosclerotic CVD, and all other forms of chronic ischemic CHD[6].

Cardiovascular Disease Mortality Statistics

Each day nearly 2,300 Americans die of CVD, at an average of one death every 38 seconds. On every year since 1900 except 1918, CVD has accounted for more deaths than any other major cause of death in the country. Yearly, CVD claims more lives than cancer, chronic lower respiratory diseases (CLRD), and accidents combined. The Centers for Disease Control and Prevention (CDC), National Center for Health Statistics (NCHS) 2006 mortality data show that CVD was the underlying cause of death in one out of every 2.9 deaths in the country. The 2006 overall death rate due to CVD was 262.5 (per every 100,000). Death rates by race and gender were: 306.6 for white males, 422.8 for black males, 215.5 for white females, and 298.2 for black females. In the same year the leading causes of death in women 65 years of age

and older were diseases of the heart, cancer, stroke, and CLRD, in decreasing order. In older men, the leading causes were diseases of the heart, cancer, CLRD, and stroke, also in decreasing order. Interestingly, the actual number of deaths due to CVD declined 12.9 percent per year from 1996 to 2006, leading to a total CVD death rate decline of 29.2 percent (Figure 1)[6]. Reductions in serum cholesterol, BP, and cigarette smoking may in part explain this decline[12].

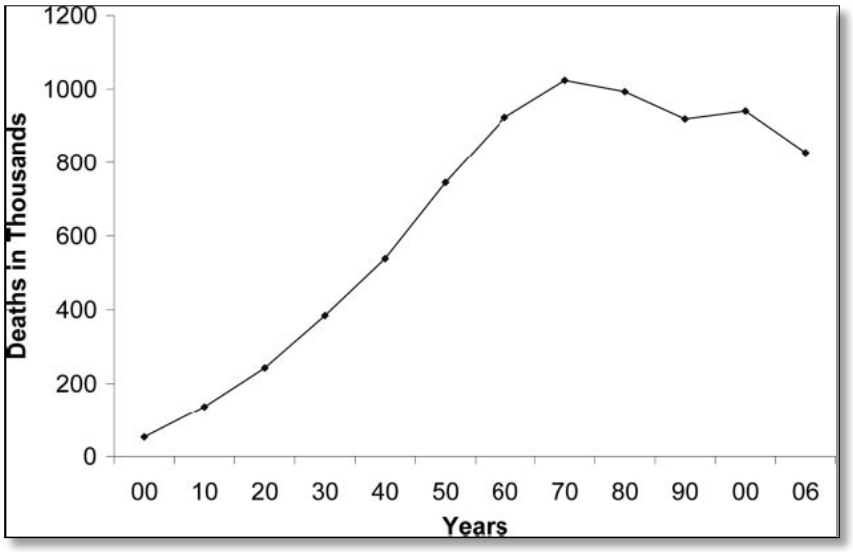

Figure 1. *Deaths due to CVD (United States: 1900–2006). CVD does not include congenital CVD.* Source: Lloyd-Jones et al., 2010[6]

Cardiovascular Disease Morbidity Statistics

In spite of the declining CVD death rate, "the burden of disease remains high", according to the AHA's 2010 Heart Disease and Stroke Statistics. This is shown in that one in three or about 81.1 million adults in the country has one or more types of CVD. According to the CDC's, National Health Interview Survey (2008), the age-adjusted prevalence estimates for white adults 18 years of age and older reveal

that 12.1 percent have heart disease, 6.5 percent have CHD, 23.3 percent have HT, and 2.7 percent have had a stroke. Among blacks, 10.2 percent have heart disease, 5.6 percent have CHD, 31.8 percent have HT, and 3.6 percent have had a stroke. Among Hispanics or Latinos, 8.1 percent have heart disease, 5.7 percent have CHD, 21.0 percent have HT, and 2.6 percent have had a stroke[6].

Cardiovascular Disease Incidence Statistics

Based on data from NHLBI's Framingham Heart Study (FHS), average annual rates of first CVD events rise from three per 1,000 men at ages 35 to 44 to 74 per 1,000 men at ages 85 to 94. Comparable rates occur 10 years later among women, with the gap narrowing with advancing age (Figure 2). Before 75 years of age, a higher proportion of CVD events due to CHD occur in men than in women, and a higher proportion of events due to stroke occur in women than in men. The lifetime risk for all CVD in recipients free of disease at 40 years of age is two in three for men and more than one in two for women. Analysis of FHS data among participants free of CVD at 50 years of age demonstrated that the lifetime risk for developing CVD is 51.7 percent for men and 39.2 percent for women. Median overall survival is 30 years for men and 36 years for women[6].

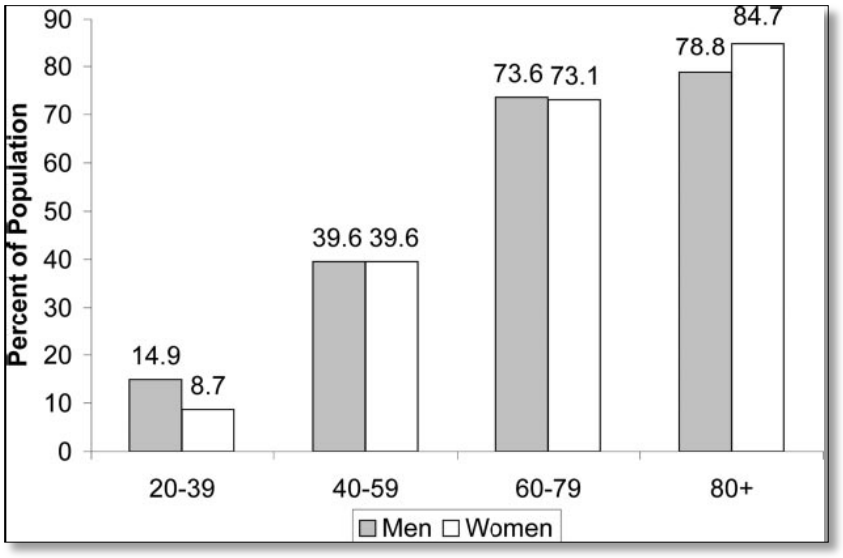

Figure 2. *Prevalence of CVD among adults ≥ 20 years of age by age and sex (NHANES: 2003–2006). These data include CHD, HF, stroke, and HT.* Source: Lloyd-Jones et al., 2010[6]

Coronary Heart Disease: the Deadliest Cardiovascular Disease

As shown in figure 3, CHD leads to the highest number of deaths among all cardiovascular diseases. In 2006, this disease alone caused one out of six deaths in the U.S. An estimated 17,600,000 Americans 20 years of age and older have CHD based on NHANES 2003-2006 estimates. Total CHD prevalence is 7.9 percent in U.S. adults 20 years of age and older. CHD prevalence is 9.1 percent for men and 7.0 percent for women. Among NHW's, CHD prevalence is 9.4 percent for men and 6.9 percent for women. Among NHB's, CHD prevalence is 7.8 percent for men and 8.8 percent for women. MA's have the lowest prevalence of the disease with 5.3 percent men and 6.6 percent women suffering from the disease.

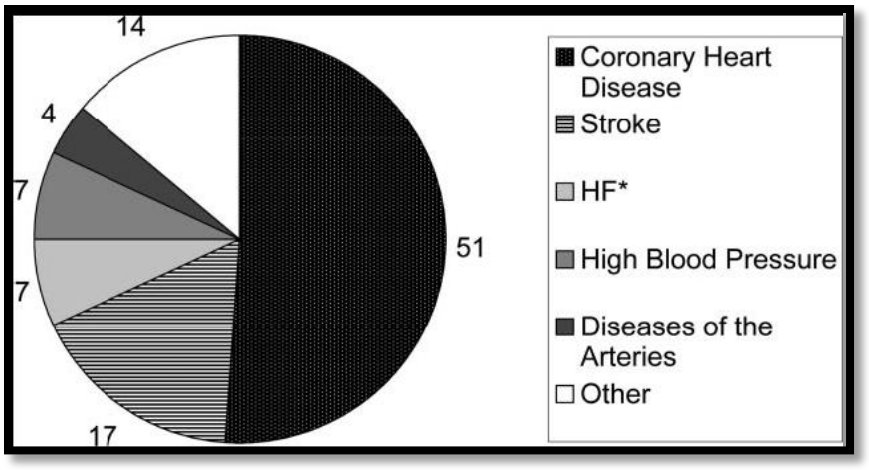

Figure 3. *Percentage breakdown of deaths due to CVD (United States: 2006). *Not a true underlying cause. May not add to 100 because of rounding.* Source: Lloyd-Jones et al., 2010[6]

Detection of Cardiovascular Disease

In 2001 the NHLBI of the NIH redefined the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults III (ATP III; Table 1). According to this new ATP III revision elevated blood levels of LDL cholesterol (≥ 160mg/dL) is the major risk factor for CHD. In keeping with this ATP III revision, goals for LDL cholesterol may be modified according to other concomitant risk factors. These other risk factors are: cigarette smoking, HT, low HDL cholesterol (< 40 mg/dL), family history of premature CHD (CHD in male first degree relative < 55 years; CHD in female first degree relative < 65 years), and age (men ≥ 45 years; women ≥ 55 years) (Table 2)[13].

Table 1. ATP III classification of LDL, total, and HDL cholesterol (mg/dL)

LDL Cholesterol – Primary Target of Therapy	
< 100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline High
160-189	High
≥ 190	Very High
Total Cholesterol	
< 200	Desirable
200-239	Borderline high
≥ 240	High
HDL Cholesterol	
< 40	Low
≥ 60	High

Source: ATP III, 2001[13]

Table 2. Major risk factors (exclusive of LDL) that modify LDL goals

- Cigarette smoking
- Hypertension (Blood pressure ≥ 140/90 mmHg or on antihypertensive medication)
- Low HDL cholesterol (< 40 mg/dL)*
- Family history of premature CHD (CHD in male first degree relative < 55 years); CHD in female first degree < 65 years)
- Age (men ≥ 45; women ≥ 55 years)

***** HDL cholesterol ≥ 60 mg/dL counts as a "negative" risk factor; its presence removes one factor from total count.
Source: ATP III, 2001[13]

The Metabolic Syndrome and its Definitions

The AHA and the NHLBI describe the MS, also known as 'Syndrome X', the 'Deadly Quartet', the 'Dysmetabolic Syndrome', and the 'Insulin resistance

Syndrome', as "a group of multiple, interrelated risk factors of metabolic origin that appear to promote the development of atherosclerotic cardiovascular disease (ASCVD) and type 2 diabetes mellitus (or its risk)"[5, 14]. According to a statement from the IDF, "the MS is a cluster of the most dangerous heart attack risk factors: diabetes and prediabetes, abdominal obesity, high cholesterol and high BP"[7]. People with the MS are three times as likely to have a heart attack or stroke compared with people without the syndrome and twice as likely to die from these. People with MS also have a five-fold greater risk of developing type 2 diabetes[7, 15]. Furthermore, CVD and type 2 diabetes are not the only clinical syndromes associated with the MS, HT, polycystic ovarian syndrome, non-alcoholic liver disease, sleep disordered breathing, fatty liver, cholesterol gallstones, gout, depression, musculoskeletal disease, and certain types of cancer have also been found to be associated with the disorder[4, 15, 16].

The MS appears to promote the development of ASCVD at various levels[17, 18]. Elevations of apolipoprotein B (apo B) containing lipoproteins initiate atherogenesis and start lesion development. This plaque development is accelerated by low circulating levels of HDL and elevated BP, by inflammatory cytokines, among these interleukin 6, tumor necrosis factor alpha, and CRP, and by elevated plasma glucose. Advanced plaques become unstable and they begin to rupture. When ruptures occur, a prothrombotic state promotes propagation of thrombi which can worsen existing cardiovascular conditions[15].

Like for CHD risk, ATP III has proposed a set of diagnostic criteria for the diagnosis of the MS (Table 3). According this criteria the presence of three out of five of the following abnormalities constitutes the MS: elevated WC (≥ 102 cm in men, ≥

88 cm in women), elevated TG (≥ 150 mg/dL, or drug treatment for elevated TG), reduced HDL (< 40 mg/dL in men, < 50 mg/dL in women, or drug treatment for reduced HDL), elevated BP (≥ 130 mm Hg systolic BP or ≥ 85 mm Hg diastolic BP, or drug treatment for elevated BP), and/or elevated FPG (≥ 100 mg/dL, or treatment for elevated glucose)[5]. These conditions, when clustered, not only indicate a diagnosis for the MS, but also help identify patients at risk for advanced CVD and offer an opportunity for early and more aggressive intervention[19].

Table 3. NCEP's ATP III diagnostic criteria for the Metabolic Syndrome

According to the ATP III definition, for a person to be defined as having the MS they must have three out of the five following:

Indicator	**Level indicative of MS**
Elevated waist circumference	≥ 102 cm (≥ 40 in.) in men ≥ 88 cm (≥ 35 in.) in women
Elevated triglycerides	≥ 150 mg/dL or drug treatment for elevated triglycerides
Reduced HDL cholesterol	< 40 mg/dL in men < 50 mg/dL in women or drug treatment for low HDL
Elevated blood pressure	≥ 130 mmHg systolic blood pressure or ≥ 85 mmHg diastolic blood pressure or drug treatment for elevated blood pressure
Elevated fasting glucose	≥ 100 mg/dL or drug treatment for elevated fasting glucose

Source: Grundy et al., 2005[5]

It is important to note that in the 2001 ATP III definition of the MS, threshold level of FPG was set at 110 mg/dL. In 2004 this cutoff was modified to be 100 mg/dL, in accordance with the American Diabetes Association's update of the definition of impaired fasting glucose[5, 20, 21].

Among the key underlying factors for the MS are abdominal obesity and insulin resistance, but other associated conditions include physical inactivity, aging, hormonal imbalances, and genetic predisposition[22]. Prospective population studies have shown that the MS significantly increases long-term risk ASCVD events and diabetes, nonetheless additional research is required to better understand the pathophysiology of the MS[5]. It is known that the concurrent presence of the metabolic abnormalities observed in individuals with the MS confer a substantial cardiovascular risk over and above the sum of the risk of each abnormality[7]. When clustered, these abnormalities not only indicate a diagnosis but more importantly help identify patients at risk for accelerated CVD[19].

The clustering of risk factors that characterize the MS is now considered to be the driving force for a worldwide CVD epidemic[7]. In light of this, the IDF has established a definition for the MS to be used worldwide in clinical practice (Table 4). This definition classifies a person as having the MS if they have central obesity defined as a WC of 94 cm or greater for Europid men and 80 cm or greater for Europid women, as well as two of the following four factors: elevated TG levels (≥ 150 mg/dL) or treatment for elevated TG, reduced HDL (< 40 mg/dL in males and < 50 mg/dL in females) or treatment for reduced HDL, raised BP (systolic BP ≥ 130 or

diastolic BP ≥ 85 mm Hg) or treatment for elevated BP, elevated FPG (≥ 100 mg/dL) or having been previously diagnosed with type 2 diabetes[23].

Table 4. The International Diabetes Federation definition of the Metabolic Syndrome

According to the new IDF definition, for a person to be defined as having the MS they must have:

Central obesity (defined as a waist circumference ≥ 94 cm for Europid men and ≥ 80 cm for Europid women, with ethnic specific values for other ethnic groups) ***plus any two of the following four factors:***

- Raised TG level: ≥ 150 mg/dL, or specific treatment for this lipid abnormality
- Reduced HDL cholesterol: < 40 mg/dL in males and < 50 mg/dL in females, or specific treatment for this lipid abnormality
- Raised blood pressure: systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg, or treatment of previously diagnosed HT
- Raised fasting plasma glucose ≥ 100 mg/dL, or previously diagnosed type 2 diabetes
  [If > 100 mg/dL, an oral glucose tolerance test is strongly recommended but is not necessary to define presence of the syndrome]

Source: Grundy et al., 2005[5]; IDF, 2009[23]

In order to make this MS definition applicable worldwide, the IDF has also specified different WC cutoffs for central obesity which are specific to gender and ethnic group (not country of residence). These include: Europids, South Asians, Chinese, Japanese, Ethnic South and Central Americans, Sub-Saharan Africans, and Eastern Mediterranean and Middle East (Arab) populations (Table 4)[5, 23].

Table 5. The International Diabetes Federation Metabolic Syndrome definition - ethnic specific values for waist circumference

Country/ Ethnic group		**Waist circumference† (as measure of central obesity)**
*Europids**	Males	≥ 94 cm
	Females	≥ 80 cm
*South Asians***	Males	≥ 90 cm
	Females	≥ 80 cm
Chinese	Males	≥ 90 cm
	Females	≥ 80 cm
*Japanese****	Males	≥ 85 cm
	Females	≥ 90 cm
Ethnic South and Central Americans	**Use South Asian recommendations until more specific data are available**	
Sub- Saharan Africans	Use European data until more specific data are available	
East Mediterranean and Middle East (Arab) populations	Use European data until more specific data are available	

* In the USA, the ATP III values (102 cm male; 88 cm female) are likely to continue to be used for clinical purposes

** Based on a Chinese, Malay and Asian Indian population

*** Subsequent data analyses suggest that Asian values (male, 90cm; female 80cm) should be used for Japanese populations until more data are available.

†In future epidemiological studies of populations of Europid origin, prevalence should be given using both European and North American cut-points to allow better comparisons.

Although a higher cut-point is currently used for all ethnic groups in the USA for clinical diagnosis, it is strongly recommended that for epidemiological studies and, wherever possible, for case detection, ethnic group specific cut-points should be used for people of the same ethnic group wherever they are found. Thus the criteria recommended for Japan would also be used in expatriate Japanese communities, as would those for South Asian males and females regardless of place and country of residence.

Sources: Grundy et al., 2005[5]; IDF, 2009[23]

In addition, the WHO also has proposed working criteria for the MS similar to that constructed by ATP III. These criteria are similar in that they focus on obesity, dyslipidemia, hyperglycemia, and HT but differ in their specific constituents used to measure these as well as in their threshold levels (Table 6)[24].

Table 6. The World Health Organization's definition of the Metabolic Syndrome

Subjects are identified as having the MS if they have **hyperinsulinemia** (defined as the upper quartile of the non-diabetic population), a **2-hour glucose** ≥ 140 mg/dL, a **fasting plasma glucose** ≥ 110 mg/dL, or taking medication for diabetes **and have two or more of the following metabolic abnormalities**:

- Waist-to-hip ratio > 0.90 in men *and* > 0.85 in women or a BMI ≥ 30 kg/m^2
- TG levels ≥ 1.7 mmol/L (150 mg/dL) ***or*** ASCVD HDL < 0.9 mmol/L (35 mg/dL) in men *and* < 1.0 mmol/L (39 mg/dL) in women
- Blood pressure ≥ 140/90 mm Hg (or treated HT)
- Microalbuminuria (urinary albumin excretion rate ≥ 20 μg/min or albumin:creatinine ratio ≥ 30 mg/g)

Sources: Meigs et al., 2003[24]; Hunt et al., 2004[25]

In 1999, after the WHO established its definition of the MS, the EGIR also constructed its own. This definition would be more useful in epidemiological trials but it can only be applied to non-diabetic individuals. Table 7 presents the criteria established by EGIR for the diagnosis of the MS[3].

Table 7. The European Group for the Study of Insulin Resistance's definition of the Metabolic Syndrome

Insulin resistance (defined as hyperinsulinemia - top 25% of fasting insulin values among the non-diabetic population)

Plus two of the following:

Fasting plasma glucose: ≥ 6.1 mmol/L (110 mg/dL) but non-diabetic
Blood pressure: ≥ 140/90 mmHg or treatment
Triglycerides: > 2.0 mmol/L(178 mg/dL) or treatment

and/or

HDL cholesterol: < 1.0 mmol/L (39 mg/dL) or treatment
Obesity as defined by waist circumference:
Men: ≥ 94 cm
Women: ≥ 80 cm

Source: Alberti et al., 2006[26]

Metabolic Syndrome Statistics

One quarter of the world's adult population has the MS[7]. In 2007 the AHA estimated that an estimated 76 million U.S. residents 20 years and older had the MS[1]. This is in sharp contrast with the 47 million residents that had the MS as of 1994[2]. The age-adjusted prevalence of MS in the nation according to NHANES 2003-2006 is approximately 34 percent. The age-adjusted prevalence is 35.1 percent for men and 32.6 percent for women. Age-adjusted prevalences of men with MS by race and ethnicity are 37.2 percent for NHW, 25.3 percent for NHB, and 33.2 percent for MA men. Among women, the percentages are 31.5 percent for NHW, 38.8 percent for NHB, and 40.6 percent for MA women[1].

Racial and Ethnic Differences in Prevalence of the Metabolic Syndrome

As we have observed the prevalence of the MS is lower overall among blacks compared to other racial and ethnic groups. However, this seems paradoxical due to the fact that blacks have one of the highest CVD rates not only in the country, but in the world[7, 27]. In blacks HT occurs 50 percent more frequently, is seen earlier, is more severe, and is often associated with target organ damage, left ventricular hypertrophy, heart failure, end-stage renal disease, fatal and nonfatal stroke, and CHD-related mortality[19]. Besides having a greater prevalence of HT, blacks have higher rates of overall obesity, central obesity, and diabetes, hyperglycemia, and insulin resistance as compared to whites. They also tend to have higher CVD morbidity and mortality, even in the absence of diabetes, than whites[8, 10, 28].

Lipid and Lipoprotein Differences between Racial/Ethnic Groups

One of the proposed reasons for this ambiguity is that blacks tend to have what appears to be a more favorable lipid profile and so do not as easily meet the criteria the MS proposes[29, 30]. The tendency is for blacks to have lower TG levels and higher HDL cholesterol levels even in the presence of higher insulin levels, diabetes, and obesity than their white and MA counterparts[31, 32]. In light of this, several research groups question the utility of the present MS criteria across different groups and suggest that criteria specific to race or ethnic group should be utilized to diagnose the MS[8, 10, 19, 31, 33, 34].

In a study 29 white American and 22 African American women, MacLean and colleagues observed that obese, diabetic African American women had a greater

prevalence of CVD even without having the alterations in lipid concentrations observed among their obese, diabetic white American counterparts. The white diabetic women in this study exhibited more atherogenic lipid concentrations compared to lean and obese white women without diabetes, as is generally expected. Interestingly, the lipid concentrations of the diabetic African American women were relatively similar to those found among the non-diabetic, lean and obese African American women. What is more, the black American women cohort demonstrated higher HDL and lower TG and LDL concentrations, regardless of level of obesity or presence of diabetes compared to the white American women. Nevertheless, the investigators note that although the increased CVD rate among obese, diabetic white subjects can be partly attributed to increased lipid concentrations, elevated CVD incidence persists among obese, diabetic African American subjects in spite of the absence of the expected increases in lipid concentrations. In other words, the dyslipidemia observed in African Americans does not seem to play a role in their CVD risk[31].

On a related note, MacLean and colleagues add that in the presence of diabetes and obesity, subtle racial differences may exist not only in terms of lipid concentrations, but also in lipid particle size and in lipoprotein subpopulation distributions. According to the researchers, in African Americans lipoprotein subpopulation distributions may be more predictive of vascular disease than lipid concentrations alone. In view of this and of the racial differences in lipoprotein distributions in the presence of obesity and diabetes, the authors conclude by

suggesting that race-specific criteria are needed in clinical settings to better identify patients at high risk for CVD[31].

A similar argument was presented by Ferdinand and Clark in their 2004 review of MS among African Americans. In it the authors draw attention to the fact that among African American men there appears to be an unexpected lower rate of MS as compared to white and MA men, which they argue is specifically caused by an underestimation of the presence of the MS. This underestimation is due in turn to higher HDL cholesterol and to lower TG and LDL cholesterol levels observed among this group. Like MacLean et al., the study group adds that the presence of these apparently more favorable lipoprotein levels does not appear to be protective against the negative effects of CHD and that in fact, CHD-related death rates within this population remain not only the highest in the country, but also in the world[19].

More recently, Sumner, in his 2009 review of racial and ethnic lipid and lipoprotein differences, argued that even though the cause of lower TG and higher HDL levels in blacks is largely unknown, the relative absence of dyslipidemia of insulin resistance in blacks may explain their lower-than-expected prevalence of the MS. The author claims that "it is also possible that the adult thresholds used to define hypertriglyceridemia (≥ 150 mg/dL) and low HDL (< 40 mg/dL in men, < 50 mg/dL in women) are not set at the appropriate level to identify high risk for diabetes and CVD risk in blacks." In view of this, the author concludes that ethnic-specific guidelines for lipids may be necessary. He adds that alternatively, blacks with the MS may transition so quickly from having the MS into CVD and diabetes that cross-sectional prevalence studies fail to capture the rate of MS in blacks[10].

Meanwhile, Gaillard and colleagues, in their review of MS definitions and classifications, challenge the current established definitions for the MS and suggest that the current ATP III, WHO, and IDF definitions of the MS should be redefined among different racial and ethnic populations, particularly in blacks. They surmise that based on the higher CVD outcomes in blacks despite of their lower rates of MS, there are racial/ethnic differences in the impact of the five components of MS for detecting future CVD and type 2 diabetes. Therefore, the relationships between several components of the MS and of insulin resistance are well established in whites but these relationships remain controversial in blacks[8].

Among blacks themselves, it has been argued that because there is limited data from studies based on sub-Saharan Africans, it is difficult to make recommendations in terms of components of the MS that are generalizable for all black populations. Preliminary studies nonetheless have shown that Ghanians and South African blacks both are more insulin resistant than whites. Lower prevalences of the MS have been reported in Cameroonians who live in rural areas versus urban areas. Also, the metabolic components of the MS in Ghanians, such as BP and lipids and lipoproteins have been observed to be comparable to those of African Americans, South Africans, and Afro-Caribbeans. According to Gaillard and colleagues, these studies collectively confirm that people of the African Diaspora are similar in this sense, regardless of their country of origin, once obesity and physical activity are accounted for[8, 35].

Racial and Ethnic Differences in Visceral Adiposity

As previously mentioned, blacks have higher rates of overall obesity and central obesity as compared to whites and MA's. According to Gaillard et al., "the distribution of excess adipose mass in adults may be more important than total fat in conferring metabolic and cardiovascular risk[8]." Excess fat in the upper body region, particularly abdominal or visceral adipose tissue, is linked with a more atherogenic plasma lipid profile and greater insulin resistance. Abdominal obesity has been shown to be associated with the MS, particularly among individuals with higher amounts of visceral adipose tissue[36]. In fact, central obesity, measured by WC, is one of ATP III's criteria for the MS[8]. Racial differences nonetheless have been reported in the relationship of body fatness to visceral adipose tissue accumulation, with whites being more prone to visceral adipose tissue deposition than blacks for any level of total body fat[37, 38].

Studies performed in white populations have shown that excess visceral adipose tissue accumulation in obese subjects is related to reduced plasma HDL levels[39]. As mentioned before, whites tend to have higher visceral adipose tissue compared to blacks, even when they have comparable BMI's and WC, and in spite of the fact that black women have greater total fat. It is probable that one reason why more favorable TG and HDL cholesterol levels are so often observed among blacks is precisely their lower visceral tissue accumulation[8, 37, 38, 40].

The Role of Lipases

Previous studies have shown that the TG lipases, lipoprotein lipase (LPL) and hepatic lipase (HL), are important correlates of plasma HDL cholesterol levels. LPL, found in the capillary endothelial cells in muscle and adipose tissue, is the enzyme responsible for clearing TG-containing lipoproteins from circulation. A deficiency of LPL leads to hypertriglyceridemia. Insulin leads to the synthesis of LPL and to its placement on the capillaries. Over time it has been repeatedly shown that subjects with high plasma LPL activity have increased HDL and decreased TG levels. Conversely, HL is expressed in the liver and the adrenal glands and its primary function is to convert intermediate density lipoproteins to LDL. Unlike LPL, HL is inversely correlated to plasma HDL levels, leading to decreased HDL levels in subjects with high HL activity[41].

The association between abdominal obesity and TG and HDL cholesterol was observed in a study of 723 subjects (32% black) using data from the Health, Risk Factors, Exercise Training, and Genetics (HERITAGE) Family Study[37]. The authors set out to test the hypothesis that lower accumulation of visceral adipose tissue could be responsible for the higher plasma HDL cholesterol levels in blacks those in whites. What they observed was that visceral adipose tissue accumulation, measured by computer tomography, showed a stronger correlation than total fat mass to TG, apo B, and total cholesterol to HDL ratio, as well as a negative correlation with HDL. White men had higher visceral adipose tissue deposition than black men, regardless of the fact that both groups had similar BMI and total body fat mass. Among women, both groups had similar levels of visceral adipose tissue regardless of the higher total

adiposity of black women, which in turn suggested that white women were more prone to visceral adipose tissue deposition than black women. White men showed increased TG and apoB concentrations and a higher ratio of total cholesterol to HDL cholesterol. White women had higher cholesterol, TG, and apoB levels. It is important to note that both white men and women showed lower LPL and higher HL activity than black men and women. These results illustrate that the generally more cardioprotective plasma lipoprotein profile found in abdominally obese black versus white individuals are explained to an extent, by a lower visceral adipose tissue deposition and a higher plasma LPL activity in blacks[37].

Previous studies have attributed the antiatherogenic properties of HDL to the reverse cholesterol transport mechanism. Furthermore, HDL has been suggested in recent studies to play an important role in the prevention of oxidative modification of LDL, which in turn contributes to the pathogenesis of atherosclerosis. Still, in spite of the seemingly protective HDL levels in blacks, still it is not known if HDL levels are truly cardioprotective in this racial group. If HDL levels are not cardioprotective, it is likely that other factors mitigate the potential cardiovascular beneficial effects of HDL in blacks. This is an issue remains to be investigated within this population. Gaillard et al. argue that in order to achieve the presumed antiatherogenic effects of HDL blacks, levels far in excess of the 50 mg/dL should be recommended for blacks in ATP III[8, 29].

Racial and Ethnic Differences in Insulin Resistance

It is widely known that insulin resistance is often characterized by elevated TG levels. However, studies elucidating this relationship have mostly been performed in primarily white populations, meaning that in blacks the relationship between insulin resistance and TG has not been well established. In blacks lower levels of TG levels are observed even when they have more insulin resistance, which in turn is caused by decreased hepatic insulin extraction in this racial group. Although the reasons for these racial differences are not clear, it has been suggested that the higher activity of LPL may in part be the reason for this lack of association in blacks[37, 42]. What is more, in addition to having relatively lower serum TG, blacks have larger LDL particle sizes, which are more buoyant and less atherogenic when compared to whites[8].

The mechanism whereby insulin resistance increases TG levels is by increasing hepatic TG production and secretion of very low density lipoproteins (VLDL) and by decreasing clearance of VLDL'S and chylomicrons, both TG-rich lipoproteins, from circulation[43]. Previous studies have suggested that insulin resistance leads to an impairment in LPL activity[42]. However, studies elucidating this mechanism of action of insulin resistance and TG have been primarily performed in whites. More recent studies including blacks have shown that such a relationship is not as apparent in this racial group. In one such study of 107 non-diabetic African Americans enrolled in the Triglyceride and Cardiovascular Risk in African Americans (TARA) of the NIH, Sumner and colleagues observed precisely this. The investigators observed that in African American men TG and insulin sensitivity were

significantly inversely correlated. However, in African American women this correlation was not significant. For men, TG was significantly higher among individuals with higher insulin resistance, but for women, TG did not change according to changes in insulin resistance. When the interaction between sex and insulin sensitivity was considered, the effect of insulin resistance was significant with TG rising as insulin resistance increased in men but not in women. In contrast, visceral adipose tissue was associated with a rise in TG levels in both men and women. What is more, visceral adipose tissue had an even greater impact on women than on men. The study group also measured gender differences in LPL activity where they observed no significant differences among the groups. For both men and women, TG levels were inversely correlated with LPL significantly. Based on these analyses, the authors affirmed that LPL activity appears to be a major determinant of TG levels. Of great importance was the fact that LPL activity did not change by tertile of insulin resistance both for the whole population, as well as when men and women were analyzed separately. In multiple regression analyses with LPL as the dependent variable and insulin sensitivity, BMI, and sex as independent variables, the contribution of insulin resistance was not significant. Their data suggest that LPL activity is independent of insulin status in this racial group. In light of this, Sumner and colleagues concluded that "the relationship between LPL activity and insulin resistance in African Americans is different from that observed in Caucasians and MA's." All in all, in whites insulin resistance leads to impairment of LPL and subsequent elevated TG levels, but in blacks TG is cleared from circulation even in the presence of insulin resistance and plasma TG levels do not rise[11, 42].

Why insulin resistance does not appear to adversely affect the lipid profile in blacks is still unknown and currently under investigation. According to Sumner differences in diet do not account for the lower TG and higher HDL levels observed in this racial group. What is known is that, as mentioned before, in blacks, LPL levels are higher and HL levels are lower, and insulin resistance does not appear to impair LPL activity. Such factors lead to unimpaired clearing of TG's from circulation even in the presence of insulin resistance in this population[10]. Moreover, it has been reported that blacks residing in diverse geographic locations have lower visceral adiposity despite increased insulin resistance when compared to whites. This has been confirmed in urban black South African when compared to white South Africans. The reason for this remains paradoxical. Thus, there is also a disassociation between insulin resistance and body fat distribution and composition in blacks, which is consistent with the metabolic and obesity paradox in this racial group[8].

Attempts to Find More Suitable Lipid and Lipoprotein Thresholds

These racial and ethnic differences in circulating TG and HDL concentrations warrant the need to revise the current cutoffs used to classify people as dyslipidemic. This is seen in that the use of one TG value in particular might be leading to the underestimation of the prevalence of the MS in blacks as compared to whites and MA's[44]. According to Sumner et al., "the consequence of under diagnosing insulin resistance and MS in blacks is that the opportunity for intervention to prevent CVD and diabetes in this group could be lost"[11]. Without understanding the relationship between and TG levels in African Americans, there is a risk that physicians may see

low-normal or normal TG levels in African Americans and underdiagnose the presence of CVD and related diseases[11, 42].

In order to ameliorate the failure of the MS to detect insulin resistance in the black population, McLaughlin and colleagues set out to determine the lipid criteria that were most sensitive markers of insulin resistance. The study group observed that the cutoffs that were more predictive of insulin resistance were TG levels of 130 mg/dL or greater and TG to HDL ratio values of 3.0 or greater. It is important to note though that this study was carried out in a primarily white population. The study sample consisted of healthy volunteers classified as overweight or obese which were 87 percent white, nine percent Asian American, three percent Hispanic, and one percent black. The authors concluded that different markers or different cutoffs might best predict insulin resistance in African Americans and even also in Asian Americans[45].

A couple of years later, Sumner et al. also set out to determine whether TG levels or the TG to HDL ratio adequately predicted insulin resistance in overweight and obese African Americans. Using a sample of 125 African Americans from the TARA study, the study group observed that fasting insulin level, BMI, and WC increased across tertiles of insulin resistance but that TG and the TG to HDL ratio did not. However, as in McLaughlin's study, this investigation included a small sample size. It also included a relatively young population of 20 to 50 years old. Still, the researchers concluded that using lipid criteria, specifically TG or the TG to HDL ratio in African Americans to diagnose insulin resistance, will lead to an underestimation of risk for disorders related to insulin resistance. Therefore before recommendations

using these markers of insulin resistance in African Americans they urge testing these criteria in a large population of African Americans over a wide age range[11].

All the above-mentioned observations provide evidence that the criteria for predicting vascular diseases may need to be race/ethnic-specific. Given the prevalence of obesity and diabetes in blacks and the substantial health care costs that are involved in treating vascular disease in these patients, studies designed to clarify the relationship between lipoprotein subpopulation distribution and vascular disease in the black population are needed[31].

Chapter 4: Methods

Survey Data

The data used for this study was obtained from the 1999-2006 National Health and Nutrition Examination Survey (NHANES). All datasets as well as the pertaining documentation are accessible to the general public at *http://www.cdc.gov/nchs /nhanes.htm.* Four survey cycles in NHANES were combined together to increase the survey sample size and produce estimates with greater statistical reliability.

The NHANES is a group of studies designed to assess the health and nutritional status of adults and children in the U.S. The survey combines interviews and physical examinations. NHANES is a major program of the NCHS, CDC and has the responsibility for producing vital and health statistics for the country. The NHANES began in the early 1960's when it was conducted as a series of separate surveys until 1999 when the survey became continuous. Since then the datasets are released in two year increments. The survey examines a nationally representative sample of about 5,000 persons yearly. These persons are located in counties across the country, 15 of which are visited each year. The NHANES interview includes demographic, socioeconomic, dietary, and health-related questions. The examination component consists of medical, dental, and physiological measurements, as well as laboratory tests administered by highly trained medical personnel[46].

NHANES data are not obtained using a simple random sample. Rather, a complex, multistage, probability sampling design is used to select participants representative of the civilian, non-institutionalized U.S. population. The sample does

not include persons residing in nursing homes, members of the armed forces, institutionalized persons, or U.S. nationals living abroad. The sampling procedure for NHANES consists of four stages. In stage one, primary sampling units (PSU's) are selected. These are mostly single counties or, in some cases, groups of contiguous counties with probability proportional to a measure of size (PPS). In the second stage, the PSU's are divided up into segments (generally city blocks or their equivalent). As with each PSU, sample segments are selected with PPS. In the third stage, households within each segment are listed, and a sample is randomly drawn. In geographic areas where the proportion of age, ethnic, or income groups selected for oversampling is high, the probability of selection for those groups is greater than in other areas. In stage four, individuals are chosen to participate in NHANES from a list of all persons residing in selected households. Individuals are drawn at random within designated age-sex-race/ethnicity screening groups. On average, 1.6 persons are selected per household[46].

NHANES samples larger numbers of certain subgroups of particular public health interest. Oversampling is done to increase the reliability and precision of estimates of health status indicators for these population subgroups. Examples of oversampled subgroups include: African Americans, MA's, low income white Americans (beginning in 2000), adolescents aged 12 to19 years, and persons age 60 years or older[46].

Human subject approval was granted for this study by the University of Maryland, College Park Institutional Review Board (2009).

Subjects: Inclusion and Exclusion Criteria

The study population selected for this study consisted of NHW, NHB, and MA male and female adults 20 years old and older, who fasted at least eight but no more than 24 hours, and who attended the morning in-person medical examination at the NHANES mobile examination centers. Pregnant and breastfeeding women, people with nephrotic syndrome (urinary albumin to creatinine ratio ≥ 3000) or those using insulin to treat their diabetes (a likely indication of type I diabetes) since all these are factors that are known to have an effect on blood TG and HDL levels. Lastly, participants of other races and ethnicities were also excluded from the analyses. Individuals with diabetes and women taking exogenous hormones were counted in for descriptive purposes, but were excluded from the analyses.

Variable Selection and Definition

Race/ethnicity was classified according to self-report of race and/or ethnicity. ***Age group*** was classified into subgroups as *20 to 39, 40 to 59,* and *60 years old or older* for descriptive purposes. It was also used as a continuous variable for mean determination as well as for inclusion in the statistical analyses.

Economic status was classified according to the poverty income ratio (PIR), for which the corresponding categories thresholds are *1*, *2*, *3*, *4* and *5*. According to the U.S. Census Bureau, "the income-to-poverty ratios represent the ratio of family or unrelated individual income to their appropriate poverty threshold. Ratios below 1.00 indicate that the income for the respective family or unrelated individual is below the official definition of poverty, while a ratio of 1.00 or greater indicates income above

the poverty level. A ratio of 1.25, for example, indicates that income was 125 percent above the appropriate poverty threshold"[47]. ***Education level*** was divided to three categories: *less than eight years*, *eight to 12 years*, and *more than 12 years*. ***Health insurance coverage*** was classified as *covered* or *not covered*, according to self-report.

Smoking status was defined as a categorical variable indicating *past* smokers, *present* smokers, and individuals who *never* smoked, as well as a continuous variable listing the amount of cigarettes smoked in the past 30 days. *Past* smokers were those who reported that they had smoked at least 100 cigarettes in their lifetime but who did not currently smoke cigarettes.

Alcohol intake was defined as a continuous variable listing the amount of alcoholic beverages consumed in the past 30 days, as well as a categorical variable indicating *0 to 30 drinks*, *31 to 60*, *61 to 100*, and *over 100 drinks per month*. One drink was considered a 12 ounce beer, five ounces of wine, and one and a half ounces of liquor.

Daily physical activity level was defined as a four level categorical variable: *1. sitting during the day and not walking about very much; 2. standing or walking about a lot during the day, but not carrying or lifting things very often; 3. lifting loads or having to climb stairs or hills often*; and *4. doing heavy work or lifting heavy loads*. ***Household physical activity*** was defined as a continuous variable measuring how many minutes in the last 30 days were spent doing housework chores and activities such as raking leaves, mowing the lawn or heavy cleaning that caused light sweating or slight to moderate increase in heart rate or breathing (moderate physical

effort) for at least 10 minutes. For the purpose of description, the ***average household physical activity*** was also categorized as *0 minutes, 1 to 450 minutes, 450 to 900 minutes, 900 to 1,800 minutes*, and *more than 1,800 minutes*, based on the distribution.

Weight, ***height***, and ***WC*** were measured while in the in-person examination using standardized techniques and equipment. WC was measured at the uppermost lateral border of the right ilium. Blood samples were taken to measure blood lipid, lipoprotein, fasting blood glucose, and ***CRP*** concentrations. Urine samples were taken to detect pregnancy and to detect and measure urinary albumin and creatinine levels.

BMI was calculated from weight and height measurements obtained in-person at the mobile examination center and by dividing weight in kilograms by the square of height in meters. *Overweight* and *obesity* were defined as a BMI 25 to 29.9 and 30 kg/m^2 or higher, respectively, according to WHO criteria[48].

Presence of the MS and presence of MS risk factors were defined using the ATP III criteria, where having of three out of five of the following abnormalities indicates the presence of the MS: elevated WC (≥ 102 cm in men, ≥ 88 cm in women), elevated TG (≥ 150 mg/dL, or drug treatment for elevated TG), reduced HDL (< 40 mg/dL in men, < 50 mg/dL in women, or drug treatment for reduced HDL), elevated BP (≥ 130 mm Hg systolic BP or ≥ 85 mm Hg diastolic BP, or drug treatment for elevated BP), and/or elevated fasting glucose (≥ 100 mg/dL, or treatment for elevated glucose). In order to make more fair comparisons with statistics released by other research groups prior to the modification of the FPG

threshold in 2004, we also calculated MS prevalences using the FPG cutoff of 110 mg/dL.

In order to calculate average BP up to four BP readings were measured in the mobile examination center. For people with three to four readings, three BP readings were used and averaged according to the following rules: if only one BP reading was obtained, that reading was considered as the average. If there was more than one BP reading obtained, the first reading was always excluded from the average. If only two BP readings were obtained, the second BP reading was considered as the average. Systolic blood pressure could not be greater than 300 or smaller than diastolic blood pressure. If there was no systolic blood pressure, then the diastolic blood pressure was not considered. Diastolic blood pressure could be zero but if all diastolic readings were zero, the average would be zero, except if there was one diastolic reading of zero and one (or more) with a number above zero. In this case the diastolic reading with zero was not used to calculate the diastolic average. If two out of three readings were zero, the one diastolic reading that was not zero was used to calculate the diastolic average. All BP measurements were obtained after a five minute seated rest and on the right arm. If measurement was not able to be done on the right arm, then the left arm was used for BP measurements.

Presence of CVD was determined by self-report of a physician's diagnosis for the following: heart failure, coronary heart disease, angina pectoris, heart attack, stroke, and HT. The latter was also considered if the measured BP measurements at the mobile examination center were ≥ 140 mm Hg systolic BP or ≥ 90 mm Hg

diastolic BP or if the individual reported taking antihypertensive medication, according to ATP III classification.

Presence of diabetes was determined by self-reported physician's diagnosis of diabetes and/or as undiagnosed diabetes in individuals with blood glucose levels ≥ 126 mg/dL as measured in the mobile examination center.

Menopausal status was defined in women by self-report of cessation of periods and/or of removal of both ovaries.

Use of lipid and lipoprotein medication was assessed by reported intake of HMG-CoA reductase inhibitors (statins), fabric acid derivates, and antihyperlipidemic combinations (statins and fibric acid derivates, and/or niacin or Ezentibe). These drug types were selected for their ability to alter TG and HDL levels in the blood.

Basic Statistical Concerns

Sample Design: Because the sampling design of NHANES is a complex, multistage, probability sampling design rather than a random sampling design, appropriate sampling design parameters were taken into account. In our analysis, *with replacement* (WR) design was specified through all the analysis below to account for the complex survey design.

Weighting: In the NHANES datasets, a sample weight was assigned to each sample person. This weight is a measure of the number of people in the population represented by that sample person in NHANES and reflects the unequal probability of selection, non-response adjustments, and adjustments to independent population controls. When an unequal selection probability is applied, sample weights are used

to produce an unbiased national estimate[46]. For our analysis, eight-year weights from 1999-2006 were constructed by using the four-year weights from 1999-2002, the two year weights from 2003-2004, and the two year weights from 2005-2006 to provide estimates that were representative of the U.S. population.

Variance Estimation: In order to ensure statistical reliability for all survey estimates, variance of estimates (sampling errors) were calculated. For complex sample surveys, general mathematical formulas for variance estimates are usually not available, so variance approximation procedures are required to provide reasonable estimates of the sampling errors. In this study, the common method Taylor Series Linearization procedure was executed for this purpose, which accounts for the complex sample design and the computed design effects.

The detailed descriptive analyses for the variables of interest mentioned above were carried out as follows:

Normality testing (for continuous variables): In order to detect outliers and whether or not log transformations were needed, normality tests were carried out to test for normality of continuous variables using the procedure UNIVARIATE in SAS.

Outlier determination (for continuous variables): Based on the distribution of the continuous variables, the outliers of each variable in each category of gender and race were determined and subsequently removed before performing the analyses.

Descriptive Statistics: For the discrete variables, population characteristics such as counts, prevalences, and the standard errors of prevalences were calculated. For this the CROSSTAB procedure in SUDAAN was executed.

For continuous variables, descriptive statistics such as means (of the non-log transformed variables), standard errors were obtained. For this the DESCRIPT procedure in SUDAAN was executed.

Age-adjusting: As we know, age can confound comparisons when the groups being compared have different age distributions and when age is related to the outcome of interest (e.g. death or the prevalence of disease). Age-adjusting, which uses age standard proportions, is done to roughly remove the confounding effect of age in order to make more relatively fair comparisons. Age-adjusting was used in this analysis for the determination of prevalence of MS and CVD. The DESCRIPT procedure in SUDAAN was used to generate age-adjusted percentages (prevalence rates) and standard errors.

Hypothesis Testing

For the specific events, such as *presence of MS* and *CVD*, Chi square statistics were first used to detect whether or not there were significant differences between unadjusted prevalences of the MS and of CVD across racial/ethnic and gender groups using the CROSSTAB procedure in SUDAAN was executed. The specific contrasts between different levels of racial/ethnic and gender groups were detected by using logistic regression with Bonferroni adjustments for multiple comparisons. For this the RLOGIST procedure in SUDAAN was executed. To compare the age-adjusted prevalences of the MS and CVD, *t*-tests with and without Bonferroni adjustments were carried out across racial/ethnic groups and gender groups.

Similarly, the significant differences across racial/ethnic groups in terms of prevalences of MS risk factors were determined using Chi square tests, also with Bonferroni adjustments for multiple comparisons. For this the CROSSTAB procedure in SUDAAN was executed.

For the continuous variables, the differences between means across racial/ethnic groups were detected by using multiple regression analyses with Bonferroni adjustments for multiple comparisons. The REGRESS procedure in SUDAAN was executed for this purpose.

In addition, the differences between the current prevalences of MS and the updated prevalence of MS using the newly calculated lipid cutoffs were detected by using *t*-tests.

Differences in hypothesis testing were considered significant at the $p \leq 0.05$ level and extremely significant at the $p \leq 0.01$ level for two-sided tests.

Logistic Regression Analysis and Model Selection

Power analysis was performed to determine the adequate sample size needed to detect significant differences across racial/ethnic groups. As mentioned before, variables used in the regression analysis were examined for outliers, which were subsequently removed. The explanatory variables were tested for normality and linearity with the response variable, as well as for homogeneity of residual variances. Additionally, the explanatory variables were tested for interactions and no significant interactions were detected. Lastly, based on the normality test and distributions, we

performed logarithmic transformations for TG, HDL, LDL, and CRP due to their non-normal distributions.

Logistic regression analyses were performed to assess the association of logTG and logHDL with presence of the MS, while adjusting for potential confounders. The logistic regression model was formulated as follows: The vector of observations ***y***, *i.e.* presence of the MS was distributed as a binary distribution, *i.e.* ***y*~*Bi*(1, π)**; the linear predictor was expressed as: **(logit (π) = βx**, where **π** was the vector of probabilities for presence of the MS when all the other parameters **β** were applied. **β** was the vector of all effects that might influence the presence of the MS, and includes the variables *age, gender, race/ethnicity, education , income (PIR), health insurance coverage* (yes/no), *smoking status* (*past*, *present*, *never*), *number of drinks in the past 30 days, daily average physical activity* (categorical variable levels *1-4*), *minutes of household chores activity in the past 30 days, BMI* (*overweight* and *obese*), *WC, average systolic BP, average diastolic BP, logTG, logHDL, log LDL, blood glucose, and log CRP*. **Logit (π) = *ln* (π /1- π)** was the link function for the analysis. Standardized regression coefficients were estimated to enable comparisons across variables with different metric scales. Odds ratios and their upper and lower limits were estimated from the logistic regression analysis and based on the standardized regression coefficients. The RLOGIST procedure in SUDAAN was executed to perform the logistic regression analysis.

Determination of the New Lipid and Lipoprotein Cutoffs

The Receiver Operating Characteristic (ROC) curve is a useful method to determine precise and accurate cutoffs of the predictor variables of interest. The basic theory for ROC curve analysis is as follows:

For each predictor variable of interest (in our case TG and HDL), a series of cutoffs X*i* (*i*=1, 2,…c) are proposed. For each X*i*, frequencies of true positives (TP), false positives (FP), false negatives (FN), and true negatives (TN) are estimated according to the classifications on table 8. In the table, the columns represent the true or actual condition and the rows represent the predicted test results.

Table 8. Sensitivity and Specificity Contingency Table

	TRUE Condition (Outcome)			
		Positive	**Negative**	**Total**
TEST Result (Predicted)	**Positive**	True Positive (**TP)**	False Positive **(FP)**	**(TP + FP)** = all positive tests
	Negative	False Negative **(FN)**	True Negative **(TN)**	**(FN + TN)** = all negative tests
	Total	**(TP + FN)** = all true positives	**(FP + TN)** = all true negatives	***N*** (total sample size)

Using the information on this table, estimates of sensitivity and specificity and related statistics were calculated using the corresponding formulas:

Sensitivity (SN) = TP / [TP + FN]
Ability of the test to correctly identify those cases with the condition.

Specificity (SP) = TN / [TN + TN]

Ability of the test to correctly identify those cases that do not have the condition.

Positive Predictive Value (PPV) = TP/ TP + FP
The proportion of cases that have the condition among those classified without the condition.

Negative Predictive Value (NVP) = TN/ FN + TN
The proportion of cases that do not have the condition among those classified without the condition.

Youden Index = SN + SP – 1
Overall measure of test accuracy (+1 is perfect prediction).

Total Accuracy (TA) = TP + TN/ N
The proportion of cases whose tests accurately predict the true outcome.

Matthews Correlation Coefficient (MCC) = TPTN – FPFN/ √(TP + FN)(TP + FP)(TN + FP)(TN + FN)
Another overall measure of test accuracy (+1 is perfect prediction).

A ROC curve is drawn by plotting sensitivity versus specificity for each cutoff (see Appendix B: Figures 4, 8 & 12). Usually, the ultimate optimal cutoff is determined by maximizing both sensitivity and specificity, which is equivalent to maximizing the Youden Index. The better the classification, the closer the curve will be to the upper left corner of the plot. A Youden Index value of +1 indicates perfect prediction as it achieves both 100 percent sensitivity and 100 percent specificity. A Youden Index value of 0.5 indicates that the test is not better than random classification. Calculations of the Total Accuracy (TA) and Matthew Correlation Coefficient (MCC) can also be used to determine the optimal cutoff points.

For our analysis, the ROC curve method was used to determine the most sensitive and specific cutoff values of TG and HDL to detect the presence of the MS for all three racial/ethnic groups. In the instance of HDL, ROC curves were drawn

separately for males and females due to the fact that the current recommendations include distinct values for both genders.

The cutoffs (*Xi*) for TG and HDL were calculated according to the following formula: cutoff = minimum value of TG or HDL + (I – 1) (maximum value of TG or HDL – minimum value of TG or HDL)/x, where x equaled 300 or 50, and I was an integer from one to x + 1. The maximum values used were the relative values based on distribution rather than the exact maximums. For TG this maximum value was 300 mg/dL and for HDL, 110 and 120 mg/dL were considered the maximum values for males and females, respectively. The minimum values used were the exact minimum values. To determine the optimum cutoff value, 300 was used as the denominator (x), while 50 was used as the denominator (x) when drawing the ROC curve. For each cutoff, sensitivity and specificity were calculated as well as the Youden Index, which was used to determine the optimum cutoffs for TG and HDL. The ROC curves of calculated sensitivity versus specificity were drawn under *R* environment.

For purposes of cross-examination, the cutoffs were calculated using the exact values of TG and HDL. For this, logistic regression analyses were performed. Also for cross examination, sensitivity, specificity, Youden Index, TA and MCC were calculated and plotted and used to confirm the cutoffs previously determined. Here the maximum value of the Youden Index was utilized to determine the optimal cutoff points for TG and HDL in each group. The plots of sensitivity and specificity, the Youden Index, TA, and MCC were plotted using SAS.

All statistical analyses and plots were calculated and conducted using SAS v9.2, SUDAAN (v10.0.1), and the *R* v2.10.1 software program.

Chapter 5: Results

The study population consisted of 6,306 male (51.41%) and female (48.59%) adults ages 20 and over. Of these 23.50 percent were MA (52.63% male, 47.37% female), 55.96 percent were NHW (51.83% male, 48.17% female), and 20.54 were NHB (48.88% male, 51.12% female) (Table 9).

Population Characteristics: Means of Socioeconomic and Lifestyle Factors

The mean age of the population was 46.41 ± 0.41 years. On average, NHW's (47.89 ± 0.46) were significantly older than MA's (38.81 ± 0.55) and NHB's (42.98 ± 0.48). The average population PIR was 3.12 ± 0.05 meaning that the average PIR was 312 percent over the national poverty line. MA's had the lowest average PIR (2.05 ± 0.07), followed by NHB's (2.46 ± 0.07), and lastly by NHW's (3.31 ± 0.06), who had the highest average PIR scores. All groups were significantly different from each other in terms of PIR. The average number of cigarettes smoked in the past 30 days for smokers was 2.65 ± 0.55. There were no significant differences in the average number of cigarettes smoked across groups. The average number of alcoholic beverages drunk in the past 30 days was 19.75 ± 0.67. NHW's drank significantly more alcoholic beverages on average per month (20.02 ± 0.83) as compared to MA's (17.96 ± 1.26) and NHB's (18.74 ± 1.99) (Table 10).

In terms of minutes of household physical activities performed in the past 30 days, the average was 589.88 minutes, with NHW's (658.97 ± 39.22) being

significantly more active in housekeeping activities than MA's (316.69 ± 28.52) and NHB's (290.71 ± 24.81), who were the least active in this category (Table 10).

Population Characteristics: Prevalences of Socioeconomic and Lifestyle Factors

In terms of education, the highest prevalence fell upon the *more than 12 years* education group (54.87% ± 1.26), with NHW's having the highest prevalence in this education subgroup (58.82% ± 1.53) versus MA's (25.68% ± 1.61) and NHB's (48.01% ± 1.73). MA's had the highest prevalence of individuals with *less than 12 years* education (53.14 ± 1.73) compared to NHW's (12.76% ± 0.93) and NHB's (28.14% ± 1.80). NHW's also had a higher prevalence (86.67% ± 0.99) of health insurance coverage as compared to MA's (50.89% ± 2.47) and NHB's (75.86% ± 1.87) (Table 13).

NHW's had the highest prevalence of *past* smokers (48.07 ± 1.43), NHB's had the highest prevalence of *present* smokers (62.99 ± 2.32), and MA's had the highest prevalence of people who had *never* smoked (10.61 ± 2.13). When it came to drinking status all groups had a prevalence of roughly 80 percent of individuals who drank from *0 to 30* alcoholic beverages in the past 30 days (Table 13).

On average, all groups had the highest number of individuals whose *daily physical activity level* was *(2) standing or walking about a lot during the day, but not carrying or lifting things very often* (all groups prevalence 49.89% ± 0.92). NHB's in particular had 54.15% ± 1.58 of its population in this group compared to MA's (56.15% ± 1.43) and NHW's (48.64% ± 1.01) (Table 13).

The prevalence of all menopausal women in the sample was 27.95 percent ± 1.30. NHW women had the highest prevalence of menopausal women (30.00% ± 1.63), followed by NHB women (21.75% ± 2.36), and lastly by MA women (15.95% ± 2.30) (Table 15).

Means of Metabolic Syndrome Risk Factors

The total population's mean BMI was 28.35 ± 0.11 with NHB's being significantly more overweight than MA's and NHW's (29.86 ± 0.22 vs. 28.48 ± 0.16 MA and 28.12 ± 0.14 NHW) (Table 9). In terms of WC, NHW men had the highest mean WC (101.73 ± 0.45) compared to MA men (96.88 ± 0.76) and NHB men (95.57 ± 0.77) (Table 11). On the other hand, NHW women had significantly lower mean WC (92.95 ± 0.50) compared to MA women (94.94 ± 0.69) and NHB women (99.04 ± 0.64), who had the highest mean WC among women (Table 12).

As was expected, NHB's had significantly higher mean HDL levels (55.04 ± 0.47) compared to MA's (49.39 ± 0.43) and NHW's (52.94 ± 0.37). Also as expected, NHB's had significantly lower mean TG levels (105.91 ± 2.22) compared to MA's (149.65 ± 4.62) and NHW's (144.09 ± 2.01). NHB's had significantly higher mean systolic BP (126.04 ± 0.61) and mean diastolic BP (73.45 ± 0.36) than MA's (119.02 ± 0.68 systolic, 70.52 ± 0.40 diastolic) and NHW's (122.15 ± 0.39 systolic, 71.60 ± 0.32 diastolic). NHB's had similar mean FPG levels (100.15 ± 0.75) than NHW's (100.29 ± 0.51) but MA had significantly higher mean FPG levels (102.13 ± 0.98) compared to NHW's and NHB's. NHB's also had a significantly lower mean TG to HDL ratio (2.21 ± 0.06) compared to MA's (3.52 ± 0.16) and NHW's (3.22 ± 0.06).

Lastly, NHB's had significantly higher mean CRP (0.51 ± 0.03) as compared to MA's (0.42 ± 0.02) and NHW's (0.38 ± 0.01) (Table 10).

Prevalences of Metabolic Syndrome Risk Factors

NHB's had the lowest percent of overweight individuals compared to MA's and NHW's (28.40% ± 1.34 vs. 40.59% ± 1.70 MA and 34.11% ± 1.00 NHW), but had the highest percent of obese individuals (44.28% ± 1.53 vs. 32.37% ± 1.37 MA and 31.26% ± 0.96 NHW). In terms of elevated WC, NHB's had the highest prevalence (54.62% ± 1.61) although compared to NHW's (52.50% ± 1.17) these prevalences were not significantly different. MA's had a significantly lower elevated WC prevalence (48.22% ± 2.05) compared to NHB's but not to NHW's (Table 17).

As it is expected and as the group means have already indicated, NHB's had a significant lower prevalence of low HDL levels (30.54% ± 1.46) compared to MA's (39.68% ± 1.78) and NHW's (39.43% ± 1.09). NHB's also had a significantly lower prevalence of elevated TG levels (22.30% ± 1.24) compared to MA's (38.36% ± 1.95) and NHW's (40.64 ± 1.09) (Table 17).

NHB's had a significantly higher prevalence of HT (49.38% ± 1.59) compared to MA's (26.94% ± 1.70) and NHW's (42.65% ± 1.03), as well as a significant higher prevalence of diabetes (12.09% ± 0.90) compared to NHW's (8.99% ± 0.56), but not compared to MA's (10.39% ± 1.21). In terms of elevated FPG, MA's had a significantly higher prevalence as compared to NHW's (40.73 ± 1.99), but not as compared to NHW's (37.59 ± 1.40). When the threshold for FPG of 110 mg/dL was used to calculate elevated FPG prevalence, no significant differences

were observed between all racial/ethnic groups (17.11% ± 1.44 MA, 15.72% ± 0.76 NHW and 15.31% ± 1.07 NHB). It is important to note that all elevated FPG prevalences were more than doubled when using the current FPG cutoff of 100 mg/dL versus the previously established FPG cutoff of 110 mg/dL (Table 17).

Prevalence of the Metabolic Syndrome

The age-adjusted prevalence of the MS for the total population was 38.14 percent (± 0.87), with the age-adjusted prevalence being significantly higher in males (40.51% ± 1.06) than in females (35.73% ± 1.15). The age-adjusted prevalence of the MS was higher among MA's (41.03% ± 1.48), followed by NHW's (38.51% ± 1.09) and lastly by NHB's (34.49% ± 1.11), who had the lowest prevalence of the MS in agreement with the reported lower MS prevalence rates among NHB's. Among men, NHW men had the highest age-adjusted MS prevalence (42.35% ± 1.21), followed by MA men (37.96% ± 2.00), and lastly by NHB men (29.08% ± 1.95). All the MS prevalence estimates among men were significantly different. The pattern of MS prevalence was different for women with MA women (43.98% ± 1.74) having the greatest prevalence, followed by NHB women (38.85% ± 1.50), and last by NHW women (34.64% ± 1.45). All the MS prevalence estimates among women were significantly different as well (Table 19).

Using the previous FPG cutoff of 110 mg/dL the prevalences of the MS were markedly lower across all groups. Using this cutoff the age-adjusted prevalence of the MS for the total population was 32.29 percent (± 0.73), with the age-adjusted prevalence being significantly higher in males (33.59% ± 1.05) than in females

(30.99% ± 1.09). The age-adjusted prevalence of the MS was higher among MA's (34.38% ± 1.58), followed by NHW's (32.75% ± 0.89) and lastly by NHB's (28.38% ± 1.17), who had the lowest prevalence of the MS in agreement with the reported lower MS prevalence rates among NHB's. Among men, NHW men had the highest age-adjusted MS prevalence (35.07% ± 1.22), followed my MA men (31.41% ± 1.99), and lastly by NHB men (24.24% ± 1.76). All the MS prevalence estimates among men were significantly different. The pattern of MS prevalence was different for women with MA women (37.22% ± 1.80) having the greatest prevalence, followed by NHB women (31.77% ± 1.50), and last by NHW women (30.43% ± 1.38). Like for males, all the MS prevalence estimates among women were significantly different. All in all the total group MS prevalence increased by an average of five percentage points when utilizing the current FPG cutoff of 100 mg/dL (38.14% ± 0.87) as compared to using the previous cutoff point of 110 mg/dL (32.29% ± 0.73) (Table 20).

Prevalence of Cardiovascular Disease

The age-adjusted CVD prevalence for the entire study population was 38.82 percent (± 0.78), with males having a significantly higher CVD age-adjusted prevalence (39.84% ± 1.05) than women (37.66% ± 1.08). In accordance to previously reported CVD age-adjusted prevalence rates, NHB's had a significantly higher prevalence of CVD (46.71% ± 1.14) compared to MA's (33.37% ± 1.38) and NHW's (38.45% ± 0.89). NHB men had significantly higher age-adjusted CVD prevalences (44.78% ± 2.13) as compared to their MA (31.90% ± 1.68) and NHW

(40.29% ± 1.20) counterparts. The same was true for NHB women (48.08% ± 1.91 vs. 34.65% ± 2.05 MA and 36.48% ± 1.29 NHW). NHB (44.78% ± 2.13) and MA (31.90% ± 1.68) men had significantly lower age-adjusted CVD prevalences than NHB (48.08% ± 1.91) and MA women (34.65% ± 2.05), respectively, but NHW men had significantly a higher age-adjusted CVD prevalence (40.29% ± 1.20) compared to NHW women (36.48% ± 1.29) (Table 21).

Logistic Regression Analysis

When the logistic regression model was fit we observed that the variables age (p= 0.0110), gender (p=0), smoking status (p=0.0429), BMI (p=0.0726), WC (p=0.0002), systolic BP (p=0.0001), FPG (p=0), logTG (p=0), logHDL (p=0), and logLDL (p=0) were significant predictors of MS. On the other hand, race/ethnicity, economic status (PIR), education, health insurance coverage, smoking status, daily activity level, household physical activity, diastolic BP, and log CRP were not significant predictors of the MS. The R^2 value that resulted from the model equaled 0.472761, hence approximately 47 percent of the variability in MS was accounted for by the joint predictive ability of the significant model variables (Table 22).

The parameter estimators (β coefficients) for the significant variables that resulted from the logistic regression analysis were as follows: -1.43 ± 0.31 for male (gender),0.02 ± 0.01 for age, 0.09 ± 0.02 for WC, 0.04 ± 0.01 for systolic BP, 0.11 ± 0.01 for FPG, 2.07 ± 0.22 for logTG, -2.64 ± 0.47 for logHDL, and -1.62 ± 0.28 for logLDL. The estimators for race/ethnicity, education, smoking status, health insurance coverage, economic status (PIR), daily activity level, household activity,

alcohol intake, BMI, diastolic blood pressure, and logCRP were not significant (Table 23).

When examining the odds ratio that resulted from the logistic regression analysis we can appreciate that being male significantly decreased the odds of having the MS by 76 percent as compared to being female. In terms of race/ethnicity, MA's had 54 percent higher odds of having the MS as compared to NHB's and NHW's had 22 percent increased odds of having the MS as compared to NHB's, although these trends were not significant. On the other hand, the odds ratios for race/ethnicity, education, smoking status, health insurance coverage, and daily activity level were not significant among the categorical variables included in the model (Table 24).

When examining the odds ratios for the continuous variables we can observe that for a one unit increase in age, the odds of having the MS increased two percent. For a one unit increase in WC, there was and nine percent increase in the odds of having the MS. For every one unit increase in systolic blood pressure the odds of having the MS increased four percent. For every one unit increase in FPG, the odds of having the MS increased ten percent. In terms of TG, for every one unit increase in logTG, the odds of having the MS increased 7.89 times. Conversely, for every one unit increase in logHDL, the odds of having the MS decreased 93 percent. Interestingly, for every one unit increase in logLDL, the odds of having the MS decreased by 80 percent. Meanwhile, the odds ratios for economic status (PIR), household activity, alcohol intake, BMI, diastolic BP, and logCRP were not significant among the continuous variables included in the model (Table 24).

New TG and HDL Cutoff Determination

After drawing ROC curves and calculating the Youden Index for TG by racial/ethnic group we obtained the following optimal TG cutoffs: 137 mg/dL for MA's, 140 mg/dL for NHW's, and 110 mg/dL for NHB's (Figures 4-7).

When conducting the TG cutoff calculations using the FPG cutoff of 110 mg/dL we obtained the following optimal TG cutoffs: 140 mg/dL for MA's, 149 mg/dL for NHW's, and 121 mg/dL for NHB's.

ROC curves were drawn and the Youden Index calculated for HDL by race/ethnicity and by gender. The calculated optimal HDL cutoff values for males were as follows: 40 mg/dL for MA's, 40 mg/dL for NHW's, and 42 mg/dL for NHB's (Figures 8-11). The same was done for HDL cutoffs in females and the following resulted: 50 mg/dL for MA's, 50 mg/dL for NHW's, and 50 mg/dL for NHB's (Figures 12-15).

When conducting the HDL cutoff calculations for males using the FPG cutoff of 110 mg/dL we obtained the following: 40 mg/dL for MA's, 39 mg/dL for NHW's, and 40 mg/dL for NHB's. The same was done for HDL cutoffs in females and the following resulted: 50.5 mg/dL for MA's, 49.5 mg/dL for NHW's, and 49.5 mg/dL for NHB's.

As we can observe new TG values were suggested for all racial/ethnic groups. In particular, looking at the suggested values of 137mg/dL for MA's and 110mg/dL for NHB's, we can see that they stand in stark contrast to the current universal cutoff of 150 mg/dL. In terms of HDL, the results obtained for all racial/ethnic and gender

groups were close enough to the currently established cutoff values of 40mg/dL for males and 50mg/dL for females.

Prevalence of the Metabolic Syndrome Based on the Newly Determined TG Cutoffs

Using the proposed new cutoffs of 137 mg/dL for MA's, 140 mg/dL for NHW's, and 110 mg/dL for NHB's we arrived at the following MS prevalence estimates. The new age-adjusted prevalence would be 39.83% ± 0.86 versus the current age-adjusted prevalence of 38.14% ± 0.87 ($p < 0.01$). For MA's the new age-adjusted prevalence would be 42.19% ± 1.49 versus the current age-adjusted prevalence of 41.03% ± 1.48. The new age-adjusted prevalence for NHW's would be 39.86% ± 1.06 versus the current age-adjusted prevalence of 38.51% ± 1.09. For NHB's the new age-adjusted MS prevalence would be 38.23% ± 1.08 in contrast to the current age-adjusted prevalence of 34.49% ± 1.11 ($p < 0.01$). The age-adjusted MS prevalences calculated for the new cutoffs remained significantly different across all racial/ethnic groups (Table 25).

For males the new age-adjusted prevalence would be 41.86% ± 1.05 in contrast to the current age-adjusted prevalence of 40.51% ± 1.06 ($p < 0.01$). For MA males the new age-adjusted MS prevalence would be 38.63% ± 1.97 versus the current age-adjusted prevalence of 37.96% ± 2.00. For NHW males the new age-adjusted MS prevalence would be 43.55% ± 1.20 versus the current age-adjusted prevalence of 42.35% ± 1.21 ($p < 0.01$). For NHB males the new age-adjusted MS prevalence would be 31.88% ± 1.98 in contrast to the current age-adjusted prevalence

of 29.08% ± 1.95 ($p < 0.01$). The age-adjusted prevalences remained significantly different across all racial/ethnic groups (Table 25).

For females the new age-adjusted prevalence would be 37.80% ± 1.18 versus the current age-adjusted prevalence of 35.73% ± 1.15 ($p < 0.01$). For MA females the new age-adjusted prevalence would be 45.69% ± 1.86 versus the current age-adjusted prevalence of 43.98% ± 1.74. For NHW females the new age-adjusted prevalence would be 36.35% ± 1.45 versus the current age-adjusted prevalence of 34.64% ± 1.45. For NHB females the new age-adjusted MS prevalence would be 43.38% ± 1.57 in contrast to the current age-adjusted prevalence of 38.85% ± 1.50 ($p < 0.01$). Here also the age-adjusted prevalences remain significantly different across all racial/ethnic groups (Table 25).

For descriptive purposes the same statistics were calculated utilizing the FPG cutoff of 110 mg/dL for the determination of MS prevalence. These results are presented in Table 26.

Chapter 6: Discussion and Conclusions

It has been observed over the years that blacks in the country have higher rates of CVD, diabetes, insulin resistance, HT, and obesity as compared to whites[30, 49-51]. Paradoxically, in spite of this they have lower prevalence rates of the MS, which purpose essentially is to help detect and prevent these same conditions. It is argued that this is due to the fact that blacks have lower TG levels and higher HDL levels compared to other racial/ethnic groups, which means that they do not as easily meet the lipid and lipoprotein criteria proposed to detect the MS. The goal of this study was to find new TG and HDL cutoffs that would accommodate these lipid and lipoprotein variations in NHB's and to further support that definitions for the MS should reflect these kinds of variations across racial/ethnic groups.

In our study we were able to see the same expected patterns of risk factors that have been identified in the black populations in the country through various surveys, among these, earlier versions of NHANES. As this analysis of NHANES data shows, NHB's smoke more and perform less household physical activity as compared to NHW's and MA's. Furthermore, they have lower average incomes, education, and health insurance coverage when compared to NHW's. NHB's are less overweight but more obese than NHW's and MA's. NHW men have lower WC as compared NHW's, but NHB women have the highest WC among the three racial/ethnic groups. As expected, NHB's have the lowest average serum TG levels as well as highest average serum HDL levels. They also have the lowest prevalences of elevated TG and of low HDL levels. What is more, concurrent with the literature, they have higher BP levels

and a higher HT prevalence when compared to MA's and to NHW's. In terms of diabetes they also have a higher prevalence when compared NHW's. All in all, NHB's have the highest prevalence of CVD and CVD risk factors but the lowest prevalence of MS of all the racial and ethnic groups. It is exactly this scenario that calls into question the validity of the current criteria for the detection of the MS syndrome in blacks.

Unadjusted and age-adjusted prevalences of the MS based on NHANES III (1988-1994) were 21.8 percent and 23.7 percent, respectively. MA's had the highest age-adjusted prevalence of the MS (31.9%), followed by NHW's (23.8%) and NHB's (21.6%)[30]. Our results based on NHANES 1999-2006 and using the previous FPG cutoff of 110 mg/dL (in order to make fair comparisons), indicate that the most current unadjusted and age-adjusted MS prevalence have since then increased to 32.86 percent and 32.29 percent, respectively. Using this FPG cutoff, among MA's the age-adjusted prevalence has increased to 34.38 percent, among NHW's to 32.75 percent, and among NHB's to 28.38 percent. The greater prevalences likely reflect the ever-increasing overweight and obesity rates in the country as well as the population growth that has taken place in the time period from the late 1980's to the late 2000's[30]. Utilizing the newly proposed FPG cutoff of 100 mg/dL, the unadjusted and age-adjusted prevalences increase an average of approximately five percentage points up to 38.80 percent and 38.14 percent, respectively. Using this FPG cutoff, among MA's the age-adjusted prevalence has increased to 41.03 percent, among NHW's to 38.51 percent, and among NHB's to 34.49 percent. Despite variations and

increases in the prevalences, it is always clearly observed that NHB's have the lowest MS syndrome prevalence across all racial/ethnic groups.

The relationships between serum lipids and lipoproteins and insulin resistance, the major underlying driving factor of the MS, have shown to be associated to different degrees in blacks as compared to whites and people of other races/ethnicities but the reasons are controversial and currently under investigation. Some researchers speculate that the reasons of the disconnect between lipid and lipoprotein levels and CVD levels in blacks is probably be due to the fact that in blacks the presence of HDL seem to be 'dysfunctional'. In other words, it is not unlikely that blacks are resistant to the cardioprotective effects of HDL and that the anti-inflammatory and antioxidant effects of HDL in blacks are impaired. It is also a possibility that in addition to having lowered TG levels, blacks have larger LDL particle sizes, which are more buoyant and less atherogenic when compared to whites[29]. In our study we observed that, in agreement with this statement, with increasing logLDL, the odds of having the MS in fact decreased.

Another nonconventional cause for the disassociation between risk factors and CVD in blacks could be the role of proinflammatory cytokines, which are primarily derived from adipose tissue and adipocytes. These peptides include adiponectin, tumor necrosis factor-alpha, resistin, leptin, interlukin-6, and CRP[8, 39, 52, 53]. Circulating CRP concentrations tend to be higher in adults with the MS, and increased CRP is an independent risk factor for type 2 diabetes and CVD[52]. We should note that our results show that NHB's have significantly higher CRP levels as

compared to MA's and NHW's but in contrast with the current literature, our logistic regression analysis showed that CRP was not a significant predictor of the MS.

Serum adiponectin has been found to be associated with improved insulin sensitivity and to be predictive the MS. Serum adiponectin levels are decreased in the presence of obesity and insulin resistance in blacks and in whites. On the other hand, tumor necrosis factor-alpha and interlukin-6 levels are increased in obese individuals. Both these cytokines have been associated with increased diabetes rates. What is more, blacks have greater oxidative stress as measured by F2 isoprostane levels when compared to whites. Here, either the generation of free oxygen radicals are higher or their clearance is impaired, or both, compared to whites. These disturbances in oxidative stress could play a greater role than that conferred by the protective effects of the observed levels of TG and HDL in the development of atherosclerosis in blacks[8].

Our study results indicated that being female as well as being MA, increases the odds of developing the MS. MS odds also increased with increasing age, WC, systolic blood pressure, logTG, and blood glucose. It is important to note that with every unit increase in logTG the odds of having the MS increased nearly eight-fold. This serves to support the fact that having TG as part of the MS criteria is of great value. Some research groups argue that the components of the ATP III MS criteria should be weighted differently to predict CVD in all racial/ethnic groups[8]. If this is the case, and in light of our findings, TG's predictive ability should not be weighed too lightly. What is more, better than weighing the MS criteria differently could be

providing race/ethnic-specific TG and HDL cutoffs much like the IDF has provided specific WC cutoffs for different racial groups (Table 5).

Other modifications to the criteria for the MS in blacks could also involve using BP as a base requirement for detection of the syndrome, much like central obesity is for the IDF definition and insulin resistance is for the WHO and EGIR definitions (Tables 5-7). This is due to the well established fact that blacks have higher prevalence of HT as well as suffer more severe consequences from it[9].

The main goal of our study was precisely to illustrate if different TG and HDL cutoffs should be instituted in the ATP III definition of the MS. We succeeded in finding that the TG level most indicative of the MS in NHB's is 40 points lower than that currently suggested by the ATP III criteria of 150 mg/dL. In this sense, our results further support to our hypothesis that lower TG lipid cutoffs would accomplish exactly this. We also observed that that for MA' a more predictive cutoff is 13 points lower that the currently proposed TG cutoff. Surprisingly, we also observed a new TG cutoff for NHW's that is 10 points lower than the currently proposed cutoff. An interesting observation is that when using the previously established FPG cutoff of 110 mg/dL the TG cut off for all groups was about 10 points higher, in which case the currently established TG cutoff for NHW's would prove to be adequate. This points to the fact that when the FPG threshold levels were decreased by 10 points, perhaps this should have been followed by a concurrent 10 point decrease in the TG threshold.

These differences in lipid threshold levels are enough to significantly increase the prevalence of the MS not only for NHB's, but also for the study population as a whole. Using our newly proposed TG cutoffs we calculated the total population's

unadjusted and age-adjusted MS prevalences and observed that even though this prevalence increased only by 1.69 percentage points, this increase was enough to be statistically significant. Furthermore, using the new TG of 110mg/dL for NHB's the age-adjusted prevalence of the MS for NHB's increased by a very significant 3.74 percentage points. The same pattern was observed for MA and for NHW men and women in that the MS prevalences increased modestly but nonetheless significantly with the newly proposed TG cutoffs.

In addition to revealing new cutoffs for TG, we set out to find new HDL cutoffs for NHB's. Unfortunately, we were not able to identify HDL levels that were convincingly different than the 40 mg/dL currently recommended for detecting MS in men and the 50 mg/dL in women. The same was observed for MA's and NHW's. Nonetheless, these results support the fact that the current ATP III HDL cutoff criteria are set at adequate levels to detect the MS in NHB, NHW, and MA men and women. In relation to our research hypothesis, these results fail to support the premise that higher HDL cutoffs would be more adequate to detect MS in NHB's.

In summary, approximately 38 percent of U.S. adults have the MS as defined by ATP III. NHB's have the lowest prevalence of the MS despite of the fact that they have the highest CVD prevalence in the country. This disconnect is likely due in part to racial and ethnic differences in lipid and lipoprotein metabolism. In light of this we set out to find more accurate and precise TG and HDL cutoffs for the prediction of CVD and diabetes risk. Our results confirm that a "one-size fits all" definition for the MS is not equally useful among racial and ethnic populations. With the increases in obesity and the decrease in physical activity as well as the increases in the number of

elderly people expected in the future, it is imperative that physicians and patients are provided with the appropriate and effective tools to counteract the impending increased risks of chronic disease.

Importance and Benefits of this Study

In light of the increasing obesity, diabetes, and CVD epidemic the country is facing and will increasingly continue to face, we anticipate that the results of this study serves to provide more adequate lipid and lipoprotein parameters for the detection of MS among blacks. The definition of the MS was developed as an instrument to detect insulin resistance and risk for diabetes and CVD with the expectation that physicians and patients may be warned in time to prevent these often deadly chronic diseases. However, as the current research literature states, the current definition of the MS is only an adequate tool for the identification of the MS in some segments of the population but not in others, and particularly among blacks.

It was the purpose of our study to use data representative of the U.S. population to find lipid and lipoprotein parameters, particularly TG and HDL, that are indicative of the presence of the MS among U.S. blacks. Through our findings we aim to shed light on the fact that the current criteria used to detect metabolic abnormalities in this group should be revisited and revised, which may help physicians of African American patients to more effectively screen for risk of diabetes and CVD. Furthermore, we expect that researchers and epidemiologists will find this information valuable as they consider the present utility of the MS, and as

they work to make it a more effective instrument for the detection and prevention of chronic disease.

Appendices

Appendix A: Tables

Table 9. Study sample distribution. U.S. adults ages ≥ 20 years old, NHANES 1999-2006

	All races/ethnicities (% (n))	Mexican American (% (n))	Non-Hispanic whites (% (n))	Non-Hispanic blacks (% (n))
Both genders	6306	23.50 (1482)	55.96 (3529)	20.54 (1295)
Males	51.41 (3242)	52.63 (780)	51.83 (1829)	48.88 (633)
Females	48.59 (3064)	47.37 (702)	48.17 (1700)	51.12 (662)

Table 10. Population characteristics (means ± S.E)

	All races/ ethnicities (mean ± S.E., CI))	Mexican Americans (mean ± S.E., (CI))	Non-Hispanic whites (mean ± S.E., (CI))	Non-Hispanic blacks (mean ± S.E., (CI))
Age	46.41 ± 0.41 (45.79-47.43)	38.81 ± 0.55† (37.71-39.91)	47.89 ± 0.46‡ (46.98-48.81)	42.98 ± 0.48§ (42.02-43.95)
Economic status (PIR)	3.12 ± 0.05 (3.03-3.21)	2.05 ± 0.07† (1.91-2.20)	3.31 ± 0.06‡ (3.20-3.43)	2.46 ± 0.07§ (2.33-2.59)
Number cigarettes per month	2.65 ± 0.55 (1.55-3.74)	2.31 ± 0.42 (1.46-3.16)	2.72 ± 0.68 (1.36-4.07)	2.40 ± 0.59 (1.22-3.58)
Number of drinks per month	19.75 ± 0.67 (18.41-21.08)	17.96 ± 1.26 (15.43-20.48)	20.02 ± 0.83‡ (18.37-21.68)	18.74 ± 1.99 (14.76-22.73)
Minutes household activity per month	589.88 ± 34.17 (521.50-658.26)	316.69 ± 28.52 (259.62-373.76)	658.97 ± 39.22‡ (580.50-737.45)	290.71 ± 24.81§ (241.06-340.36)
BMI ***(kg/m^2)***	28.35 ± 0.11 (28.12-28.58)	28.48 ± 0.16† (28.15-28.81)	28.12 ± 0.14 (27.84-28.40)	29.86 ± 0.22§ (29.43-30.29)
Total cholesterol (mg/dL)	199.61 ± 0.89 (197.84-201.39)	195.95 ± 1.34† (193.26-198.64)	201.06 ± 1.01‡ (199.04-203.08)	191.76 ± 1.06§ (189.65-193.87)
LDL cholesterol (mg/dL)	119.10 ± 0.77 (117.56-120.63)	117.67 ± 1.15 (115.37-119.97)	119.72 ± 0.88 (117.96-121.48)	115.71 ± 1.14§ (113.43-117.99)
HDL cholesterol (mg/dL)	2.89 ± 0.30 (52.29-53.49)	49.39 ± 0.43† (48.53-50.25)	52.94 ± 0.37‡ (52.20-53.69)	55.04 ± 0.47§ (54.10-55.98)
Triglycerides (mg/dL)	140.31 ± 1.77 (136.77-143.85)	149.65 ± 4.62† (140.40-158.90)	144.09 ± 2.01 (140.07-148.12)	105.91 ± 2.22§ (101.46-110.36)
Systolic blood pressure	122.34 ± 0.36 (121.63-123.05)	119.02 ± 0.68† (117.66-120.38)	122.15 ± 0.39‡ (121.37-122.94)	126.04 ± 0.61§ (124.83-127.26)
Diastolic blood pressure	71.72 ± 0.27 (71.17-72.27)	70.52 ± 0.40† (69.72-71.31)	71.60 ± 0.32‡ (70.96-72.24)	73.45 ± 0.36§ (72.72-74.17)
Fasting glucose (mg/dL)	100.58 ± 0.45 (99.69-101.47)	102.13 ± 0.98† (102.13-106.07)	100.29 ± 0.51‡ (99.27-101.31)	100.15 ± 0.75 (98.65-101.65)
CRP	0.40 ± 0.01 (0.38-0.42)	0.42 ± 0.02 (0.37-0.46)	0.38 ± 0.01 (0.36-0.40)	0.51 ± 0.03§ (0.46-0.57)
TG:HDL	3.13 ± 0.05 (3.02-3.23)	3.52 ± 0.16† (3.20-3.83)	3.22 ± 0.06 (3.09-3.34)	2.21 ± 0.06§ (2.09-2.32)

† Statistically significant difference between MA and NHB
‡ Statistically significant difference between MA and NHW
§ Statistically significant difference between NHW and NHB

Table 11. Population characteristics (means ± S.E) – males

	All races/ ethnicities (mean ± S.E. (CI))	Mexican Americans (mean ± S.E., (CI))	Non-Hispanic whites (mean ± S.E., (CI))	Non-Hispanic blacks (mean ± S.E., (CI))
Age	45.37 ± 0.46 (44.44-46.29)	37.57 ± 0.56† (36.46-38.68)	46.70 ± 0.53‡ (45.65-47.75)	42.05 ± 0.66§ (40.76-43.37)
Economic status (PIR)	3.22 ± 0.05 (3.12-3.32)	2.07 ± 0.08† (1.91-2.23)	3.44 ± 0.07‡ (3.31-3.57)	2.57 ± 0.08§ (2.42-2.73)
Number cigarettes per month	2.74 ± 0.64 (1.46-4.02)	3.44 ± 0.76 (1.91-4.96)	2.50 ± 0.79 (0.92-4.07)	4.00 ± 1.13 (1.75-6.26)
Number drinks per month	27.90 ± 1.10 (25.70-30.10)	24.17 ± 1.66 (20.86-27.49)	29.42 ± 1.39 (25.63-31.21)	27.19 ± 3.20 (20.79-33.59)
Minutes household activity per month	656.92 ± 41.26 (574.36-739.48)	304.75 ± 31.21 (242.29-367.21)	748.77 ± 47.93‡ (652.87-844.67)	262.43 ± 27.15§ (208.11-316.75)
BMI (kg/m^2)	28.29 ± 0.13 (28.02-28.56)	27.90 ± 0.25 (27.39-28.41)	28.41 ± 0.16 (28.08-28.73)	27.72 ± 0.28 (27.16-28.29)
WC	100.64 ± 0.39 (99.86-101.42)	96.88 ± 0.76 (95.35-98.41)	101.73 ± 0.45‡ (100.82-102.64)	95.57 ± 0.77§ (94.04-97.11)
Systolic blood pressure	123.24 ± 0.41 (122.42-124.05)	120.11 ± 0.77† (118.56-121.66)	123.11 ± 0.45‡ (122.21-124.01)	127.00 ± 0.80§ (125.40-128.60)
Diastolic blood pressure	72.94 ± 0.29 (72.36-73.51)	70.99 ± 0.63† (69.73-72.26)	72.92 ± 0.32‡ (72.28-73.56)	74.83 ± 0.83§ (73.72-75.95)
Total cholesterol (mg/dL)	197.67 ± 1.06 (195.56-199.79)	198.80 ± 1.64† (195.52-202.09)	198.41 ± 1.25 (195.91-200.91)	190.85 ± 1.34§ (188.17-193.52)
LDL cholesterol (mg/dL)	120.36 ± 0.89 (118.58-122.13)	122.49 ± 1.34† (119.82-125.17)	120.60 ± 1.07 (118.46-122.74)	116.64 ± 1.46 (113.72-119.55)
HDL cholesterol (mg/dL)	47.53 ± 0.34 (46.85-48.20)	46.27 ± 0.45† (45.38-47.16)	47.14 ± 0.41 (46.32-47.97)	51.66 ± 0.66§ (50.35-52.98)
Triglycerides (mg/dL)	152.69 ± 2.71 (147.26-158.12)	160.28 ± 7.49† (145.28-162.85)	156.61 ± 3.12 (150.36-162.85)	115 ± 3.53§ (107.93-122.07)
Fasting glucose (mg/dL)	103 ± 0.59 (102.26-104.63)	104.62 ± 1.09 (102.44-106.79)	103 ± 0.70 (102.14-104.93)	101.70 ± 1.12 (99.46-103.94)
CRP	0.31 ± 0.01 (0.29-0.34)	0.31 ± 0.03 (0.25-0.37)	0.31 ± 0.01 (0.28-0.34)	0.35 ± 0.03 (0.29-0.40)
TG:HDL	3.72 ± 0.09 (3.55-3.89)	4.01 ± 0.26† (3.49-4.53)	3.84 ± 0.10 (3.65-4.04)	2.53 ± 0.10§ (2.34-2.73)

† Statistically significant difference between MA and NHB
‡ Statistically significant difference between MA and NHW
§ Statistically significant difference between NHW and NHB

Table 12. Population characteristics (means ± S.E) – females

	All races/ ethnicities (mean ± S.E. (CI))	Mexican Americans (mean ± S.E., (CI))	Non-Hispanic whites (mean ± S.E., (CI))	Non-Hispanic blacks (mean ± S.E., (CI))
Age	47.83 ± 0.46 (46.91-48.75)	40.46 ± 0.76† (38.94-41.98)	49.06 ± 0.52‡ (48.03-50.09)	43.77 ± 0.72§ (42.32-45.22)
Economic status (PIR)	3.02 ± 0.05 (2.92-3.12)	2.03 ± 0.10 (1.84-2.23)	3.19 ± 0.06‡ (3.08-3.31)	2.36 ± 0.09§ (2.18-2.54)
Number cigarettes per month	2.56 ± 0.79 (0.98-4.14)	0.98 ± 0.25 (0.48-1.47)	2.92 ± 0.98 (0.95-4.89)	1.25 ± 0.61 (0.04-2.47)
Number drinks per month	10.17 ± 0.53 (9.11-11.23)	5.25 ± 0.59† (4.07-6.42)	10.58 ± 0.59‡ (9.40-11.75)	9.41 ± 1.36 (6.69-12.13)
Minutes household activity per month	523.74 ± 34.84 (454.01-593.46)	332.55 ± 43.42 (245.66-419.43)	571.17 ± 40.73‡ (489.67-652.66)	314.74 ± 35.87§ (242.97-386.51)
BMI (kg/m^2)	28.41 ± 0.16 (28.08-28.73)	29.25 ± 0.33† (28.59-29.91)	27.84 ± 0.19‡ (27.45-28.23)	31.65 ± 0.27§ (31.11-32.20)
WC	93.82 ± 0.40 (93.01-94.63)	94.94 ± 0.69† (93.57-96.32)	92.95 ± 0.50 (91.94-93.95)	99.04 ± 0.64§ (97.75-100.32)
Systolic blood pressure	121.45 ± 0.50 (120.45-122.45)	117.57 ± 1.01† (115.55-119.59)	121.22 ± 0.58‡ (120.07-122.37)	125.23 ± 1.12§ (123.00-127.47)
Diastolic blood pressure	70.52 ± 0.34 (69.84-71.20)	69.88 ± 0.51† (68.87-70.89)	70.31 ± 0.40 (69.51-71.11)	72.26 ± 0.64§ (70.98-73.54)
Total cholesterol (mg/dL)	201.56 ± 1.06 (199.43-203.68)	192.16 ± 1.79 (188.58-195.74)	203.70 ± 1.14‡ (201.41-205.98)	192.55 ± 1.83§ (188.89-196.20)
LDL cholesterol (mg/dL)	117.88 ± 1.00 (115.88-119.88)	111.48 ± 1.58 (108.32-114.65)	118.87 ± 1.08‡ (116.71-121.03)	114.92 ± 1.88 (111.17-118.68)
HDL cholesterol (mg/dL)	58.26 ± 0.48 (57.30-59.21)	53.54 ± 0.63† (52.27-54.81)	58.71 ± 0.60‡ (57.52-59.90)	57.94 ± 0.61 (56.72-59.17)
Triglycerides (mg/dL)	127.92 ± 1.80 (124.31-131.54)	135.58 ± 3.25† (129.08-142.09)	131.66 ± 2.18 (127.30-136.02)	98.12 ± 2.33§ (93.45-102.78)
Fasting glucose (mg/dL)	97.75 ± 0.49 (96.76-98.74)	103.42 ± 1.75 (99.91-106.93)	97.11 ± 0.57‡ (95.97-98.24)	98.82 ± 0.88 (97.07-100.58)
CRP	0.48 ± 0.01 (0.46-0.51)	0.56 ± 0.04 (0.48-0.63)	0.45 ± 0.02‡ (0.42-0.48)	0.65 ± 0.04§ (0.58-0.73)
TG:HDL	2.53 ± 0.05 (2.43-2.63)	2.86 ± 0.09† (2.69-3.03)	2.59 ± 0.06 (2.47-2.72)	1.92 ± 0.06§ (1.81-2.04)

† Statistically significant difference between MA and NHB
‡ Statistically significant difference between MA and NHW
§ Statistically significant difference between NHW and NHB

Table 13. Prevalence of socioeconomic and lifestyle factors

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Age				
20-39	36.79 ± 1.00 (1964)	58.79 ± 1.82 (537)	33.51 ± 1.07 (939)	44.08 ± 1.41 (488)
40-59	40.07 ± 0.71 (2032)	30.41 ± 1.34 (442)	41.10 ± 0.86 (1148)	39.68 ± 1.45 (442)
≥ 60	23.14 ± 0.95 (2310)	10.79 ± 1.10 (503)	25.39 ± 1.13 (1442)	16.24 ± 1.15 (365)
Missing (n)	(0)	(0)	(0)	(0)
Economic status (PIR)				
0 - 0.99	11.14 ± 0.72 (960)	27.73 ± 2.34 (380)	7.97 ± 0.77 (321)	21.99 ± 1.77 (259)
1 - 1.99	20.51 ± 0.93 (1526)	33.39 ± 1.82(463)	18.46 ± 1.16 (742)	26.00 ± 1.62 (321)
2 - 2.99	15.60 ± 0.78 (959)	15.37 ± 1.39 (211)	15.48 ± 0.93 (545)	16.62 ± 1.14 (203)
3 - 3.99	15.21 ± 0.76 (770)	11.27 ± 1.18 (138)	15.93 ± 0.92 (486)	12.81 ± 1.14 (146)
4 - 4.99	11.01 ± 0.61 (529)	4.92 ± 0.79 (74)	12.04 ± 0.72 (359)	7.95 ± 1.06 (96)
5	26.54 ± 1.22 (1167)	7.32 ± 1.21 (106)	30.12 ± 1.54 (886)	14.63 ± 1.38 (175)
Missing (n)	(395)	(110)	(190)	(95)
Education level				
< 12 years	17.83 ± 0.82 (1869)	53.14 ± 1.73 (884)	12.76 ± 0.93 (586)	28.14 ± 1.80 (399)
12 years	27.30 ± 0.86 (1545)	21.18 ± 1.35 (252)	28.42 ± 0.99 (987)	23.85 ± 1.33 (306)
> 12 years	54.87 ± 1.26 (2886)	25.68 ± 1.61 (344)	58.82 ± 1.53 (1952)	48.01 ± 1.73 (590)
Missing (n)	(6)	(2)	(4)	(0)
Health insurance coverage	82.53 ± 0.95 (4989)	50.89 ± 2.47 (891)	86.67 ± 0.99 (3110)	75.86 ± 1.87 (988)
Missing (n)	(45)	(15)	(13)	(16)
Smoking status				
Past	46.57 ± 1.32 (1613)	44.20 ± 2.55 (338)	48.07 ± 1.43 (1061)	34.09 ± 2.28 (214)
Present	47.18 ± 1.44 (1351)	45.19 ± 2.96 (236)	45.66 ± 1.56 (795)	62.99 ± 2.32 (320)
Never	6.25 ± 0.53 (197)	10.61 ± 2.13 (60)	6.28 ± 0.57 (120)	2.93 ± 0.74 (17)
Missing (n)	(3145)	(848)	(1553)	(744)
Drinking status				
0 - 30	79.53 ± 0.94 (3140)	80.07 ± 1.78 (702)	79.19 ± 1.14 (1857)	82.08 ± 2.07 (581)
31 - 60	11.69 ± 0.57 (435)	12.21 ± 1.45 (101)	11.98 ± 0.70 (275)	8.77 ± 1.11 (59)
61 - 100	5.53 ± 0.47 (197)	4.76 ± 0.94 (38)	5.71 ± 0.55 (128)	4.66 ± 0.82 (31)
> 100	3.24 ± 0.30 (127)	2.96 ± 0.69 (28)	3.13 ± 0.34 (69)	4.48 ± 1.24 (30)
Missing (n)	(2407)	(613)	(1200)	(594)
Daily physical activity level				
1	24.22 ± 0.79 (1510)	16.48 ± 1.20 (273)	24.80 ± 0.93 (891)	25.57 ± 1.34 (346)
2	49.89 ± 0.92 (3312)	56.15 ± 1.42 (861)	48.64 ± 1.01 (1753)	54.15 ± 1.58 (698)
3	17.80 ± 0.64 (1001)	13.40 ± 1.00 (182)	18.67 ± 0.70 (635)	14.82 ± 1.05 (184)
4	8.10 ± 0.62 (473)	13.97 ± 1.50 (163)	7.88 ± 0.73 (254)	5.46 ± 0.97 (65)
Missing (n)	(10)	(3)	(5)	(2)
Minutes of household activity				
0	32.33 ± 1.15 (2565)	51.77 ± 1.88 (780)	27.79 ± 1.11 (1125)	50.12 ± 2.07 (660)
1 - 450	35.29 ± 0.80 (1970)	28.80 ± 1.70 (394)	36.56 ± 0.97 (1183)	30.99 ± 1.44 (393)
451 - 900	15.29 ± 0.57 (823)	9.97 ± 1.05 (148)	16.66 ± 0.67 (551)	9.59 ± 0.77 (124)
901 - 1800	10.18 ± 0.60 (549)	5.89 ± 0.66 (89)	11.20 ± 0.68 (384)	6.15 ± 0.82 (76)
> 1800	6.91 ± 0.62 (384)	3.57 ± 0.68 (68)	7.79 ± 0.75 (276)	3.15 ± 0.57 (40)
Missing (n)	(15)	(3)	(10)	(2)

Table 14. Prevalence of socioeconomic and lifestyle factors – males

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Age				
20-39	39.28 ± 1.24 (1060)	62.74 ± 2.10 (315)	35.62 ± 1.36 (495)	46.25 ± 2.63 (250)
40-59	40.21 ± 1.00 (1028)	28.68 ± 1.86 (219)	41.69 ± 1.11 (609)	39.16 ± 2.48 (200)
≥ 60	20.51 ± 1.00 (1154)	8.58 ± 0.90 (246)	22.69 ± 1.18 (725)	14.59 ± 1.24 (183)
Missing (n)	(0)	(0)	(0)	(0)
Economic status (PIR)				
0 - 0.99	10.29 ± 0.67 (474)	26.50 ± 2.58 (191)	7.15 ± 0.76 (166)	19.89 ± 2.07 (117)
1 - 1.99	18.41 ± 1.05 (745)	32.77 ± 2.19 (248)	16.06 ± 1.35 (348)	23.72 ± 1.99 (149)
2 - 2.99	16.03 ± 1.01 (515)	17.51 ± 1.87 (122)	15.45 ± 1.20 (281)	19.05 ± 1.63 (112)
3 - 3.99	15.51 ± 0.81 (400)	10.64 ± 1.49 (72)	16.33 ± 1.00 (254)	13.52 ± 1.60 (74)
4 - 4.99	11.40 ± 0.73 (287)	5.58 ± 1.12 (44)	12.43 ± 0.84 (191)	8.63 ± 1.21 (52)
5	28.37 ± 1.38 (642)	7.00 ± 1.33 (54)	32.57 ± 1.77 (496)	15.19 ± 1.75 (92)
Missing (n)	(179)	(49)	(93)	(49)
Education level				
< 12 years	17.98 ± 0.98 (989)	52.77 ± 2.22 (470)	12.16 ± 1.14 (305)	31.20 ± 2.59 (214)
12 years	27.99 ± 1.18 (797)	24.19 ± 2.17 (143)	28.79 ± 1.39 (498)	25.38 ± 1.85 (156)
> 12 years	54.03 ± 1.44 (1451)	23.04 ± 1.88 (166)	59.05 ± 1.85 (1022)	43.43 ± 2.50 (263)
Missing (n)	(5)	(1)	(4)	(0)
Health insurance coverage	80.84 ± 1.08 (2523)	50.31 ± 2.70 (459)	85.68 ± 1.15 (1600)	70.93 ± 2.32 (464)
Missing (n)	(23)	(8)	(7)	(8)
Smoking status				
Past	46.24 ± 1.45 (986)	43.33 ± 2.82 (235)	48.49 ± 1.64 (637)	28.42 ± 2.66 (114)
Present	47.43 ± 1.51 (808)	46.89 ± 3.30 (166)	45.16 ± 1.73 (439)	68.63 ± 2.84 (203)
Never	6.33 ± 0.73 (117)	9.77 ± 2.49 (38)	6.36 ± 0.83 (69)	2.95 ± 0.99 (10)
Missing (n)	(1331)	(341)	(684)	(306)
Drinking status				
0 - 30	71.36 ± 1.28 (1644)	72.23 ± 2.38 (410)	70.95 ± 1.58 (935)	74.09 ± 3.18(299)
31 - 60	14.37 ± 0.76 (312)	16.50 ± 2.03 (86)	14.30 ± 0.97 (181)	12.77 ± 1.90 (45)
61 - 100	8.78 ± 8.74 (172)	7.00 ± 1.41 (37)	9.29 ± 0.87 (112)	6.25 ± 1.24 (23)
> 100	5.48 ± 0.50 (116)	4.27 ± 1.02 (26)	5.47 ± 0.60 (65)	6.89 ± 1.95 (25)
Missing (n)	(998)	(221)	(536)	(241)
Daily physical activity level				
1	21.43 ± 0.93 (693)	12.55 ± 1.41 (115)	22.54 ± 1.15 (429)	20.80 ± 1.52 (149)
2	44.74 ± 1.28 (1550)	47.96 ± 1.78 (394)	43.40 ± 1.52 (832)	51.97 ± 2.32 (324)
3	19.93 ± 0.97 (591)	16.84 ± 1.64 (125)	20.54 ± 1.14 (359)	18.03 ± 1.44 (107)
4	13.90 ± 1.03 (400)	22.66 ± 2.30 (144)	13.52 ± 1.21 (205)	9.20 ± 1.81 (51)
Missing (n)	(8)	(2)	(4)	(2)
Minutes of household activity				
0	28.29 ± 1.36 (1179)	50.25 ± 2.41 (388)	23.44 ± 1.36 (499)	45.37 ± 2.61 (292)
1 - 450	36.68 ± 0.96 (1076)	30.70 ± 2.14 (232)	37.46 ± 1.19 (621)	36.07 ± 2.08 (223)
451 - 900	15.58 ± 0.70 (439)	10.13 ± 1.37 (79)	17.02 ± 0.80 (297)	9.54 ± 1.16 (63)
901 - 1800	11.37 ± 0.73 (314)	5.75 ± 0.88 (46)	12.71 ± 0.83 (229)	6.28 ± 1.02 (39)
> 1800	8.08 ± 0.74 (226)	3.17 ± 0.68 (34)	9.37 ± 0.87 (177)	2.74 ± 0.68 (15)
Missing (n)	(8)	(1)	(6)	(1)

Table 15. Prevalence of socioeconomic and lifestyle factors – females

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Age				
20-39	34.37 ± 1.21 (904)	53.68 ± 2.32 (222)	31.47 ± 1.31 (444)	42.26 ± 1.83 (238)
40-59	39.93 ± 0.94 (1004)	32.66 ± 1.40 (223)	40.53 ± 1.12 (539)	40.12 ± 1.72 (242)
≥ 60	25.70 ± 1.09 (1156)	13.66 ± 1.54 (257)	28.00 ± 1.31 (717)	17.62 ± 1.60 (182)
Menopausal	27.95 ± 1.30 (629)	15.95 ± 2.30 (125)	30.00 ± 1.63 (395)	21.75 ± 2.36 (109)
Missing (n)	(1200)	(300)	(655)	(245)
Economic status (PIR)				
0 - 0.99	11.98 ± 0.93 (486)	29.35 ± 3.05 (189)	8.76 ± 0.99 (155)	23.82 ± 2.11 (142)
1 - 1.99	22.57 ± 0.98 (781)	34.21 ± 2.31 (215)	20.78 ± 1.15 (394)	27.99 ± 2.00 (172)
2 - 2.99	15.18 ± 0.77 (444)	12.54 ± 1.93 (89)	15.50 ± 0.89 (264)	14.50 ± 1.31 (91)
3 - 3.99	14.91 ± 0.89 (370)	12.10 ± 1.26 (66)	15.55 ± 1.05 (232)	12.19 ± 1.24 (72)
4 - 4.99	10.63 ± 0.72 (242)	4.05 ± 0.84 (30)	11.67 ± 0.85 (168)	7.36 ± 1.53 (44)
5	24.74 ± 1.25 (525)	7.75 ± 1.42 (52)	27.74 ± 1.50 (390)	14.14 ± 1.69 (83)
Missing	(216)	(61)	(97)	(58)
Education level				
< 12 years	17.69 ± 0.97 (880)	53.62 ± 2.39 (414)	13.34 ± 1.06 (281)	25.57 ± 2.16 (185)
12 years	26.62 ± 0.97 (748)	17.28 ± 1.42 (109)	28.06 ± 1.18 (489)	22.58 ±1.78 (150)
> 12 years	55.69 ± 1.53 (1435)	29.09 ± 2.14 (178)	58.60 ± 1.79 (930)	51.85 ± 2.36 (327)
Missing	(1)	(1)	(0)	(0)
Health insurance coverage	84.17 ± 1.06 (2466)	51.64 ± 3.03 (432)	87.63 ± 1.09 (1510)	79.98 ± 2.41 (524)
Missing (n)	(22)	(8)	(6)	(8)
Smoking status				
Past	46.97 ± 1.77 (627)	46.37 ± 4.52 (103)	47.58 ± 1.91 (424)	41.21 ± 3.28 (100)
Present	46.87 ± 1.89 (543)	40.92 ± 4.39 (70)	46.24 ± 1.99 (356)	55.88 ± 3.14 (117)
Never	6.16 ± 0.69 (80)	12.71 ± 2.98 (22)	6.18 ± 0.77 (51)	2.90 ± 1.17 (7)
Missing (n)	(1814)	(507)	(869)	(438)
Drinking status				
0 - 30	89.06 ± 1.00 (1496)	96.03 ± 0.95 (292)	88.38 ± 1.17 (922)	91.02 ± 1.45 (282)
31 - 60	8.57 ± 0.90 (123)	3.46 ± 0.91 (15)	9.39 ± 1.03 (94)	4.30 ± 1.37 (14)
61 - 100	1.74 ± 0.41 (25)	0.20 ± 0.20 (1)	1.71 ± 0.45 (16)	2.89 ± 1.05 (8)
> 100	0.63 ± 0.24 (11)	0.31 ± 0.22 (2)	0.52 ± 0.27 (4)	1.78 ± 0.81 (5)
Missing (n)	(1409)	(392)	(664)	(353)
Daily physical activity level				
1	26.93 ± 1.05 (817)	21.55 ± 1.52 (158)	26.99 ± 1.17 (462)	29.56 ± 2.01 (197)
2	54.90 ± 1.38 (1762)	66.73 ± 1.85 (467)	53.71 ± 1.57 (921)	55.98 ± 1.98 (374)
3	15.72 ± 0.92 (410)	8.96 ± 1.27 (57)	16.87 ± 1.10 (276)	12.13 ± 1.51 (77)
4	2.45 ± 0.42 (73)	2.76 ± 0.73 (19)	2.44 ± 0.48 (40)	2.33 ± 0.86 (14)
Missing (n)	(2)	(1)	(1)	(0)
Minutes of household activity				
0	36.27 ± 1.26 (1386)	53.73 ± 2.52 (392)	31.99 ± 1.29 (626)	54.09 ± 2.54 (368)
1 - 450	33.93 ± 1.14 (894)	26.35 ± 1.79 (162)	35.70 ± 1.36 (562)	26.75 ± 2.15 (170)
451 - 900	15.01 ± 0.80 (384)	9.75 ± 1.31 (69)	16.30 ± 1.01 (254)	9.63 ± 1.11 (61)
901 - 1800	9.02 ± 0.67 (235)	6.08 ± 1.08 (43)	9.74 ± 0.79 (155)	6.03 ± 1.12 (37)
> 1800	5.77 ± 0.75 (158)	4.09 ± 0.95 (34)	6.27 ± 0.92 (99)	3.50 ± 0.78 (25)
Missing (n)	(7)	(2)	(4)	(1)

Table 16. Prevalence of Metabolic Syndrome risk factors among U.S. adults ages ≥ 20 years old, NHANES 1999-2006

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Both genders				
BMI				
Overweight	33.98 ± 0.88 (2219)	40.59 ± 1.70 (615)	34.11 ± 1.00 (1225)	28.40 ± 1.34 (379)
Obese	32.87 ± 0.77 (2071)	32.37 ± 1.37 (486)	31.26 ± 0.96 (1033)	44.28 ± 1.53 (552)
Missing (n)*	(101)	(17)	(66)	(18)
Enlarged WC	52.40 ± 0.89 (3332)	48.22 ± 2.05 (785)†	52.50 ± 1.17 (1859)	54.62 ± 1.61 (688)
Missing (n)	(153)	(29)	(80)	(44)
Elevated TC	26.04 ± 0.87 (1699)	16.56 ± 1.08 (338)	28.05 ± 1.01 (1091)‡	18.66 ± 1.08 (270)§
Missing (n)	(63)	(9)	(29)	(25)
Elevated LDL	23.29 ± 0.81(1490)	15.10 ± 1.15 (283)	24.76 ± 0.89 (947)‡	17.96 ±1.40 (260)§
Missing (n)	(224)	(69)	(117)	(38)
Low HDL	38.43 ± 0.92 (2480)	39.68 ± 1.78 (650)†	39.43 ± 1.09 (1429)	30.54 ± 1.46 (401)§
Missing (n)	(65)	(9)	(33)	(23)
Elevated TG	38.35 ± 0.90 (2513)	38.36 ± 1.95 (667)†	40.64 ± 1.09 (1539)	22.30 ± 1.24 (307)§
Missing (n)	(73)	(11)	(35)	(27)
HT	42.16 ± 0.94 (3005)	26.94 ± 1.70 (598)†	42.65 ± 1.03 (1721)‡	49.38 ± 1.59 (686)§
Missing (n)	(148)	(37)	(69)	(42)
Elevated FPG	37.29 ± 1.21 (2658)	40.73 ± 1.99 (355)†	37.59 ± 1.40 (1481)	32.79 ± 1.55 (465)
Missing (n)	(14)	(2)	(7)	(5)
Elevated FPG*	15.79 ± 0.65 (1239)	17.11 ± 1.44 (355)	15.72 ± 0.76 (660)	15.31 ± 1.07 (224)
Missing (n)	(14)	(2)	(7)	(5)
Diabetes	9.46 ± 0.49 (774)	10.39 ± 1.21 (236)	8.99 ± 0.56 (363)	12.09 ± 0.90 (175)§
Missing (n)	(0)	(0)	(0)	(0)

† Statistically significant difference between MA and NHB
‡ Statistically significant difference between MA and NHW
§ Statistically significant difference between NHW and NHB

* *n* of total missing is for both overweight and obese. Statistically significant differences exist across racial/ethnic groups but it is not possible to determine across which
** Fasting plasma glucose ≥ 110 mg/dL

Abbreviations:
WC= waist circumference
TC= total cholesterol
LDL= low density lipoprotein cholesterol
HDL= high density lipoprotein cholesterol
TG= triglycerides
HT= hypertension
FPG= fasting plasma glucose

Table 17. Prevalence of Metabolic Syndrome risk factors among U.S. males ages ≥ 20 years old, NHANES 1999-2006

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Males				
BMI				
Overweight	40.34 ± 1.20 (1315)	46.43 ± 2.14 (367)	40.67 ± 1.36 (736)	32.50 ± 1.96 (212)
Obese	30.83 ± 1.06 (939)	26.73 ± 1.92 (216)	31.22 ± 1.25 (528)	31.53 ± 2.18 (195)
Missing (n)*	(44)	(4)	(28)	(12)
Enlarged WC	43.52 ± 1.26 (1351)	32.20 ± 2.62 (290)	46.36 ± 1.43 (847)‡	31.95 ± 2.23 (214)§
Missing (n)	(74)	(12)	(39)	(23)
Elevated TC	25.65 ± 1.08 (837)	17.74 ± 1.32 (169)	27.62 ± 1.28 (545)‡	17.63 ± 1.73 (123)§
Missing (n)	(16)	(4)	(2)	(10)
Elevated LDL	24.23 ± 1.03 (782)	17.27 ± 1.49 (151)	25.75 ± 1.20 (500)‡	18.85 ± 1.90 (131)§
Missing (n)	(135)	(44)	(70)	(21)
Low HDL	36.58 ± 1.22 (1191)	31.79 ± 2.21 (285)†	39.07 ± 1.38 (750)‡	22.00 ± 1.91 (156)§
Missing (n)	(15)	(4)	(3)	(8)
Elevated TG	43.51 ± 1.22 (1419)	42.67 ± 2.58 (366)†	45.93 ± 1.43 (883)	25.88 ± 1.80 (170)§
Missing (n)	(22)	(6)	(4)	(12)
HT	44.06 ± 1.21 (1574)	27.90 ± 2.17 (307)†	45.15 ± 1.40 (928)‡	49.86 ± 2.59 (339)
Missing (n)	(59)	(16)	(28)	(15)
Elevated FPG	44.78 ± 1.40 (1565)	46.04 ± 2.21 (413) †	46.14 ± 1.61 (919)	33.53 ± 1.94 (233)§
Missing (n)	(2)	(0)	(1)	(1)
Elevated FPG*	18.70 ± 1.02 (726)	18.30 ± 1.77 (198)	19.13 ± 1.18 (412)	15.86 ± 1.46 (116)
Missing (n)	(2)	(0)	(1)	(1)
Diabetes	10.47 ± 0.71 (410)	9.17 ± 1.13 (113)	10.56 ± 0.83 (213)	10.92 ± 1.11 (84)
Missing (n)	(0)	(0)	(0)	(0)

† Statistically significant difference between MA and NHB
‡ Statistically significant difference between MA and NHW
§ Statistically significant difference between NHW and NHB

* *n* of total missing is for both overweight and obese. Statistically significant differences exist across racial/ethnic groups but it is not possible to determine across which
** Fasting plasma glucose ≥ 110 mg/dL

Abbreviations:
WC= waist circumference
TC= total cholesterol
LDL= low density lipoprotein cholesterol
HDL= high density lipoprotein cholesterol
TG= triglycerides
HT= hypertension
FPG= fasting plasma glucose

Table 18. Prevalence of Metabolic Syndrome risk factors among U.S. females ages ≥ 20 years old, NHANES 1999-2006

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Females				
BMI				
Overweight	27.75 ± 1.09 (904)	32.96 ± 1.99 (248)	27.73 ± 1.23 (489)	24.99 ± 1.67 (167)
Obese	34.86 ± 1.02 (1132)	39.73 ± 2.51 (270)	31.31 ± 1.23 (505)	54.86 ± 1.92 (357)
Missing (n)*	(57)	(13)	(38)	(6)
Enlarged WC	61.04 ± 1.22 (1981)	69.18 ± 2.79 (495)	58.43 ± 1.59 (1012)‡	73.46 ± 1.84 (474)§
Missing (n)	(79)	(17)	(41)	(21)
Elevated TC	26.42 ± 1.06 (862)	15.03 ± 1.32 (169)	28.48 ± 1.23 (546)‡	19.53 ± 1.48 (147)§
Missing (n)	(47)	(5)	(27)	(15)
Elevated LDL	22.19 ± 1.02 (708)	12.39 ± 1.47 (132)	23.82 ± 1.17 (447)‡	17.22 ± 1.89 (129)§
Missing (n)	(89)	(25)	(47)	(17)
Low HDL	40.25 ± 1.27 (1289)	49.90 ± 2.04 (365)†	39.79 ± 1.55 (679)‡	37.76 ± 2.30 (245)
Missing (n)	(50)	(5)	(30)	(15)
Elevated TG	33.25 ± 1.10 (1094)	32.81 ± 2.18 (301)†	35.44 ± 1.38 (656)	19.28 ± 1.54 (137)§
Missing (n)	(51)	(5)	(31)	(15)
HT	40.29 ± 1.18 (1431)	25.68 ± 2.60 (291)†	40.22 ± 1.36 (793)‡	48.96 ± 2.41 (347)§
Missing (n)	(89)	(21)	(41)	(27)
Elevated FPG	29.97 ± 1.24 (513)	33.85 ± 2.97 (299)	29.29 ± 1.47 (562)	32.17 ± 1.77 (232)
Missing (n	(12)	(2)	(6)	(4)
Elevated FPG*	11.71 ± 0.64 (513)	15.55 ± 1.97 (157)	12.42 ± 0.80 (248)	14.85 ± 1.09 (108)
Missing (n)	(12)	(2)	(6)	(4)
Diabetes	8.48 ± 0.54 (364)	11.97 ± 1.84 (123)	7.47 ± 0.59 (150)	13.07 ± 1.33 (91)§
Missing (n)	(0)	(0)	(0)	(0)

† Statistically significant difference between MA and NHB
‡ Statistically significant difference between MA and NHW
§ Statistically significant difference between NHW and NHB

* *n* of total missing is for both overweight and obese. Statistically significant differences exist across racial/ethnic groups but it is not possible to determine across which
** Fasting plasma glucose ≥ 110 mg/dL

Abbreviations:
WC= waist circumference
TC= total cholesterol
LDL= low density lipoprotein cholesterol
HDL= high density lipoprotein cholesterol
TG= triglycerides
HT= hypertension
FPG= fasting plasma glucose

Table 19. Prevalence of the Metabolic Syndrome among U.S. adults ages ≥ 20 years old, NHANES 1999-2006, calculated using the fasting plasma glucose cutoff of 100 mg/dL

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Both genders				
Unadjusted	38.80 ± 0.99 (2688)	33.12 ± 1.75^{A} (659)	40.36 ± 1.20^{B} (1572)	31.99 ± 1.07^{A} (457)
Age-adjusted	38.14 ± 0.87 (2688)	41.03 ± 1.48^{A} (659)	38.51 ± 1.09^{B} (1572)	34.49 ± 1.11^{C} (457)
Males				
Unadjusted	^{A}40.13 ± 1.19 (1364)	^{A}29.72 ± 2.26^{A} (311)	^{A}43.25 ± 1.33^{B} (861)	^{A}25.88 ± 1.95^{A} (192)
Age-adjusted	^{A}40.51 ± 1.06 (1364)	^{A}37.96 ± 2.00^{A} (311)	^{A}42.35 ± 1.21^{B} (861)	^{A}29.08 ± 1.95^{C} (192)
Females				
Unadjusted	^{B}37.49 ± 1.26 (1324)	^{B}37.50 ± 2.44 (348)	^{B}37.55 ± 1.57 (711)	^{B}37.11 ± 1.59 (265)
Age-adjusted	^{B}35.73 ± 1.15 (1324)	^{B}43.98 ± 1.74^{A} (348)	^{B}34.64 ± 1.45^{B} (711)	^{B}38.85 ± 1.50^{C} (265)

$^{A, B, C}$ Uppercase = significance level is $p \leq 0.01$

$^{a, b, c}$ Lowercase = significance level is $p \leq 0.05$

Superscripts before prevalence value indicate significant differences between genders by unadjusted and age adjusted prevalence

Table 20. Prevalence of the Metabolic Syndrome among U.S. adults ages ≥ 20 years old, NHANES 1999-2006, calculated using the fasting plasma glucose cutoff of 110 mg/dL

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Both genders				
Unadjusted	32.86 ± 0.84 (2300)	26.65 ± 1.80^{A} (562)	34.47 ± 1.0^{B} (1360)	26.09 ± 1.05^{A} (378)
Age-adjusted	32.29 ± 0.73 (2300)	34.38 ± 1.58^{A} (562)	32.75 ± 0.89^{B} (1360)	28.38 ± 1.17^{C} (378)
Males				
Unadjusted	33.13 ± 1.13 (1146)	^{a}23.46 ± 2.11^{A} (257)	35.84 ± 1.33^{B} (727)	^{A}21.21 ± 1.76^{A} (162)
Age-adjusted	^{A}33.59 ± 1.05 (1146)	^{A}31.41 ± 1.99^{A} (257)	^{A}35.07 ± 1.22^{B} (727)	^{A}24.24 ± 1.76^{C} (162)
Females				
Unadjusted	32.61 ± 1.22 (1154)	^{b}30.79 ± 2.36 (305)	33.15 ± 1.53 (633)	^{B}30.18 ± 1.54 (216)
Age-adjusted	^{B}30.99 ± 1.09 (1154)	^{B}37.22 ± 1.80^{A} (305)	^{B}30.43 ± 1.38^{B} (633)	^{B}31.77 ± 1.50^{C} (216)

$^{A, B, C}$ Uppercase = significance level is $p \leq 0.01$

$^{a, b, c}$ Lowercase = significance level is $p \leq 0.05$

Superscripts before prevalence value indicate significant differences between genders by unadjusted and age adjusted prevalence

Table 21. Prevalence of Cardiovascular Disease among U.S. adults ages ≥ 20 years old, NHANES 1999-2006

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Both genders				
Unadjusted	39.47 ± 0.99 (2888)	24.38 ± 1.66^{A} (564)	40.50 ± 1.14^{B} (1692)	42.94 ± 1.37^{B} (632)
Age-adjusted	38.82 ± 0.78 (2888)	33.37 ± 1.38^{A} (564)	38.45 ± 0.89^{B} (1692)	46.71 ± 1.14^{C} (632)
Males				
Unadjusted	39.00 ± 1.21 (1455)	^{a}21.99 ± 1.92^{A} (271)	40.81 ± 1.36^{B} (888)	^{a}40.19 ± 2.32^{B} (296)
Age-adjusted	^{A}39.84 ± 1.05 (1455)	^{A}31.90 ± 1.68^{A} (271)	^{A}40.29 ± 1.20^{B} (888)	^{A}44.78 ± 2.13^{C} (296)
Females				
Unadjusted	39.94 ± 1.29 (1433)	^{b}27.46 ± 2.49^{A} (293)	40.20 ± 1.53^{B} (804)	^{b}45.24 ± 2.4^{B} (336)
Age-adjusted	^{B}37.66 ± 1.08 (1433)	^{B}34.65 ± 2.05^{A} (293)	^{B}36.48 ± 1.29^{B} (804)	^{B}48.08 ± 1.91^{C} (336)

$^{A, B, C}$ Uppercase = significance level is $p \leq 0.01$

$^{a, b, c}$ Lowercase = significance level is $p \leq 0.05$

Superscripts before prevalence value indicate significant differences between genders by unadjusted and age adjusted prevalence

Table 22. Significance of the predictor variables

Covariates	*P*
Age	0.0110
Gender	0
Race/ethnicity	0.4260
Economic status (PIR)	0.8847
Education	0.4260
Health insurance	0.2730
Smoking status	0.0429
Alcohol intake	0.2853
Daily activity	0.3183
Household activity	0.3751
BMI	0.0726
Waist circumference	0.0002
Systolic blood pressure	0.0001
Diastolic blood pressure	0.0877
Fasting glucose	0
logTG	0
logHDL	0
logLDL	0
logCRP	0.3003

$R^2 = 0.472761$

Abbreviations:
PIR= poverty income ratio
BMI = body mass index
TG= triglycerides
HDL= high density lipoprotein cholesterol
LDL= low density lipoprotein cholesterol
CRP= C-reactive protein

Table 23. Beta estimates of the predictor variables

	β	β S.E.	Lower Limit	Upper Limit	*t* - test	*P*
Intercept	-16.38	3.25	-22.89	-9.87	-5.03	0.0000
Categorical						
Gender						
Male	-1.43	0.31	-2.04	-0.81	-4.65	0
Female	0	0	0	0	.	.
Race/Ethnicity						
MA	0.43	0.33	-0.23	1.09	1.30	0.1982
NHW	0.20	0.26	-0.33	0.72	0.75	0.4567
NHB	0	0	0	0	.	.
Education						
< 12 years	-0.05	0.28	-0.61	0.50	-0.19	0.8490
12 years	0.44	0.27	-0.09	0.98	1.65	0.1042
> 12 years	0	0	0	0	.	.
Smoking status						
Past	0.35	0.44	-0.54	1.23	0.79	0.4349
Present	-0.21	0.40	-1.02	0.59	-0.53	0.5971
Never	0	0	0	0	.	.
Health insurance						
Covered	0.35	0.31	-0.28	0.97	1.11	0.2730
Not covered	0	0	0	0	.	.
Daily activity level						
1	0.18	0.32	-0.46	0.82	0.55	0.5836
2	-0.32	0.32	0.95	0.31	-1.02	0.3100
3	-0.10	0.33	-0.75	0.56	-0.29	0.7698
4	0	0	0	0	.	.
Continuous						
Age	0.02	0.01	0.01	0.04	2.62	0.0110
Economic status (PIR)	0.01	0.08	-0.15	0.18	0.15	0.8847
Household activity	0	0	0	0	0.89	0.3751
Alcohol intake	0	0	-0.01	0	-1.08	0.2853
BMI	-0.09	0.05	-0.19	-0.01	-1.83	0.0726
Waist circumference	0.09	0.02	0.05	0.14	4.03	0.0002
Systolic blood pressure	0.04	0.01	0.02	0.05	4.09	0.0001
Diastolic blood pressure	0.02	0.01	0	0.04	1.74	0.0877
Fasting glucose	0.11	0.01	0.08	0.14	8.01	0
logTG	2.07	0.22	1.62	2.51	9.29	0
logHDL	-2.64	0.47	-3.59	-1.70	-5.59	0
logLDL	-1.62	0.28	-2.19	-1.06	-5.72	0
logCRP	0.09	0.09	-0.08	0.27	1.04	0.3003

Table 24. Odds ratios of the predictor variables

	Odds Ratio	Lower Limit	Upper Limit
Intercept	0	0	0.00
Categorical			
Gender			
Male	0.24	0.13	0.44
Female	1	1	1
Race/Ethnicity			
MA	1.54	0.79	2.98
NHW	1.22	0.72	2.05
NHB	1	1	1
Education			
< 12 years	0.95	0.54	1.65
12 years	1.56	0.91	2.67
> 12 years	1	1	1
Smoking status			
Past	1.42	0.58	3.43
Present	0.81	0.36	1.81
Never	1	1	1
Health insurance			
Covered	1.41	0.76	2.65
Not covered	1	1	1
Daily activity level			
1	1.19	0.63	2.27
2	0.72	0.39	1.36
3	0.91	0.47	1.75
4	1	1	1
Continuous			
Age	1.02	1.01	1.04
Economic status (PIR)	1.01	0.86	1.19
Household activity	1	1	1
Alcohol intake	0.99	0.99	1
BMI	0.91	0.82	1.01
Waist circumference	1.09	1.05	1.14
Systolic blood pressure	1.04	1.02	1.05
Diastolic blood pressure	1.02	1	1.04
Fasting glucose	1.10	1.09	1.15
logTG	7.89	5.06	12.31
logHDL	0.07	0.03	0.18
logLDL	0.20	0.11	0.35
logCRP	1.00	0.99	1.00

Table 25. Prevalence of Metabolic Syndrome with newly proposed triglyceride cutoffs among U.S. adults ages ≥ 20 years old, NHANES 1999-2006, calculated using the blood glucose cutoff of 100 mg/dL

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Both genders				
Current unadjusted	38.80 ± 0.99 (2688)	33.12 ± 1.75^{A} (659)	40.36 ± 1.20^{B} (1572)	31.99 ± 1.07^{A} (457)
New unadjusted	****40.49 ± 0.98 (2804)**	****34.33 ± 1.73^{A} (675)**	****41.80 ± 1.17^{B} (1623)**	****35.78 ± 1.07^{C} (506)**
Current age-adjusted	38.14 ± 0.87 (2688)	41.03 ± 1.48^{A} (659)	38.51 ± 1.09^{B} (1572)	34.49 ± 1.11^{C} (457)
New age-adjusted	****39.83 ± 0.86 (2804)**	****42.19 ± 1.49^{A} (675)**	****39.96 ± 1.06^{B} (1623)**	****38.23 ± 1.08^{C} (506)**
Males				
Current unadjusted	40.13 ± 1.19 (1364)	29.72 ± 2.26^{A} (311)	43.25 ± 1.33^{B} (861)	25.88 ± 1.95^{A} (192)
New unadjusted	****41.49 ± 1.19 (1412)**	****30.50 ± 2.25^{A} (316)**	****44.48 ± 1.33^{B} (886)**	****28.70 ± 2.08^{A} (210)**
Current age-adjusted	40.51 ± 1.06 (1364)	37.96 ± 2.00^{A} (311)	42.35 ± 1.21^{B} (861)	29.08 ± 1.95^{C} (192)
New age-adjusted	****41.86 ± 1.05 (1412)**	****38.63 ± 1.97^{A} (316)**	****43.55 ± 1.20^{B} (886)**	****31.88 ± 1.98^{C} (210)**
Females				
Current unadjusted	37.49 ± 1.26 (1324)	37.50 ± 2.44 (348)	37.55 ± 1.57 (711)	37.11 ± 1.59 (265)
New unadjusted	****39.52 ± 1.28 (1392)**	****39.29 ± 2.53 (359)**	****39.20 ± 1.56 (737)**	****41.71 ± 1.71 (296)**
Current age-adjusted	35.73 ± 1.15 (1324)	43.98 ± 1.74^{A} (348)	34.64 ± 1.45^{B} (711)	38.85 ± 1.50^{C} (265)
New age-adjusted	****37.80 ± 1.18 (1392)**	****45.69 ± 1.86^{A} (359)**	****36.35 ± 1.45^{B} (737)**	****43.38 ± 1.57^{C} (296)**

$^{A, B, C}$ Uppercase = significance level is $p \leq 0.01$

$^{a, b, c}$ Lowercase = significance level is $p \leq 0.05$

* Significant differences between current and new prevalence ($p < 0.05$)

** Significant differences between current and new prevalence ($p < 0.01$)

Table 26. Prevalence of Metabolic Syndrome with newly proposed triglyceride cutoffs among U.S. adults ages ≥ 20 years old, NHANES 1999-2006, calculated using the blood glucose cutoff of 110 mg/dL

	All races/ ethnicities (% ± S.E. (n))	Mexican Americans (% ± S.E. (n))	Non-Hispanic whites (% ± S.E. (n))	Non-Hispanic blacks (% ± S.E. (n))
Both genders				
Current unadjusted	32.86 ± 0.84 (2300)	26.65 ± 1.80^{A} (562)	34.47 ± 1.03^{B} (1360)	26.09 ± 1.05^{A} (378)
New unadjusted	****33.20 ± 0.86 (2342)**	****27.51 ± 1.74^{A} (577)**	**34.47 ± 1.03^{B} (1360)**	****28.34 ± 0.99^{A} (405)**
Current age-adjusted	32.29 ± 0.73 (2300)	34.38 ± 1.58^{A} (562)	32.75 ± 0.89^{B} (1360)	28.38 ± 1.17^{C} (378)
New age-adjusted	****32.62 ± 0.74 (2342)**	****35.31 ± 1.47^{A} (577)**	**32.75 ± 0.89^{B} (1360)**	****30.64 ± 1.01^{C} (405)**
Males				
Current unadjusted	33.13 ± 1.13 (1146)	23.46 ± 2.11^{A} (257)	35.84 ± 1.33^{B} (727)	21.21 ± 1.76^{A} (162)
New unadjusted	****33.30 ± 1.14 (1158)**	**23.73 ± 2.10^{A} (261)**	**35.84 ± 1.33^{B} (727)**	****22.60 ± 1.65^{A} (170)**
Current age-adjusted	33.59 ± 1.05 (1146)	31.41 ± 1.99^{A} (257)	35.07 ± 1.22^{B} (727)	24.24 ± 1.76^{C} (162)
New age-adjusted	****33.76 ± 1.05 (1158)**	***31.82 ± 1.99^{A} (261)**	**35.07 ± 1.22 (727)^{B}**	****25.51 ± 1.65^{C} (170)**
Females				
Current unadjusted	32.61 ± 1.22 (1154)	30.79 ± 2.36 (305)	33.15 ± 1.53 (633)	30.18 ± 1.54 (216)
New unadjusted	****33.09 ± 1.25 (1184)**	****32.40 ± 2.36 (316)**	**33.15 ± 1.53 (633)**	****33.14 ± 1.69 (235)**
Current age-adjusted	30.99 ± 1.09 (1154)	37.22 ± 1.80^{A} (305)	30.43 ± 1.38^{B} (633)	31.77 ± 1.50^{C} (216)
New age-adjusted	****31.47 ± 1.11 (1184)**	****38.80 ± 1.75^{A} (316)**	**30.43 ± 1.38^{B} (633)**	****34.78 ± 1.49^{C} (235)**

$^{A, B, C}$ Uppercase = significance level is $p \leq 0.01$

$^{a, b, c}$ Lowercase = significance level is $p \leq 0.05$

* Significant differences between current and new prevalence ($p < 0.05$)

** Significant differences between current and new prevalence ($p < 0.01$)

Appendix B: Figures

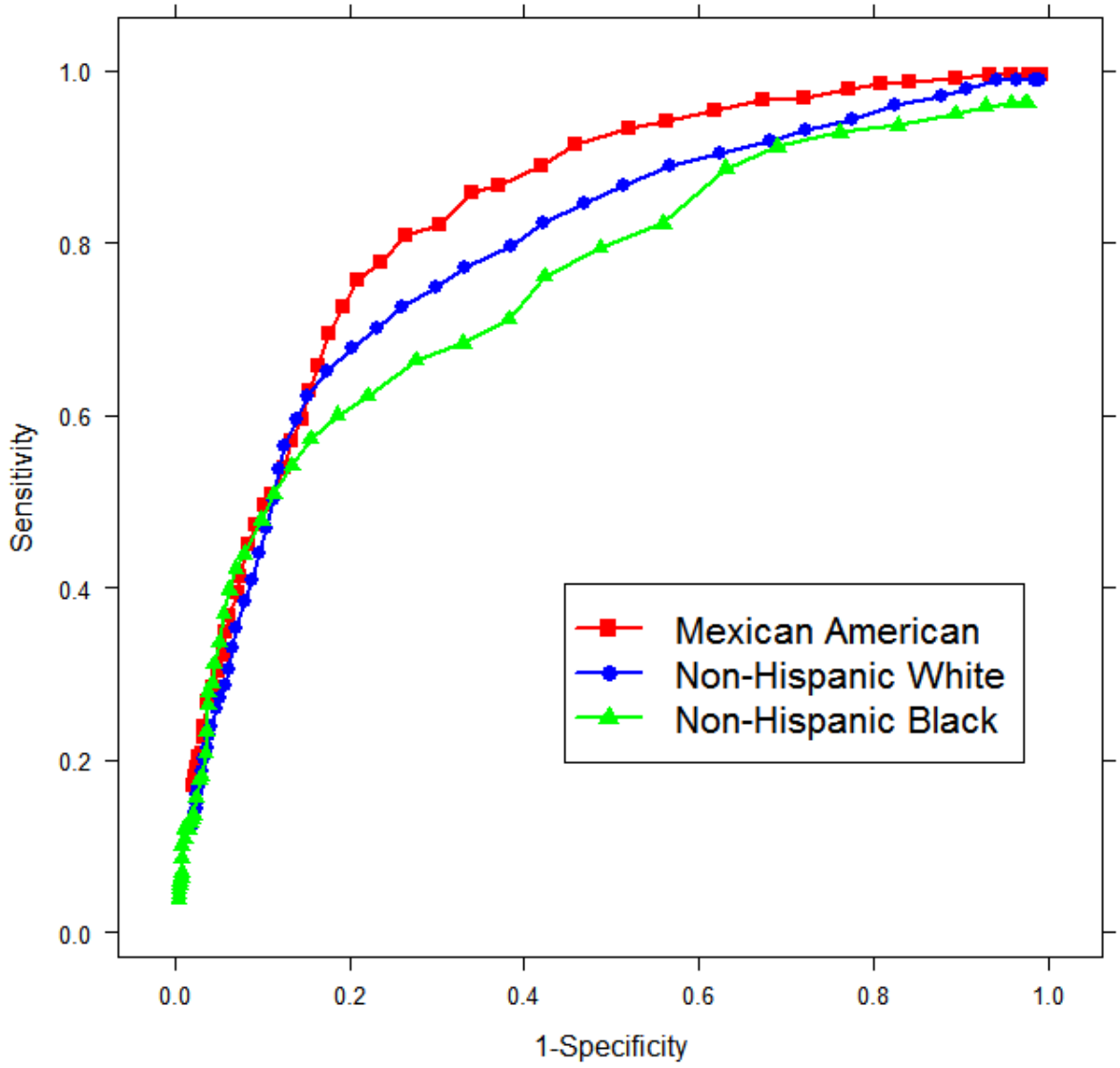

Figure 4. *ROC curve for determining triglyceride cutoffs in MA's, NHW's, and NHB's*

TG cutoff values according to Youden Index calculation:
MA: 137 mg/dL
NHW: 140 mg/dL
NHB: 110 mg/dL

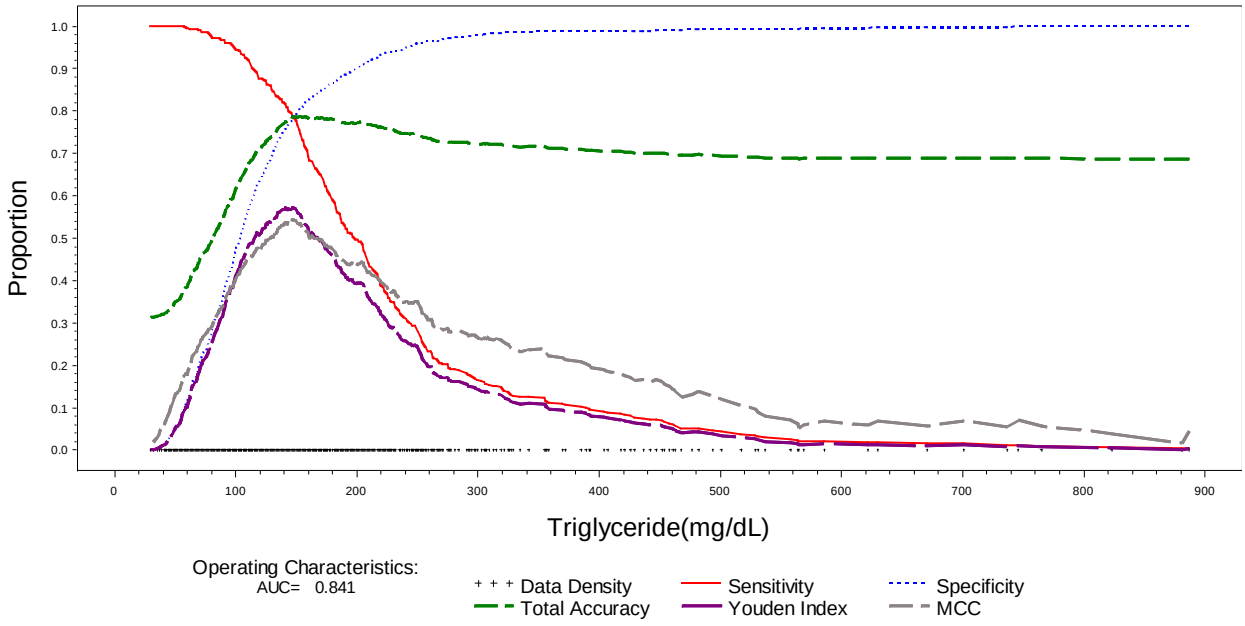

Figure 5. *Plots of sensitivity, specificity, Youden Index, Total Accuracy, and Matthew Correlation Coefficient for determining TG cutoff among MA's*

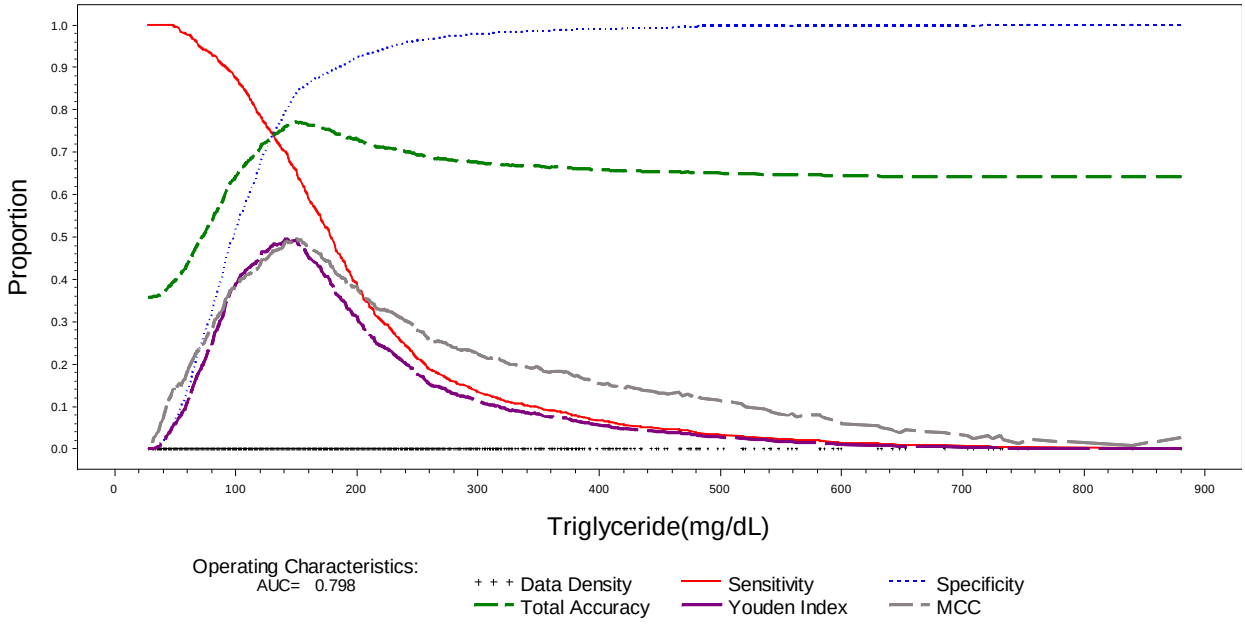

Figure 6. *Plots of sensitivity, specificity, Youden Index, Total Accuracy, and Matthew Correlation Coefficient for determining TG cutoff among NHW's*

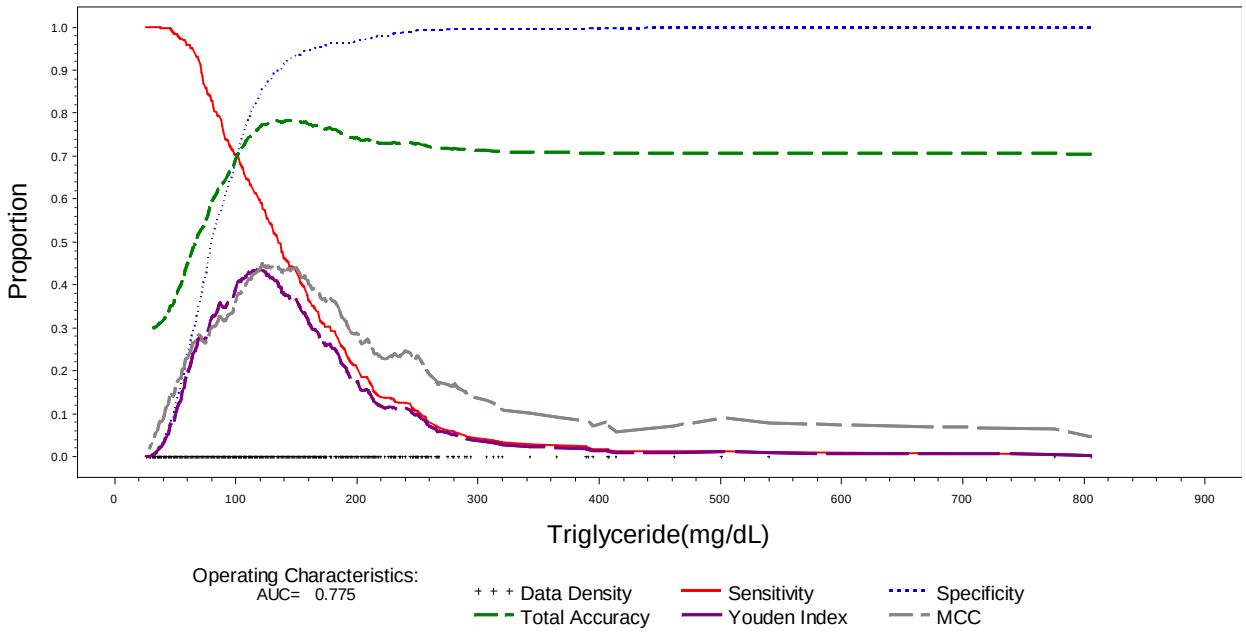

Figure 7. *Plots of sensitivity, specificity, Youden Index, Total Accuracy, and Matthew Correlation Coefficient for determining TG cutoff among NHB's*

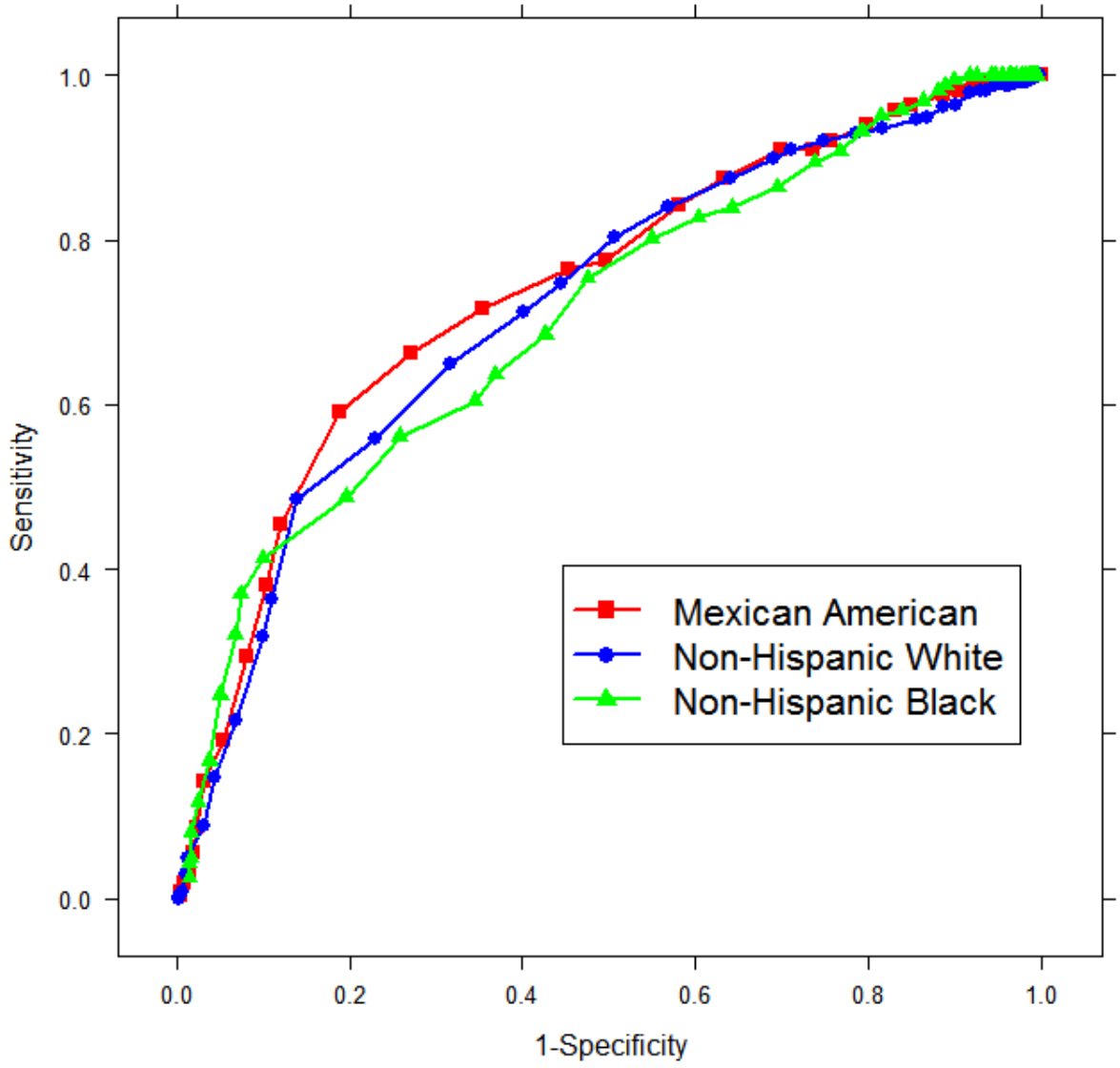

Figure 8. *ROC curve for HDL cutoffs in MA, NHW, and NHB males*

HDL cutoff values according to Youden Index calculation:
MA: 40 mg/dL
NHW: 40 mg/dL
NHB: 42 mg/dL

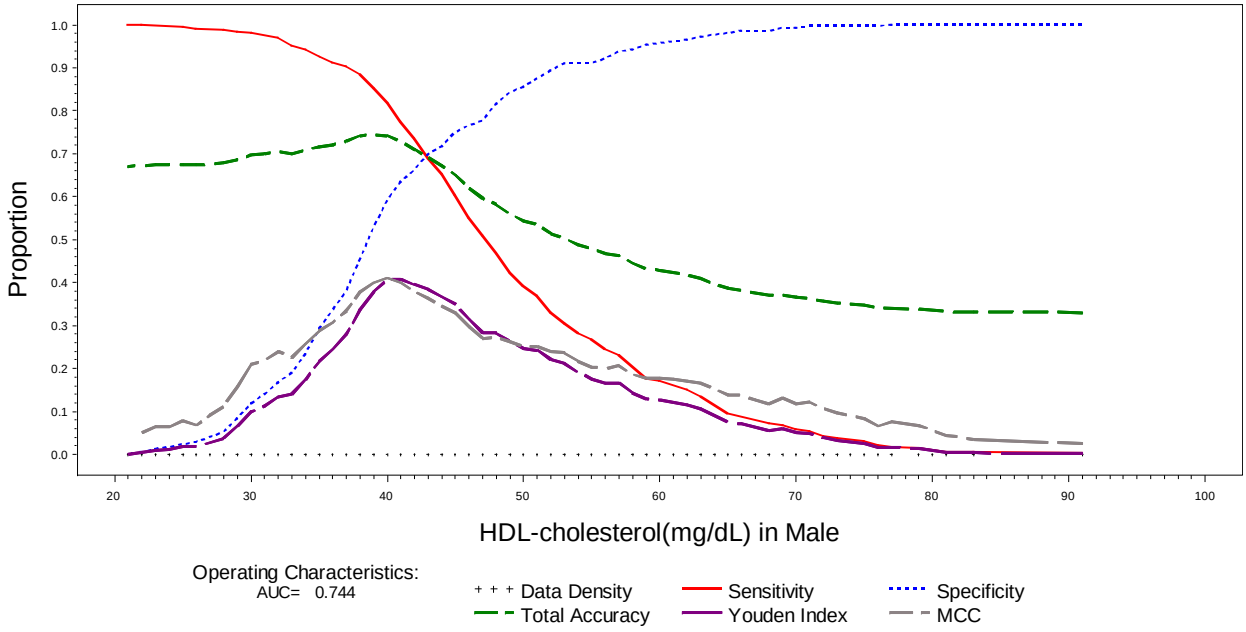

Figure 9. *Plots of sensitivity, specificity, Youden Index, Total Accuracy, and Matthew Correlation Coefficient for determining HDL cutoff among MA males*

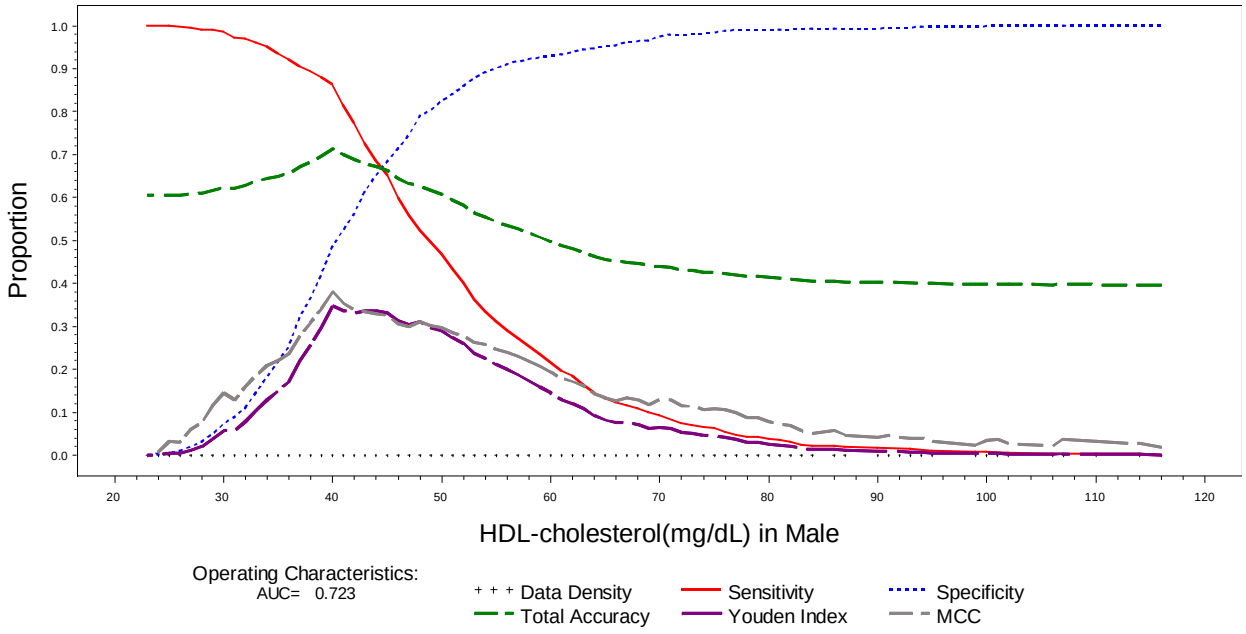

Figure 10. *Plots of sensitivity, specificity, Youden Index, Total Accuracy, and Matthew Correlation Coefficient for determining HDL cutoff among NHW males*

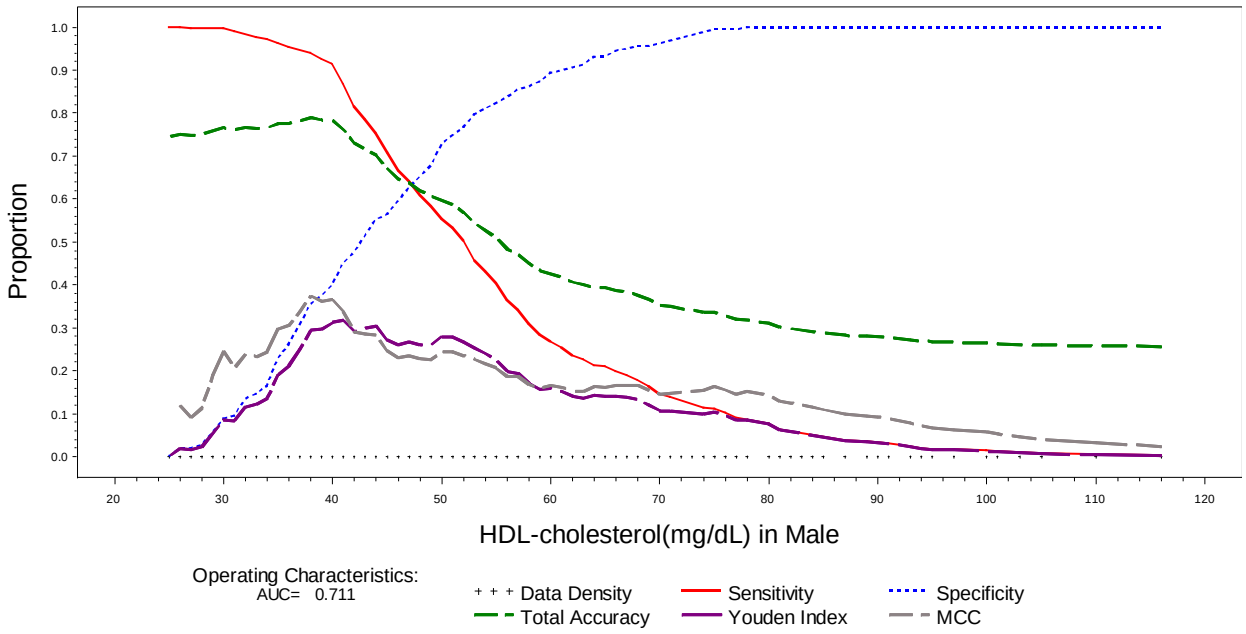

Figure 11. *Plots of sensitivity, specificity, Youden Index, Total Accuracy, and Matthew Correlation Coefficient for determining HDL cutoff among NHB males*

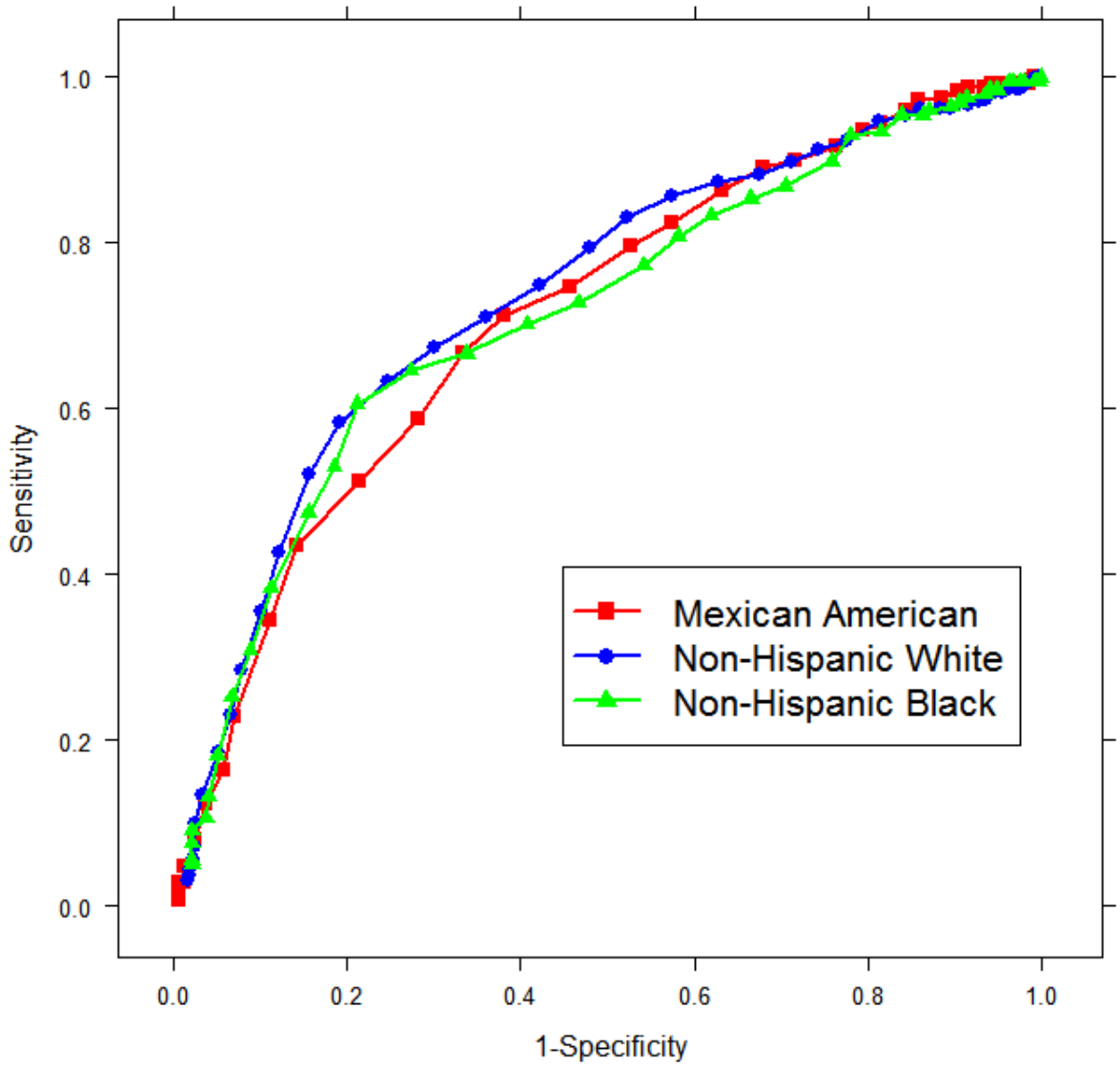

Figure 12. *ROC curve for HDL in MA, NHW, and NHB females*

HDL cutoff values according to Youden Index calculation:
MA: 50 mg/dL
NHW: 50 mg/dL
NHB: 50 mg/dL

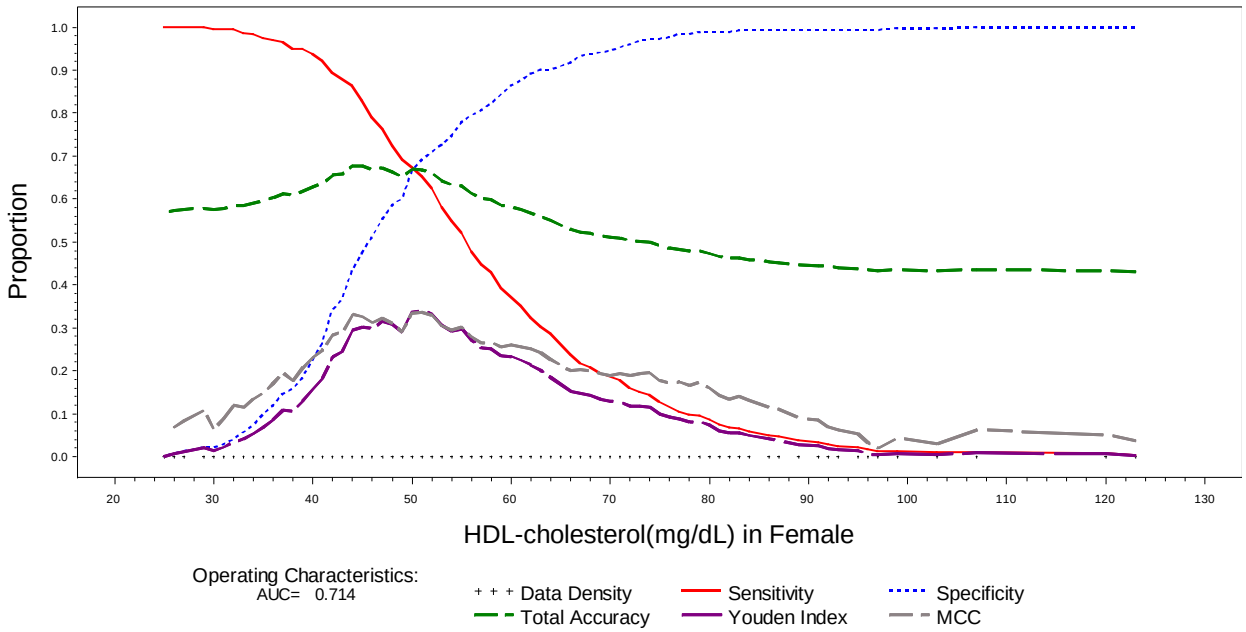

Figure 13. *Plots of sensitivity, specificity, Youden Index, Total Accuracy, and Matthew Correlation Coefficient for determining HDL cutoff among MA females*

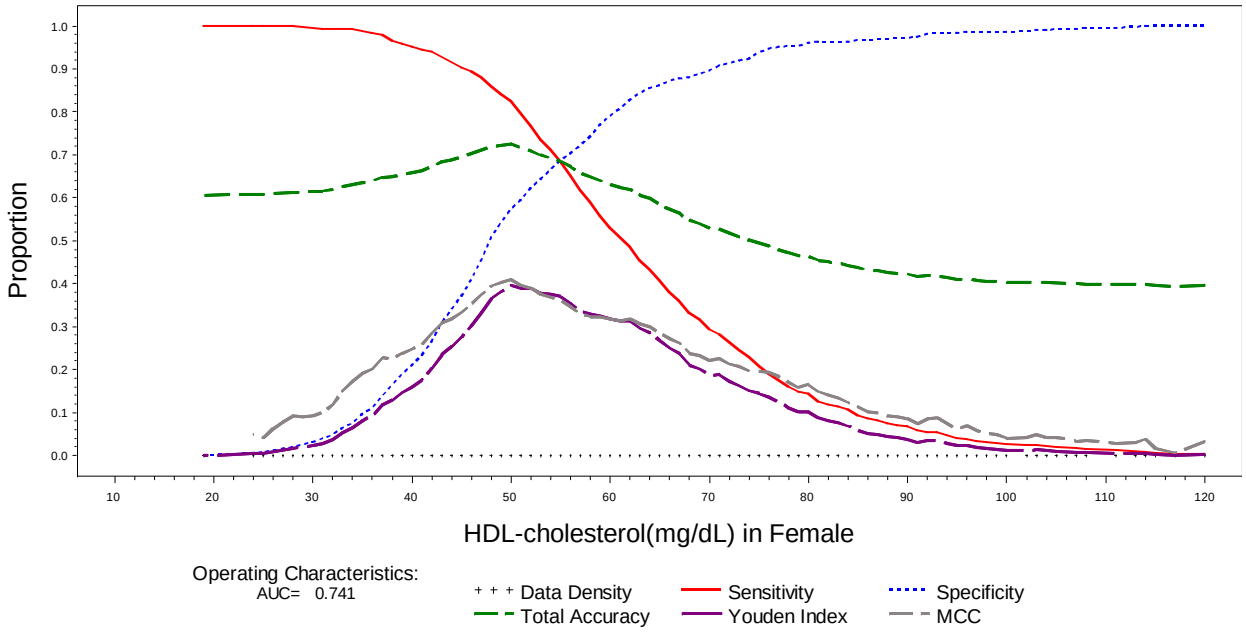

Figure 14. *Plots of sensitivity, specificity, Youden Index, Total Accuracy, and Matthew Correlation Coefficient for determining HDL cutoff among NHW females*

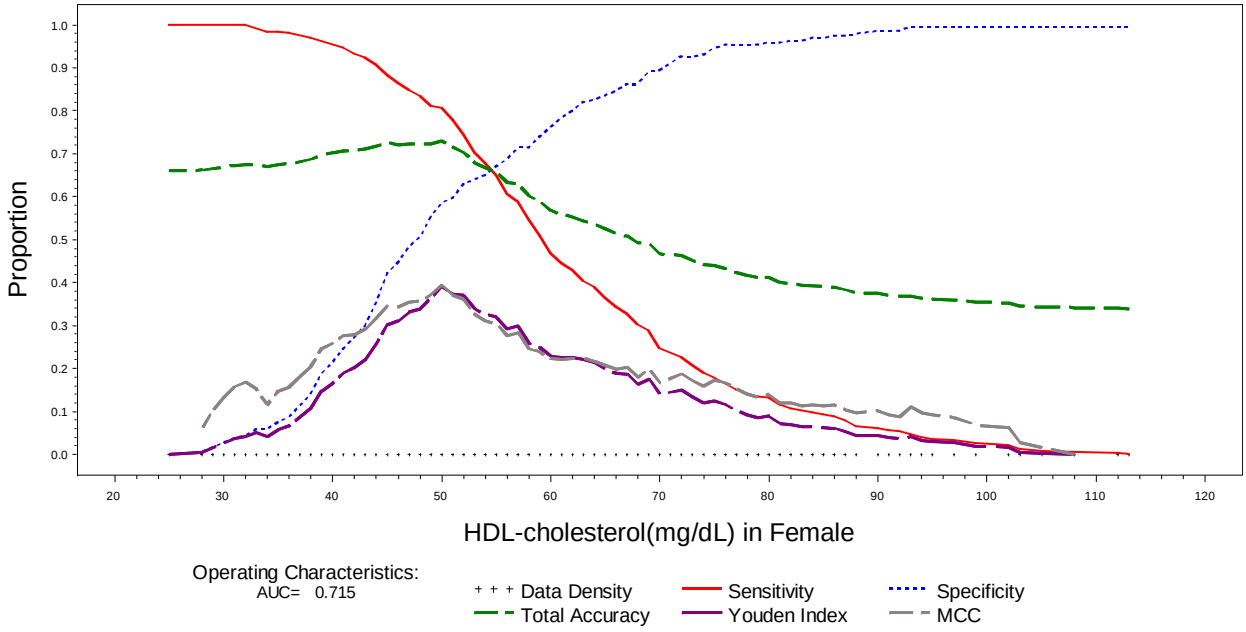

Figure 15. *Plots of sensitivity, specificity, Youden Index, Total Accuracy, and Matthew Correlation Coefficient for determining HDL cutoff among NHB females*

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