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The Role of Health and Diet in the Development of Metabolic Syndrome Stratified by Race, Sex, and Age

Michael D. Harada
Walden University

Walden University

College of Health Professions

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Michael D. Harada

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Review Committee
Dr. Lee Caplan, Committee Chairperson, Public Health Faculty
Dr. Xianbin Li, Committee Member, Public Health Faculty
Dr. Simone Salandy, University Reviewer, Public Health Faculty

Chief Academic Officer and Provost
Sue Subocz, Ph.D.

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Abstract

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Michael D. Harada

MD, Windsor School of Medicine, 2021

MPH, Walden University, 2014

MA, California State University Fullerton, 2004

BA, California State University Fullerton, 2000

BA, California State University Fullerton, 1993

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Public Health – Epidemiology

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Abstract

Obesity is now recognized as a disease in need of treatment by the medical profession and is associated with other chronic diseases including hypertension, hyperglycemia, hypertriglyceridemia, insulin-resistance, and reduced levels of high density lipoproteins. Metabolic syndrome (MetS) occurs when a combination of at least three of these chronic conditions are comorbid with each other. The purpose of this quantitative cross-sectional study was to find significant health and nutritional predictors of MetS status across race, sex, and age. The evolutionary mismatch hypothesis and health belief model provided the framework for this study. Data were collected from 2,303 participants from the 2015-2016 National Health and Nutrition Examination Survey. Findings show out of forty six variables associated with health and nutrition, four were significant predictors of MetS Status: triglyceride levels, insulin levels, testosterone levels, and vigorous recreational activities. The results showed the younger age groups had a lower prevalence of MetS compared to the middle-aged and elderly for both sexes and all race groups. Participants with MetS in the younger age groups had higher levels of triglycerides and insulin indicating poor diet. Testosterone levels in males with MetS were lower across all age groups and race compared to men without MetS. Middle-aged participants who engaged in vigorous recreational activity showed significantly less prevalence of MetS compared to those who did not. The results suggest that in order to prevent the financial costs and loss of quality of life from having MetS, the younger population must recognize that being overweight is the start of developing chronic diseases and to proactively monitor their diet and engage in physical activity to reverse unhealthy weight gain.

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Dedication

I dedicate this dissertation to all the healthcare professionals who have themselves dedicated their lives to heal their patient's diseases and improve their health through treatment and education. This study was conducted as the Covid-19 pandemic began across the globe. The infection rates and mortality statistics in the US exposed the healthcare disparities that have always existed across different levels of socioeconomic status. Covid-19's severity particularly struck Americans who were in poor metabolic health and with a high prevalence of obesity in the US, the need for public health to address this issue is only more prescient. As infections continue to decline, healthcare professionals have an opportunity to proactively educate their patients on how to maintain a healthy lifestyle so their futures can be free from chronic diseases.

Acknowledgments

I would like to acknowledge Dr. Lee S. Caplan (chair), Dr. Daniel Lee (committee member) and Jill Kaspszak (student advisor) for guiding me on this very long but worthwhile journey to reach this milestone, the completion of my dissertation. There were many detours on this long bumpy road and I lost my direction several times. However with the support of the Walden faculty, I was able to mend myself and get back onto the correct highways and finally made it to the end of my destination in good health. The journey was truly just as significant as reaching this academic milestone. Thank you Walden University.

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Chapter 1: Introduction to the Study

In 2013, the nation's largest physician group, the American Medical Association, recognized the detrimental health effects of obesity and officially classified obesity as a disease that needs medical treatment (Kyle, 2016). Obesity is an excessive accumulation of stored energy in the form of adipose tissue (body fat) located primarily in the abdominal region of the body. The etiology of obesity is complex, but is mainly caused by the overconsumption of calories, primarily in the form of fats, sugars, and refined starches without a concurrent fasted state where excess calories can be utilized for energy (Burn, 2021).

Chronic obesity is associated with other comorbidities including hypertension, hypertriglyceridemia, insulin resistance, and hyperglycemia. Eventually, obesity leads to the development of Type 2 diabetes mellitus (T2DM), atherosclerosis, and cardiovascular disease (CVD; Kumar, 2017). CVD remains the primary cause of all mortality in the United States, accounting for over 800,000 deaths per year (Benjamin, 2017).

The National Institutes of Health, which are part of the US Department of Health and Human Services, classify obesity based on a person's body mass index (BMI), which takes into account a person's height and weight. Obesity is defined as a BMI over 30 kg/m2, while a BMI in the range of 25 to 29 kg/m2 is classified as overweight (Jiang, 2016). Since the 1990s, there has been a rise in the rate of obesity among American adults which has now reached epidemic proportions, to the point where approximately two-thirds of all adults are either overweight or obese (Moore, 2017). At the same time, there have been increases in hypertension and T2DM.

Metabolic Syndrome (MetS) is defined as a cluster of at least three CVD risk factors that include abdominal obesity, elevated triglycerides, reduced levels of high-density lipoproteins, high blood pressure, and hyperglycemia (Zhang, 2016). These health conditions are all independent risk factors for CVD, but when they present as comorbidities with each other, their synergistic effects make the symptoms more severe and significantly increase the risk for premature death from CVD (Bonora, 2015). MetS is primarily driven by weight gain, making obesity the most prominent risk factor. Therefore, preventing MetS or reversing its effects can be achieved through proper dieting behavior (Han, 2016).

This chapter is organized into provides an overview of the dissertation. The first section provides the background of the study. I then present the problem statement and the purpose of the study. Following, I provide a description of the conceptual framework, the research questions and hypotheses, the nature of the study, and definitions of terms. Last, I discuss the study's assumptions, scope and delimitations, limitations, and significance.

Background

Though the components of MetS can develop independently, obesity is the disease that can be the starting point for hyperglycemia, hypertension, increased triglycerides, and low HDL. Through an inflammatory process, obesity is a cause of insulin resistance (IR). IR is the failure of cells to respond normally to insulin, leading to a decrease in the uptake of glucose by cells, thereby leaving more in the bloodstream. Without dietary intervention, hyperglycemia then develops into adult onset T2DM. There

are many pathologies associated with diabetes that affect different organ systems, and depending on the severity of diabetes progression, a person's quality of life (QoL) can significantly be reduced (Balderston, 2013). Obesity is also a factor in the development of hypertension. Stage 1 hypertension is defined by a systolic blood pressure from 130 to 140 mmHg or diastolic pressure from 80 to 89 mmHg (Whelton, 2018).

Hypertension develops from obesity through the activation of the sympathetic nervous system, development of atherosclerosis, and stimulation of the kidneys to reabsorb sodium and water (Jiang, 2016). Hypertension can also develop independent of obesity through high salt intake (Mahmoodabad, 2016).

Data from the National Health and Nutrition Examination Survey (NHANES) showed that MetS prevalence in the United States increased from 25.3% in the time period 1988 to 1994 to 34.2% in the time period 2007 to 2012 (Moore, 2017). During the interval between these two time periods, every category of the demographic variables, including age, race, and sex, showed an increase in MetS prevalence, with the greatest increases seen in non-Hispanic black men (from 15% to 26%), non-Hispanic black women (from 24% to 34%), and non-Hispanic white women (from 25% to 35%). Furthermore, obesity was the most common symptom seen in NHANES participants with MetS. However, there were nonobese participants who still met the requirements for a MetS diagnosis. The prevalence of nonobese MetS participants held steady at approximately 16% for both time periods.

There is a wide range of MetS prevalence when stratified by age. In the 2007 to 2012 NHANES data, the 18 to 29 age bracket showed the lowest prevalence with

approximately 9% for all race groups. There was an increasing trend for MetS prevalence with increasing age, from the 50 to 69 age group which had a prevalence ranging from 40% to 55% to the 70 and over group which had a prevalence range of 60% to 70%. Therefore, the 34.2% overall MetS prevalence of the American adult population masks the high MetS prevalence seen in adults over age 50 (Moore, 2017).

With well over half of older Americans suffering from this debilitating condition, research is needed to classify and quantify behaviors related to the development of MetS. Both increased awareness of MetS and knowing specific behaviors to decrease the risk of its development are what is needed to prevent MetS. Ideally, when any one of the MetS symptoms is first observed, preventive behaviors should be started to stop the development of MetS.

There are items in the NHANES self-questionnaire that ask for the duration and number of times per day for engaging in physical activities such as walking or bicycling, and also for engaging in sedentary activities such as television watching and computer usage. Identifying the behaviors that differentiate MetS status from this self-questionnaire section can provide more information for future public health prevention strategies. In other words, analyzing data that contain the same set of health and diet-related questions for those who either have MetS or do not, this study can help discern what people who have MetS are doing differently compared to those who do not. Furthermore, the results for each of the significant predictor variables were stratified by age, race, and sex. Since MetS is more prevalent in different groups, when the results are stratified by demographics, a more accurate evaluation can be made to identify the risk factors

specific for each demographic group. These results can be used in future population-based intervention efforts to prevent all the components of MetS before they develop.

Problem statement

With an estimated MetS prevalence in the United States of 33%, which is skewed to the middle-aged and older populations, MetS is a significant health and financial burden affecting the QoL of those who suffer from it, older Americans in particular. Therefore, the public health strategy to decrease the prevalence of MetS in the older age groups should focus on how to prevent MetS incidence in the younger age groups, especially those who are susceptible to MetS. The problem of recognizing the development of chronic diseases is that their symptoms often do not appear acutely, but only after physiological damage has occurred (Kovesdy, 2017).

To understand how MetS develops over a time period, those behaviors seen across all age groups that are different between those who have MetS and those who do not were identified in this study. If the behaviors of those who have MetS are also seen in the younger age groups who do not have MetS, then that is an indication for behavioral change. Since less than 10% of young adults have MetS, approximately 90% do not. It would be to the benefit of public health to keep the younger population, which is largely free of chronic disease, from developing MetS as it ages. The younger population that has not developed any of the risk factors that make up MetS can remain symptom-free if a set of dietary and physical activity behaviors are consistently performed over their lifespan. Healthy young adults can remain so, even into their elderly years.

Purpose

The purpose of this study was to identify the behavioral risk factors for developing MetS. The variables of interest were taken from the dietary and lab questionnaire sections of the NHANES survey. Questions include behavioral, dietary, and health-related topics. The risk factors that were found to be significantly associated with MetS were then stratified by age, sex, and race to identify what group is most affected by MetS. I analyzed data from the 2015-2016 NHANES in a quantitative fashion and utilized inferential statistics to conduct this study.

Framework

This study utilized one health theory and one concept from biology to guide it, the health belief model (HBM) and evolutionary mismatch. The HBM is a well-known, established health theory that can be applied to many settings because it attempts to explain why people will or will not engage in behaviors that will benefit their health. The HBM describes the likelihood of engaging in a health promoting behavior along four dimensions: perceived severity, perceived susceptibility, perceived benefits, and perceived barriers (Janz, 1984). These dimensions describe how and when a person will be ready to act to prevent a disease from occurring. The HBM was initially developed to explain why Americans were not participating in preventive screening for tuberculosis. More recently, the explanatory power of the HBM has often been used to describe noncompliance behaviors in regard to the managing or prevention of other diseases (Souza, 2009).

The evolutionary mismatch concept holds that genetic evolution has not kept pace with the relatively recent changes in our modern environment, especially in Western culture where high caloric foods and jobs that require minimal physical exertion are readily available (Grey, 2018). For most of modern human history, humans have lived as hunter-gatherers across all continents, with the exception of the Antarctic. Over thousands of years, humans have had to adapt to vastly different natural environments, including deserts, rain forests, woodlands, and the Arctic tundra to survive and reproduce (Liberman, 2013).

Periods of food scarcity were routine, which forced humans to engage in physically taxing hunting. As a means of survival, humans evolved to have a taste preference for foods that are sweet with sugar. The natural food sources that contain sugar and would be readily available in the environment would have been fruits and honey. The sugar in fruits and honey gives immediate energy, and any excess glucose can be processed and stored as abdominal fat to be used as an energy source in times of food scarcity. Thus, abdominal fat in times of food scarcity was an advantage, not a health risk, in human history. However, in today's environment, previously adaptive traits are no longer favored for survival. The lifestyle of today's American population that includes high caloric meals, processed foods, and low energy output predisposes the body to obesity because our bodies have been adapted to efficiently store unused energy in the form of abdominal fat (Konner, 2010).

This concept of evolutionary mismatch is important for the present study because prevention strategies should be seen within the context of how there is a mismatch

between what our bodies have been adapted for and how today's environment readily provides high carbohydrate and high caloric foods without the need for hunting. In developed nations, there is an expectation that public health and government agencies will provide safe and sustainable home and work environments in which to live (Schneider, 2017). This is in stark contrast to how our paleolithic ancestors once lived (Koopman, 2016).

Research Questions

Research Question 1: Will any of the following health and behavioral variables significantly predict MetS status: alcohol use, cardiovascular health, hormone levels, consumer behavior, recreational drug use, food security, insurance, immunizations, income, medical conditions, medications, physical activity, smoking, sleep, and diet?

$H_0$1: None of the health and behavioral variables will significantly predict MetS status.

H_a1: Some or all of the health and behavioral variables will significantly predict MetS status.

Research Question 2: Do the significant predictors of MetS differ among age groups, sex, and ethnicity?

$H_0$2: The significant predictors of MetS do not differ among age groups, sex, and ethnicity.

H_a2: The significant predictors for MetS will differ among age groups, sex, and/or ethnicity.

Nature of the Study

The NHANES is a cross-sectional survey and as such allows for estimates of prevalence values at the time of measurement. This study used the 2015-2016 NHANES data as secondary data and was quantitative in nature. A logistic regression was used to identify which variables significantly predict MetS status (have MetS or do not have MetS). Based on the logistic regression results, I calculated odds ratio values and also stratified the results based on demographics.

My null hypothesis was that there is no association between MetS status and the NHANES questionnaire variables. My alternative hypothesis was that the NHANES questionnaire variables are not able to predict who has MetS and who does not. The HBM and mismatch concept guided my discussion as to why some people fall into states of chronic disease while others do not and also enabled me to suggest possible methods and policies to prevent MetS from developing.

Definitions

Evolutionary Mismatch Hypothesis: This concept holds that adapted traits that were selected from past environments to maximize the fitness for survival and reproductive success of an organism are no longer favored in a different environment (Manus, 2018). In regard to humans, the genetic make-up of humans of the paleolithic era has not kept pace with the rapid change of today's modern environment which has resulted in maladaptive behaviors leading to chronic diseases (Liberman, 2013).

Adult Body Mass Index: Body Mass Index (BMI) is a person's weight in kilograms divided by the square of height in meters. A BMI less than 18.5 is considered

underweight. A BMI from 18.5 to <25 is the normal range. A BMI from 25.0 to <30 is the overweight range. A BMI of 30.0 or higher is considered obese (CDC, 2020a).

Obesity: A BMI of 30.0 or higher is considered obese and is divided into three classes. Class 1 is a BMI from 30.0 to <35.0. Class 2 is a BMI from 35.0 to <40.0. Class 3 is a BMI equal to or greater than 40 and is considered to be a severe form referred to as morbid obesity (CDC, 2019a).

Blood Pressure: Blood pressure (BP) is the force of blood pushing against the walls of the arteries as blood is pumped throughout the body. BP is measured using two parameters, systolic and diastolic pressure. Systolic BP is the pressure in blood vessels when the heart beats. Diastolic BP is the pressure in the blood vessels when the heart rests between beats. BP is measured in millimeters of mercury (mmHg) (CDC, 2020b).

Hypertension: Stage 1 hypertension is defined by a systolic BP from 130 to 139 mmHg or diastolic pressure from 80 to 89 mmHg. Stage 2 is defined as systolic pressure 140 or higher or diastolic pressure 90 or higher (American Heart Association, 2019).

HDL: High density lipoprotein is a carrier molecule that transports cholesterol from tissues and blood vessels back to the liver for storage or disposal. HDL also transports cholesterol to the adrenal glands, ovaries, and testes for the synthesis of steroid hormones. HDL levels greater than 60 mg/dL are high, and levels less than 40 mg/dL are low. Low levels of HDL is considered a risk factor for atherosclerosis, the build-up of cholesterol filled plaque in the arteries (Ferrier, 2014).

Atherosclerosis: A blood vessel disease characterized by plaque lesions of the artery that protrude into the lumen of the arterial vessel. The plaque consists mostly of

cholesterol, foam cell macrophages, calcium, and cellular debris covered by a fibrous cap. This plaque can rupture and form a blood clot called a thrombosis and block blood flow to the heart leading to coronary artery disease (Kumar, 2017)

Metabolic syndrome (MetS): A cluster of different metabolic disorders when presented together pose a significant risk for cardiovascular disease compared to when each disorder presents alone. The American Heart Association defines MetS as having three or more of the following conditions: abdominal obesity (waist circumference of greater than 40 inches in men, and greater than 35 inches in women), a triglyceride level of 150 mg/dL or greater, an HDL level less than 40 mg/dL in men or less than 50 mg/dL in women, systolic blood pressure greater than 130 mm Hg or diastolic blood pressure of 85 mm Hg or greater, and a fasting glucose level of 100 mg/dL or greater (American Heart Association, 2019).

Assumptions

Several assumptions are made regarding the collection of the data. Data were collected by the CDC staff for the 2015-2016 NHANES. Interviews were conducted at participants' homes, and physical examinations were done in trailers. I am assuming the CDC staff collected interview and lab data in a valid and reliable manner. The annual NHANES protocol changes periodically to sample larger numbers of subgroups that are of interest to public health, such as racial minorities. Therefore, I assumed the data from the participants was a representative sample of the noninstitutionalized U.S. population. As such, I can generalize the results regarding the risk factors influencing metabolic disease to the larger population.

Scope and Delimitations

The 2015-2016 NHANES collected data from over 10,000 people across 30 locations in the United States. I analyzed data from 6,113 participants, 18 to 80 years of age. The NHANES target sample is meant to be representative of the noninstitutionalized civilian resident population of the United States in terms of age, race, and sex. To get an accurate representation of this population, there was heavier sampling of racial minorities, lower income populations, and older adults (CDC, 2019). Staff hired local translators when necessary to communicate with non-English speakers and also used professional medical interpreter phone services when local translators were not available.

Limitations

NHANES did not specifically classify MetS as a variable in the dataset. There are collected data on weight, waist circumference, BMI, glucose levels, HDL levels, triglyceride levels, and blood pressure. I created a new variable and operationalized MetS in the present study. Since obesity and hyperglycemia are the main topic of this study as a precursor to MetS, I defined MetS using a BMI > 30.0 and a waist circumference over 40 inches as requirements, in addition to high blood pressure and hyperglycemia.

Significance of the Study

The significance of this study regarding positive social change is to increase awareness in Americans of all ages that there are long-term detrimental consequences from an unhealthy lifestyle, but that these consequences can be prevented through proactive behaviors. The current life expectancy in the US is 78.6 years (Murphy, 2016), and how we manage our health over our lifespan determines the QoL we will experience

in old age. The phenomenon of aging is an inevitable part of life; aging is not seen as a disease in medicine and therefore has no cure (Trevisan, 2019). There are many cellular age-related degenerative changes that cannot be stopped and will eventually lead to death (Bhar, 2016).

The 2015-2016 NHANES includes data on demographics, dietary habits, and health, as well as laboratory and physical examination data. Analyzing responses from participants helped gain more information about risk factors for MetS and also provided more specific guidelines as to what behavioral changes are needed to prevent MetS development. Past public health initiatives have not curtailed the increase in childhood obesity, with rates increasing in all age groups over the last 2 decades (Skinner, 2018). As obesity is a precursor to T2DM, the incidence of MetS closely parallels the incidence of both obesity and T2DM (Saklayen, 2018). With rates of obesity still increasing, there is no indication that MetS incidence will decrease in the near future. This is why education and awareness about dietary health and physical activity are key to preventing the development of obesity and its downstream effects.

Summary and Transition

Recognizing that obesity has risen to epidemic levels in the US and its detrimental health consequences, the American Medical Association has classified obesity as a disease (Kyle, 2016). Seventy percent of Americans are either overweight or obese, while 40% of Americans meet the criteria for obesity (CDC, 2019). The causes of obesity are multifactorial, including genetic, environmental, and behavioral factors, but overconsumption of calories, primarily in the form of processed foods with high sugar

and fat contents contribute to gaining excess weight. When coupled with a sedentary lifestyle, the calories from food are stored away as visceral fat surrounding organs located in the abdomen. Obesity is associated with other noncommunicable diseases such as hypertension, high levels of total cholesterol, and hyperglycemia. MetS arises when these conditions present at once and becomes a strong risk factor for heart disease. Heart disease remains the primary cause of death for Americans, with mortality reaching over 600,000 deaths per year (CDC, 2019).

The prevalence of MetS in the US is 33% and is skewed toward Americans over the age of 50. Since the components of MetS are chronic noncommunicable diseases, they can be prevented so that MetS never develops in the first place. This study explored which behavioral and dietary variables taken from the CDC's 2015-2016 NHANES significantly predicted MetS status. These variables were then stratified by demographics to determine which groups are most susceptible to MetS, so that recommendations to prevent MetS can be made. In Chapter 2, I will provide a background on each of the components of MetS, how each can develop from obesity and independently, and how each can be prevented.

Chapter 2: Literature Review

In this literature review, I will review and assess the development of the obesity epidemic and MetS from a macro perspective of how academic research, governmental policies, and dietary recommendations possibly led to the current obesity epidemic. I will also describe how obesity develops into MetS on an individual level through multiple physiologic processes. I will focus on past historical research and also current medical journals that explain the cellular mechanisms and pathology of fat storage from excessive amounts of sugar leading to heart disease. For example, in 2016, an article was published in JAMA about recently discovered documents describing how the sugar industry influenced academia and the US government by downplaying the effects of sugar consumption on the development of heart disease (Kearns, 2016). These documents shed light on how the dietary recommendations made by the US government may be biased and outdated. I will also review current research on modern-day hunter-gatherers living in South America and Africa and compare and contrast their health and lifestyle with Americans.

Literature Search Strategy

I used several strategies for collecting the necessary information for my literature review. To collect peer-reviewed journal articles for the present study, I used Walden Library's EBSCO database under the topic of health sciences. My study covers various health topics, so EBSCO's multiple database library was a practical source to use. EBSCO databases include MEDLINE, CINAHL (Cumulative Index to Nursing & Allied Health Literature), ProQuest Health & Medical Collection, ProQuest Nursing & Allied

Health Source, and PsycINFO. I set the search option to use the most recent journal articles; however, there were several historical articles dating to the 1950s that I also needed. I was able to obtain all the journal articles I wanted using the EBSCO databases.

The topics for my study included metabolic syndrome, obesity, heart disease, human evolution, modern-day hunter-gatherers, public health, government policies in diet, and historic research in heart disease. . I used and cited medical textbooks that were necessary to explain specific cellular mechanisms.

The keywords that I used for my search included:

- *Adipocytes*
- *Ancel Keys*
- *Atherosclerosis*
- *Cholesterol transport*
- *Food pyramid*
- *Glucose and fructose metabolism*
- *Health Belief Model*
- *Heart disease*
- *Human evolution*
- *Hunter-gatherers*
- *Hyperglycemia*
- *Hypertension*
- *Lipid metabolism*
- *Metabolic Syndrome*

- *Mis-match diseases*
- *Obesity prevalence*
- *Resistance training*
- *Sugar research*
- *Triglycerides*
- *Visceral fat*

Theoretical Framework

This study utilized the health belief model (HBM) and the concept of evolutionary mismatch as a theoretical framework to guide what past research to summarize, what variables to analyze, and how to interpret results from statistical analysis.

The focus of medicine today regarding metabolic chronic disease is on treating its symptoms, which involves mostly drugs, surgery, and long-term hospice care while not preventing the root causes (Wells, 2017). To understand why people in industrialized nations develop noncommunicable, chronic disease when they were in previously good health, it is necessary to understand their behavior and the health decisions they have made for them to slowly develop metabolic disorders. The new discipline of evolutionary medicine is helping public health scientists understand why children and adults are now more susceptible to developing chronic, noncommunicable diseases by framing such diseases as a consequence of behaviors and conditions that our human ancestors did not experience.

In 1973, geneticist Theodosius Dobzhansky wrote an article entitled “Nothing in biology makes sense except in the light of evolution.” In it, Dobzhansky criticizes

religious views on creationism and defends the concept that the diversity of life is explained by evolution (Dobzhansky, 1973). Dobzhansky's viewpoint, that evolution shaped the traits that humans and all animal life possess today, can also be applied to public health by helping to explain the etiology of obesity, T2DM, CVD, and other ''diseases of affluence'' seen in the US and other developed countries. A tenet of evolutionary theory is that organisms are selected to allocate their time and energy to maximize reproductive success, so their respective species can continue in greater numbers after individual lifespans have been completed (Pontzer, 2015). This same principle applies to the evolution of humans. The human body has been shaped through natural selection to survive the dynamic and wide range of environmental conditions in which modern humans have lived. Past homo genus populations also existed and lived in multiple continents, but none survived and are extinct. Homo sapiens are the only human species to survive and exist today. However, evolution is slow and the recent and rapid changes to the environment within the past century are not always compatible with the traits humans have developed to survive previous natural environments.

Identifying biological traits and behaviors that were once advantageous could improve the effectiveness of public health strategies targeting obesity and heart disease. By using an evolutionary perspective, public health can explain why certain behaviors are harmful and can also predict physiological outcomes. Being able to predict the severity of chronic disease would be helpful to address the metabolic consequences of poor health behavior across different demographics (Wells, 2017). Anthropological studies on modern day hunter-gatherers in South America and Africa offer a unique method to

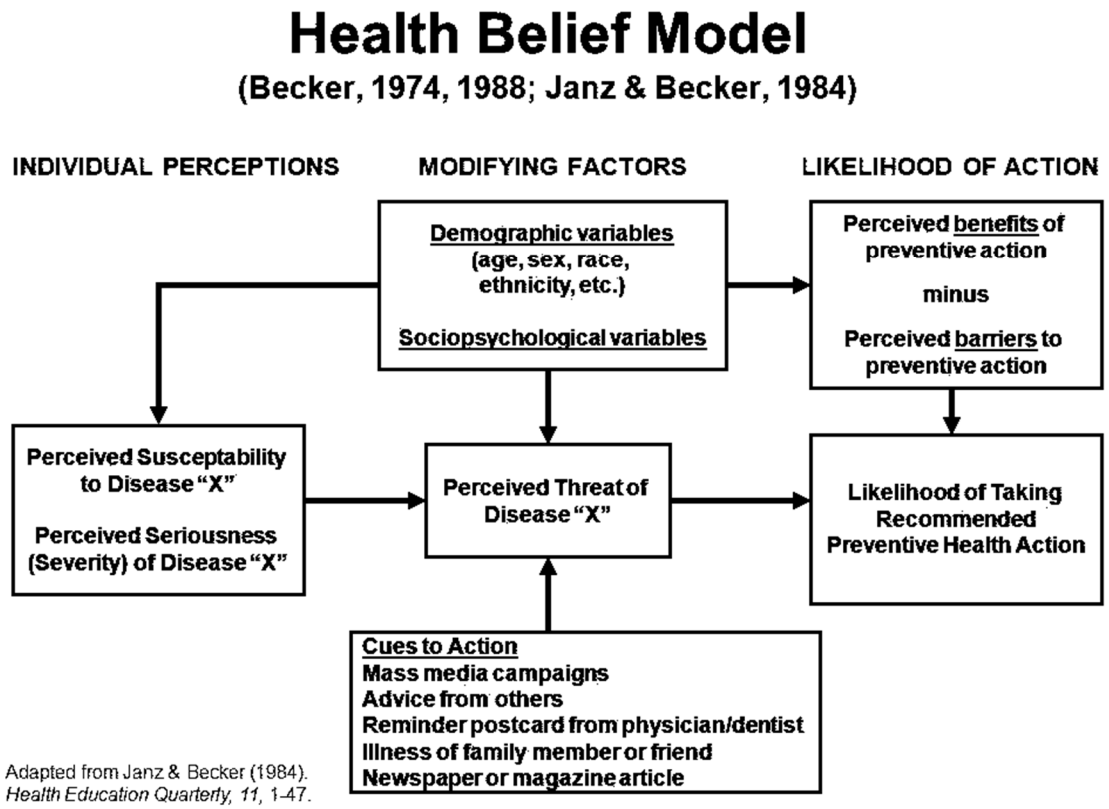
understand the root evolutionary causes of noncommunicable diseases. These indigenous populations are remarkable for having excellent metabolic and heart health while concurrently suffering from constant inflammation from infectious parasites. An approach that combines modern medicine with identified hunter-gatherer behaviors associated with excellent metabolic health would help to guide future public health and other governmental policies.

Two-thirds of Americans are overweight or obese, and for this population to change its behaviors towards reducing their weight, they first have to make a conscious decision to do so. There may not be overt symptoms relating to obesity, so those who are obese and overweight may not be aware of their ill health. To recognize that their weight is a serious health problem, they need to be knowledgeable of the subsequent complications from continued weight gain.

As shown in Figure 1, the HBM explains and predicts why people seek preventive screenings or treatment for diseases based on perceived susceptibility and harm and also the effective benefits in health improvement weighed against the barriers to seeking treatment or screening. Cues to action act as stimuli to decision making by providing information about a disease, while a person's individual socioeconomic status and demographics also influences their perception of the threat of a disease (Janz, 1984).

Figure 1

Dimensions of the Health Belief Model



Note. From *"Community Health Nursing. Promoting Health of Aggregates, Families and Individuals* (4th ed.)" by M. Stanhope & J. Lancaster, 1996, Mosby.

In the present study, conclusions and recommendations to prevent MetS from ever developing were based upon the dimensions of the HBM. The HBM has been applied to people with chronic diseases, including those with obesity, to have a positive effect on lifestyle changes (Abdeyazdan, 2017). In the present study, perceived susceptibility would be how one recognizes the vulnerability that obesity can lead to the components of MetS and ultimately heart disease. The perceived threat of obesity would be how severe each of these conditions could become if left untreated. Recognizing the value of being

healthy versus living with detrimental ailments from obesity is the perceived benefit. Perceived barriers might include resistance to diet change, reducing food intake, and increasing physical activity. Cues to action would include sources of available information about the health risks of obesity, such as visits to the doctor, advice from friends, and the news media.

Fats Vs Cholesterol as the Cause of Heart Disease

The epidemiology of the current obesity epidemic in the American population is complex. In addition to poor dieting habits (eating increased size meals, at restaurants, ready-made dinners) and reduced levels of physical activity, the multiple causal factors include biochemistry, neuroendocrinology, prenatal health, psychology, culture, and environmental factors (Lustig, 2012). Obesity was not a national health problem for much of the 20th century but then in the early 1980's obesity rates started a continual rise with no decline that continues to the present. As seen in figure 2, the rapid increase in prevalence that began in the early 1980s has since not reached a plateau. The nation's obesity prevalence is nearing 40% according to the most recent NHANES data. That equates to approximately 93 million adults and 14 million children (NCHS, 2017). The rapidity of such an increase from under 15% for most of the century to the current prevalence of almost 40% would suggest an environmental factor as the primary cause. Current obesity research points to the overconsumption of sugar, specifically high fructose corn syrup (HFCS) as one of the primary sources of obesity (Bray, 2004).

One possible reason why sugar has not been seen as the primary driver behind obesity and MetS and consequently heart disease is the dietary recommendations made

by the US Department of Agriculture (USDA), whose policies still influence the food industry and thus the American diet today. The USDA published the first edition of the Dietary Guidelines for Americans in 1980, but it based its' research on potentially biased and erroneous conclusions. The primary recommendation of the dietary guidelines was to eat a low fat, complex carbohydrate diet.

The nutritionists whom the USDA based their decisions on were initially researching the reasons behind why there was such a high rate of death from heart disease during the 1950's. In the 1950's, there was a sudden rise in heart attacks, and prominent nutritionists took interest into the causes of heart disease. Death from heart disease was not common in the early 20th century, as compared to infectious diseases. However, by midcentury, with better standards of living and vaccinations available, heart disease replaced infectious diseases as the leading cause of mortality. The death rate from heart disease peaked in 1965 at 600 deaths per 100,000 and has steadily declined to the present (Dalen, 2014). Though heart disease is still the leading cause of death in the US, the death rate from heart disease is now at its lowest since 1965. The most recent estimate of deaths due to heart disease is 165.0 per 100,000 in 2017 (CDC, 2019). This decrease is best explained by better primary prevention and better medical technology and drugs to treat patients with heart disease and those who have suffered from myocardial infarctions.

The root cause of death from a myocardial infarction is coronary atherosclerosis. Atherosclerosis is the plaque build-up in the arteries that impedes blood flow to the heart. As the plaque grows larger, it will cause a lack of blood flow in the diameter of the artery. The plaque can then rupture and travel to the coronary arteries and stop the supply

of oxygen delivered to the heart cells, which it needs for energy to perform its pumping function. A myocardial infarction is the result when the heart can no longer pump due to lack of oxygen. Prominent nutritionists working in the 1950's to the 1970's were exploring the dietary causes of atherosclerosis, and they were not always in agreement in their conclusions. Nevertheless, the USDA and US Congressional leaders in the 1970's had to make a decision on whose research to base their recommendations on.

Figure 2

Obesity Prevalence in the United States

One prominent American nutritionist was Ancel Keys. During World War II, the military assigned Keys to develop non-perishable, ready-made meals that could be shipped and stored for up to two weeks for thousands of soldiers. These pocket-sized meals were called K-rations and were a success for the military (Shanahan, 2016). After WWII, the Minnesota Department of Health hired him to research the causes of heart disease. This is where he began his Seven Country study which led to his diet-heart hypothesis. He collected data from seven countries, Japan, Italy, Greece, Finland Yugoslavia, the Netherlands, and the US and measured the amount of dietary fat and

death rates from heart disease. He plotted the data and found that the two countries with low levels of fat intake, Japan and Italy, had a lower death rate compared to other countries that had higher levels of fat intake. Based on this strong correlational data, Keys concluded that diets high in saturated fats raise serum cholesterol, which contributes to the development of atherosclerosis and heart disease. This conclusion was known as the diet-heart hypothesis. He therefore recommended a diet low in saturated fats and cholesterol under the assumption that lowering saturated fat intake would protect against the development of atherosclerosis.

However, Keys purposely left out 15 countries where data regarding fat intake and death from heart disease were available but would have made his correlation weak when plotted with the seven countries he chose. There were other countries with high fat intake but with a low death rate from heart disease. A plot of all 22 countries shows a random pattern, not one with a strong positive correlation between fat intake and heart disease. This means that an accurate prediction of heart disease cannot be made based on fat intake (Shanahan, 2016). Despite criticisms for his data manipulation, Ancel Keys became an influential figure in nutrition, and his work became a cover story for Time Magazine in 1961, the same year in which he was appointed to the American Heart Association nutrition committee (Page, 1961).

Current research shows more conflicting views on what fat does to health because there are several types of fats, some of which can be healthy. Ancel Keys used cholesterol as a biomarker for heart disease but did not show experimental proof that cholesterol itself was the cause of death from heart disease. Though the chemical

structure of cholesterol is the same, it is packaged into specialized proteins called lipoproteins known as high-density lipoproteins(HDL) and low-density lipoproteins (LDL). These lipoprotein carriers determine to where the cholesterol is transported. LDL particles travel from the liver to different tissues in the body and deposit cholesterol into cells with LDL receptors, while HDL returns excess cholesterol back to the liver to be removed from the body (Kumar, 2008).

Evidence for why LDL cholesterol is seen as a cause of heart disease comes from a genetic disease called Familial Hypercholesterolemia (FH). In FH, there is a mutation to the gene that codes for the LDL receptor. Located on chromosome 9, the mutation can lead to five subtypes of FH that differ in severity. The most severe form is called class I, where the LDL receptor is not made at all. This results in the accumulation of LDL cholesterol in the blood because the body's cells that need cholesterol cannot absorb LDL, and the liver continuously produces more LDL, because it senses that other cells need cholesterol. This results in atherosclerosis at an early age, and heart attacks are seen in people with this mutation in their 20's (Nair, 2013).

Evidence contradicting Key's conclusion came from a prospective study done in France in the early 1990's called the Lyon study. This study explored the effects of a Mediterranean- style diet compared to a low-fat diet. The Mediterranean diet is one that emphasizes healthy fats, such as olive oil, with seafood, fruits, vegetables, whole grains, legumes, and nuts. Red meat is to be eaten only occasionally. Participants eating the Mediterranean-style diet were dying at a significantly lower rate than the participants in the low-fat diet group, but the cholesterol levels in the Mediterranean diet group did not

change from the start to the end of the study. The principal investigator of the study, Michel de Lorgeril, believed that the protective effects of the Mediterranean diet were not related to serum cholesterol but to the high concentration of omega-3 fatty acids found in seed oils, meat, cereals, green leafy vegetables, and fish. The study therefore concluded that deaths due to heart disease were independent of cholesterol levels, as lowering cholesterol in the diet did not lower the risk for heart disease (Lorgeril, 1994).

Another reason why focusing on fats and their effects on cholesterol is misleading is that there are different types of fats and also different subtypes of both HDL and LDL. Generally, the higher quantity of HDL, the better for normal blood vessels, because HDL delivers excess cholesterol back to the liver to be excreted as bile in the intestines. HDL also has cardioprotective properties by inhibiting oxidation, inflammation, and coagulation. There are two subtypes for LDL cholesterol, LDL-A and LDL-B, and the main difference between them is size. LDL-A has a larger diameter (27 nm compared to 24 nm. The difference of only 3 nanometers makes a difference in their behavior. The smaller LDL-B are not cleared from the blood vessels as rapidly as LDL-A, because the LDL receptors are not able to effectively recognize LDL-B as much as LDL-A. Because of their smaller size and increased time in the blood, LDL-B are able to penetrate inflamed and damaged tissue, including the coronary arteries, causing plaque build-up and eventual atherosclerosis. (Kumar, 2017). Table 1 summarize the different lipoproteins.

Table 1

Lipoprotein Types

Lipoprotein	Source	Contents and Description
Chylomicron	Intestine	Contains triglycerides and cholesterol absorbed from the intestine and is transported to adipose and peripheral tissue.
VLDL	Liver	Contains triglycerides and cholesterol and is transported from the liver to adipose and peripheral tissue.
LDL	Remnant of VLDL	Contains cholesterol transported to tissue.
HDL	Liver	Contains cholesterol transported to liver.

United States Senate Select Committee on Nutrition and Human Needs & Dietary Recommendations

The United States (US) government also played a role in the American diet by making recommendations through non-legislative policies in the late 1970's. In 1968, Senator George McGovern of South Dakota took the role of Chairman of the Select Committee on Nutrition and Human Needs. The initial goal of this committee was to address malnutrition in the US. Later, the committee's goals expanded to include nutrition policy and to identify dietary risk factors for heart disease. In July of 1976, the select committee held hearings from many sources including non-governmental organizations, academia, health and nutrition experts, the medical community, and the public. One influential staff member on the committee was nutritionist D. Mark Hegsted who, similar to Ancel Keys, did research in the 1960's as to the causes of heart disease with a focus on saturated fats (Oppenheimer, 2014).

Senator McGovern appointed a journalist, Nick Mottern, to author the report. Mottern, who had no background in science or medicine, relied heavily on the research

done by Hegsted, who was working for Harvard's School of Public Health. The 1977 report titled Dietary Goals for the United States, also known as the "McGovern Report," suggested that Americans eat less fat, cholesterol, processed foods, and sugar and to consume more complex carbohydrates and fiber. The main conclusion of the report was that increased saturated fat consumption was the primary risk factor for heart disease, not sugar.

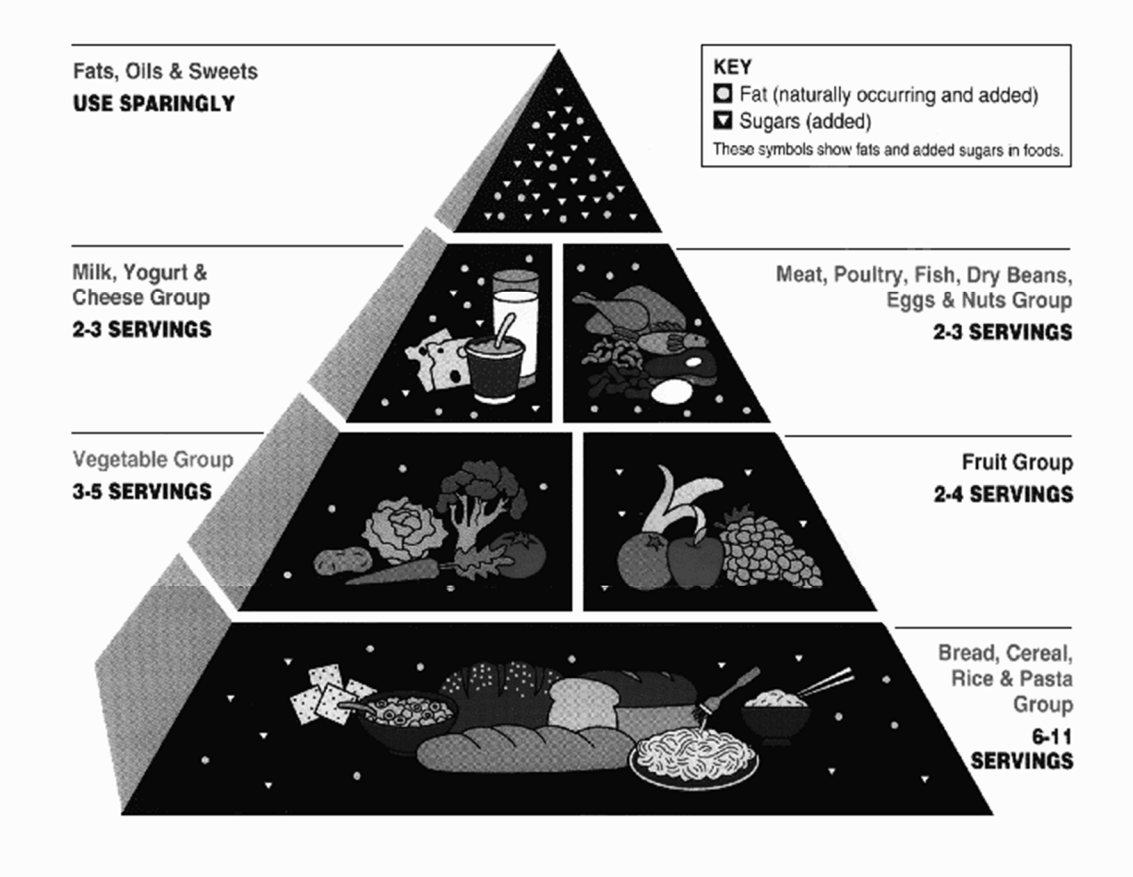
The report's influence reached the assistant secretary of the USDA, Carol Tucker Foreman. Foreman believed that the Dietary Goals for the United States report should be turned into official policy for the USDA. She was told by the Food and Nutrition Board of the National Academy of Sciences (NAS), which decides the recommended dietary allowances, that the report was not valid. Foreman, however, believed in the report and asked Senator McGovern's staff for advice. They directed her to hire Mark Hegsted (Taube, 2001). Hegsted became head of nutrition for the USDA and with his input, the USDA and Health and Human Services (HHS) produced the first edition of the USDA's Dietary Guidelines for Americans in 1980.

Following the USDA's dietary recommendations, the food industry began to lower the fat content in foods in the 1980's. Fat itself has a taste and with the removal of fat, food becomes less palatable. Sugar was therefore added to low-fat foods to make them sweeter and more palatable (Lustig. 2012). In fact, the food industry began to market its processed food products with added sugar, as if they were healthy, because they were labeled being low-fat (La Berge, 2008). By 1992, the USDA introduced the food pyramid graphic (figure 3) which was supposed to represent optimal nutritional

servings from six basic food groups: carbohydrates (breads, cereal, rice, pasta), fruits, vegetables, dairy (milk, yogurt, cheese), meats (beef, poultry, fish, dry beans, eggs, nuts), and fats. Fat, oils, and sugar were recommended to be used sparingly.

Figure 3

Food Pyramid Issued by the USDA from 1992 to 2005



Note. From "*What's a Pregnant Woman to Eat? A review of current USDA Dietary guidelines and My Pyramid*." by E. Fowles, 2006, *The Journal of Perinatal Education*, 15, p. 28-33.

The guidelines acknowledged the controversy that a single dietary recommendation would not suit everyone in the diverse American population, but like the McGovern report, the main point was to avoid saturated fats to lower the risk of heart

disease (Taube, 2001). Congress later passed the National Nutrition Monitoring and Related Research Act in 1990. The Act mandated that the Dietary Guidelines be revised and published by the USDA and HHS every five years. The 9th edition for 2020-2025 is currently under development (USDA, 2019).

Thirty six years after the first edition of the Dietary Guidelines came out, JAMA Internal Medicine published an article in 2016 about newly discovered documents describing how the sugar industry had paid Hegsted and two other nutrition researchers, Frederick Stare and Robert McGandy, the equivalent of $48,000 in the late 1960's to publish research downplaying the role of sugar in the development of heart disease (Kearns, 2016). Stare was the chairman of the Department of Nutrition at Harvard, and McGandy was a professor at the school. There was already published evidence linking sugar to heart disease. At the same time, Ancel Keys was publishing his work citing saturated fats as the cause of heart disease. The sugar industry had an interest in publicizing the findings that fat, not sugar consumption, was responsible for heart diseases.

The evidence documenting how the Harvard researchers accepted money for their sugar research was discovered in 2011 by Dr. Cristin E. Kearns, a dentist by profession, in the archives at the library of Colorado State University. At the time, Dr. Kearns was working for the Inner City Health Center in Denver, Colorado, which serves low-income patients in the community. She was surprised to find that many of her patients had severe tooth decay and bone loss and attributed this to excessive sugar consumption. She started to research the link between chronic diseases and sugar and discovered that the Great

Western Sugar Company had donated its documents to local libraries in Colorado. These documents revealed that a trade group called the Sugar Research Foundation, which still operates today as the Sugar Association, hired the Harvard nutritionists to publish their research in the New England Journal of Medicine, minimizing the link between sugar and heart disease and instead casting saturated fat as the primary cause of heart disease.

John Yudkin, a British doctor who was critical of sugar consumption, was recognized by the Sugar Research Foundation as a threat to its business. Yudkin published a series of journal articles in the late 1960's and early 1970's that pointed to sugar, not fat, as the primary cause of heart disease (Yudkin, 1969). His contemporary, Ancel Keys, acknowledged the overconsumption of sugar, but Keys would still try to refute Yudkin's work by saying that it had poor methodology and made erroneous generalizations about sugar (Keys, 1971). In 1972, Yudkin published "Pure, White, and Deadly," a book meant for the general public warning of the dangers of over consumption of sugar. In the book, he argued that fat from animals had always been a part of the human diet, while sugar was relatively new to the human diet in the copious amounts that people were consuming it (Yudkin, 1972).

Amidst published research that sugar was the cause of heart and other chronic diseases, John Hickson, the vice president of and director of research at the Sugar Research Foundation, hired Hegsted, Stare, and McGandy to refute this new evidence. Hegsted was in communication with Hickson but delayed publishing their work because they had to rewrite sections to rebut new journal articles that were being published stating sugar was responsible for coronary artery disease. Hickson was allowed to review and

approve the final paper before it was published in 1967 as “Dietary fats, carbohydrates and atherosclerotic vascular disease.” The paper did not disclose that the sugar industry was paying the authors for their work (Kearns, 2016).

Hegsted passed away in 2009, and it will never be known how much influence the sugar industry had over his research over 50 years ago. The sugar industry did not pay Hegsted to conduct research to cast sugar in a favorable light. Instead, it chose a researcher whose work already implicated fats as the culprit for heart disease This selective bias from the sugar industry steered research to focus on saturated fats and high cholesterol to be responsible for heart disease for the next decade (Teicholz, 2014).

Nutrition and Food Groups

The human body has 11 organ systems: nervous, muscular, skeletal, integumentary, lymphatic, endocrine, digestive, reproductive, respiratory, urinary, and cardiovascular. All 11 organ systems operate interdependently, and all are necessary for humans to survive and reproduce. These organ systems have their own sets of specialized cells that allow the organs to perform their respective functions (Martini, 2018). The human body is composed of approximately 37 trillion cells, and each cell requires nutrition and energy, which is derived from the foods humans eat. (Li, 2019).

Food provides the body with the vital nutrients needed for survival and allows the organ systems to function and stay healthy. The body needs six types of nutrients: carbohydrates, lipids, proteins, vitamins, minerals, and water. For the body to be able to utilize them, these nutrients first must be ingested, then broken down into their basic

components by enzymes, and finally absorbed through the gastrointestinal (GI) tract (Gropper, 2018).

Food is comprised of both macronutrients and micronutrients. The three macronutrient types are proteins, carbohydrates, and fats. These macronutrients supply the cells with calories needed for energy. The constituents of macronutrients also provide the building blocks that directly influence the structure, growth, repair, and function of cells. Micronutrients are vitamins and minerals and are only needed in small quantities, but since the human body cannot synthesize all types of micronutrients, they must be obtained through the diet. Vitamins and minerals are needed for the proper functioning of proteins and enzymes and also are required for the health of bones, nails, hair, muscles, ligaments and tendons (Chen, 2018).

Proteins are found throughout the human body, with over 40% of body protein found in skeletal muscle, 25% found in the organs, and the remainder found mostly in the skin, blood, hair, nails, enzymes, and hormones. (Gropper, 2018). There are 22 types of amino acids that provide the building blocks needed for the growth, repair, and maintenance of body tissues. Proteins from food are broken down into their constituent amino acids and digested. Then through the process of protein synthesis, amino acids are reconstructed inside different types of cells into new proteins based on a person's DNA sequence. The new proteins made then perform the unique functions of their respective cells. (Cooper, 2019). When the body is low in blood glucose, amino acids can be converted into glucose in the liver through a process called gluconeogenesis. Food

sources of proteins are mostly of animal origin and include animal meats, fish, dairy products, and eggs. Beans and nuts also contain protein (Gropper, 2018).

Carbohydrates are molecules containing the atoms hydrogen, oxygen, and carbon often in the form of pentagonal (5- sided) or hexagonal (6- sided) rings. When the rings are in the form of either a single ring or two joined rings, they are known as sugars. When the rings are combined into longer branched or unbranched chains, they become known as starches, fiber, and complex carbohydrates. Food sources of carbohydrates include breads, pasta, legumes, rice, fruits, potatoes, and many types of vegetables. The carbohydrates that are broken down and digested are eventually absorbed as monosaccharides to be used as energy by the body's cells or stored away as glycogen or fat (Gropper, 2018).

When carbohydrates are in the form of fiber, the GI tract does not have the enzymes to break them down for digestion. There two types of indigestible fiber, soluble and insoluble. Both are important for GI tract function and for the prevention of chronic diseases. In the small intestine, soluble fiber binds with water and turns into a gelatinous composition that surrounds the eaten food and slows down digestion, so nutrients have more time to be absorbed rather than being excreted. In the large intestine, insoluble fiber helps to increase stool weight, dilute toxins, and prevent constipation (Gropper, 2018).

Fiber is also a source of nutrients for the microbiome, the normal bacteria and fungi that live in our intestines (Gail, 2019). The microbiome plays an important role in digestion and gut health by aiding in the absorption of nutrients and minerals, synthesis of enzymes, vitamins and amino acids, and the production of short-chain fatty acids

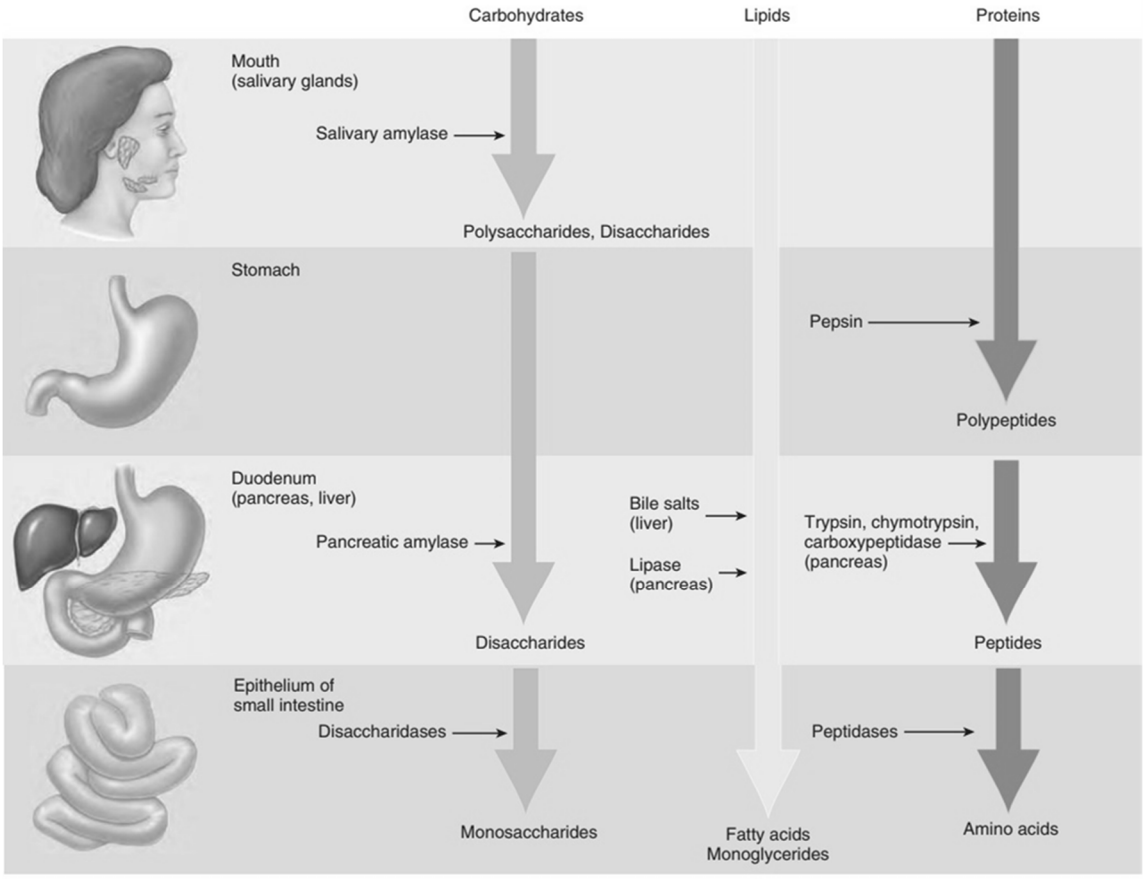
(SCFAs) through fermentation. Acetate, propionate, and butyrate are three SCFAs that are important for gut health by regulating pH, providing energy for gut epithelial cells, gut epithelial barrier integrity, and protection against pathogens (Blaak, 2019).

Fats, also known as lipids, provide the energy our cells need to function, and any excess calories are stored away as body fat. Fats from foods come in the form of triglycerides, to be explained in the Fructose Metabolism section.

Figure 4 shows how the three food groups, carbohydrates, lipids, and proteins, are broken down by enzymes at different locations in the GI Tract into their constituent components, monosaccharides, fatty acids, and amino acids, respectively. Figure 5 shows how these components can either be converted into acetyl CoA to be used as energy for cells or stored away as triglycerides.

Figure 4

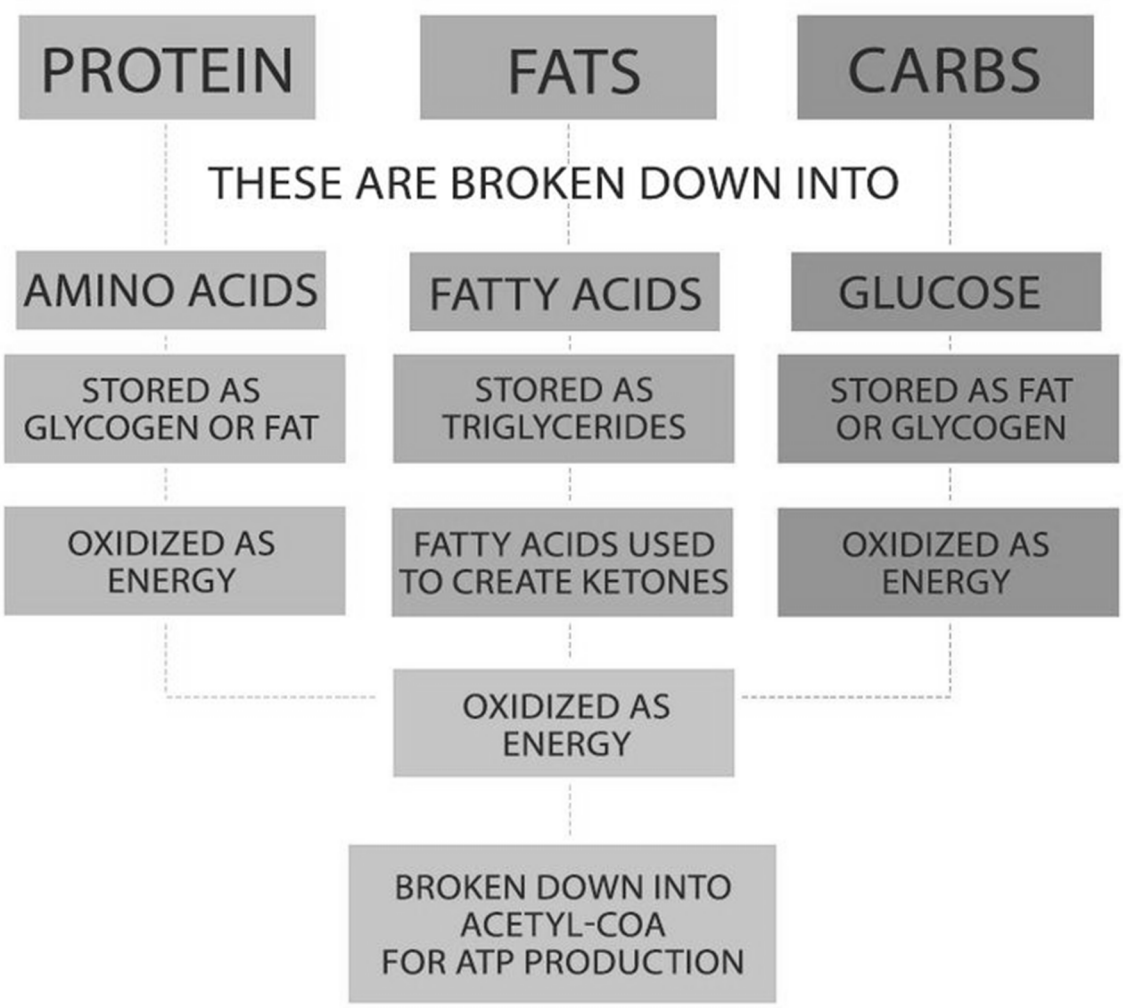
Three Food Groups and their Individual Components



Note. Carbohydrates, lipids, and proteins are broken down into the basic chemical components by specific enzymes and then digested at different parts of the gastrointestinal tract. From "*Essentials of Anatomy and Physiology"* by D. Patton, 2011, Mosby.

Figure 5

Protein, Fat, and Carbohydrate Pathways



Note. After the chemical breakdown of the three food groups, acetyl CoA is the final common molecule, which can used for energy production in the mitochondria or converted into triglycerides in the liver and then be sent out to be stored away as body fat. From Lyon, P. (2022). *Macronutrients and the Ketogenic Diet*. Ruled Me. https://www.ruled.me/macronutrients-and-ketogenic-diet.

Obesity Development

Obesity is a metabolic disorder characterized by an excess of body fat (Duran, 2018). The excess body fat comes from overconsumption of all types of foods, including fats, carbohydrates, and proteins. When greater quantities of calories enter the body than are expended, body weight increases due to the conversion of food into stored fat. Obesity is therefore caused by an unequal caloric intake versus caloric outtake. Fat is stored in the form of triglycerides inside the adipocytes. There are two types of adipose tissue, white adipose tissue (WAT) and brown adipose tissue (BAT). WAT is the storage form of fat, while BAT functions as a thermoregulator to keep the body warm and is found primarily in babies (Giordano, 2014).

The number of adipocytes increases during childhood and is stabilized by late adolescence. When children over consume foods, they develop hyperplastic obesity in which the number of adipocytes increases compared to an increased size of the fat cell. In contrast, adults develop hypertrophic obesity where the fat cells increase mostly in size. However, recent studies show that adults too can produce new adipocytes if they continually overeat (MacLean, 2015). Therefore these adults have both hyperplastic and hypertrophic obesity. A morbidly obese person could have four times as many fat cells as a lean person. For any person to lose weight, energy intake (food consumption) has to be less than energy expenditure. Besides physical activity and basal metabolism, weight loss can be induced by fasting. Fasting causes weight loss by releasing the triglycerides from the adipocytes of free fatty acids (FFA) into the bloodstream. The FFA can then be used

as fuel for all the body's cells, including muscle and neurons, instead of glucose (Puchalska, 2017).

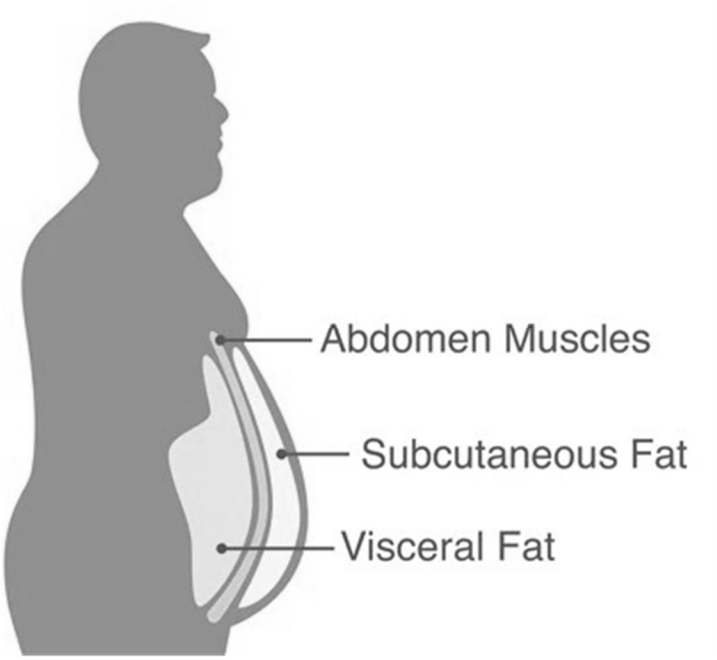
Since it is difficult to accurately measure body fat, the BMI is used as an indicator of obesity. However, the BMI is not a direct measurement of adiposity, as it does not take into account the distribution of fat and the amount of muscle a person has. Two people with BMI over 30.0 who share the same height and weight could have a different body habitus, one being overweight due to fat and the other having a muscular body type. Since obesity is associated with stored fat in the abdominal region, measuring the waistline is a better way to differentiate between a healthy physique and obesity. A waist size over 40 inches in males and 35 inches in females would be considered obese (Tyson, 2018).

There are differences in the metabolic activity of adipocytes depending on the location of these fat cells. The fat that can be felt under the skin is called subcutaneous fat, while the fat underneath the muscle within the abdominal cavity is called visceral fat as seen in figure 6. An increased amount of visceral fat is associated with the pathology in MetS. Subcutaneous fat in the abdominal region is less active and resists conversion into FFA in a process called lipolysis. FFA is the form of fat that is used for energy in muscles and other tissue when glucose levels are low. Visceral fat is more active in that it can convert to FFA more readily than subcutaneous fat. When there are low levels of blood glucose due to fasting and starvation, adipose tissue is converted into FFA. However, in obese individuals with IR, both visceral and subcutaneous fat convert to

FFA, because the body senses that it needs more sources of energy since glucose cannot be efficiently utilized (Ebbert, 2013).

Figure 6

Fat classification based on location in the body



In addition to storing fat, WAT has several endocrine functions. In healthy, nonobese individuals, weight remains relatively stable over time due to hormones known as adiponectins being released by WAT. Leptin is an adiponectin that regulates weight by inhibiting hunger by acting on the brain. Leptin is produced in the fat cells in proportion to the fat cells' size (Friedman, 2015). When more calories are consumed than are needed for energy, leptin is made and released into the bloodstream. Leptin inhibits a neuropeptide hormone called Neuropeptide Y (NPY). NPY activates the lateral hypothalamus and stimulates the sensation of hunger. By inhibiting NPY, leptin functions

as a satiety signal to cease eating. When body fat is reduced, the opposite action occurs; leptin production is reduced and hunger increases due to the effects of NPY. In obesity, high levels of leptin are produced due to increased fat cell size, but resistance to leptin's effects in the brain develops over time, and NPY continually activates the lateral hypothalamus so appetite is still present (van den Heuvel, 2014).

Sugar as a Cause for the Obesity Epidemic

The development of the obesity epidemic in the US closely coincides with the use of added sugar starting in the 1980's at the time the USDA recommended a diet low in fats. Sugar is ubiquitous in processed food items at grocery stores; 74% of all food products sold in the US contain some type of sugar (Popkin, 2016). In particular, the consumption of high fructose corn syrup (HFCS) in sodas and many other processed food products has been associated with the increased incidence of obesity and consequently T2DM and MetS (Cioffi, 2017). The addition of fructose to foods by food companies was favored over regular sugar due to its increased sweetness and palatability, lower costs, and ability to be efficiently produced in high amounts compared to sugar (Lustig, 2012). Previous studies have shown that fructose alone can induce the components of MetS, such as IR, weight gain, hypertension, and fatty liver disease (Zhang, 2014).

The metabolism of sugars ultimately ends with two outcomes, being used as energy for cells or being stored for later use. Lean body mass organs, such as the heart, liver, kidneys, brain, and muscles utilize glucose for their respective functions. Conversely, sugar can metabolize into triglycerides in the liver and stored as fat. The hormone that influences whether energy in the form of sugar is to be used for lean body

mass functions or to be stored away as fat is insulin (Hall, 2015). Insulin allows glucose to enter cells from the bloodstream to be used as energy by converting glucose into adenosine triphosphate (ATP). ATP is an unstable molecule that is universally used for energy by all cells (Goloubinoff, 2018). Foods that quickly increase glucose levels and stimulate insulin are sugars and other carbohydrates, such as bread, rice, pasta, and fruits based on their glycemic index.

The glycemic index is a ranking of carbohydrates on a scale from 0 to 100 according to how fast they raise and lower blood glucose levels two hours after a meal. Carbohydrates with a high glycemic index, which includes all sugar products, are rapidly digested, absorbed and metabolized. This results in a rapid increase in blood glucose and then a steep decrease. Carbohydrates with a low glycemic index, such as fruits and vegetables, slowly raise and lower blood glucose over the course of two hours. The fiber in foods with a low glycemic index is one reason for the stable glucose levels, because fiber slows down digestion (Lovegrove, 2017).

The normal blood glucose level is from 70 to 110 mg/dL, and insulin is able to maintain glucose levels in this range in a healthy body. Glucose is first delivered to the organs that need it the most, namely the brain and muscles, during a physically active state. In the presence of oxygen, the process where glucose is metabolized to energy in the form of ATP is called aerobic respiration. Aerobic respiration involves metabolizing glucose into carbon dioxide through a set of biochemical reactions known as glycolysis, the citric acid cycle, and oxidative phosphorylation. Glycolysis occurs within the cell's cytoplasm, and the citric acid cycle and oxidative phosphorylation occur within the

mitochondria. The mitochondria are present in every cell type except for mature red blood cells and is responsible for most of the ATP made. A single glucose molecule can produce up to 38 molecules of ATP (Hall, 2015).

During the rested postprandial or fed state, glucose is first stored in the liver and muscle in the form of glycogen. The body is able to store a relatively small amount of glycogen compared to storing glucose in the form of fat. If there is excess blood glucose after the glycogen reserves are filled, glucose is then metabolized into fat which is delivered and stored mostly in the abdomen. When a person continually eats processed carbohydrates and sodas, glucose remains high and insulin is continually secreted to convert glucose into its storage forms. In the liver and muscle, insulin stimulates the conversion of glucose to its storage form of glycogen. In the liver, excess glucose goes through the Krebs Cycle and produces citrate. Then enzymes in the liver convert citrate to acetyl CoA and then to Palmitic Acid, which is then incorporated into a triglyceride. The triglycerides are then packaged into VLDL and taken out into the circulation to be stored into adipocytes. When there is constant stimulation of insulin release over a period of years, IR develops in cells that utilize insulin Long-term IR is what leads to MetS (Indumathy, 2018).

IR occurs when the insulin receptors on cells do not respond as efficiently as they once did to insulin, and this causes hyperglycemia. This leads the pancreas to secrete more insulin, because the pancreas senses higher levels of glucose in circulation. Eventually, the pancreatic beta-cells also wear out and cannot produce any more insulin, similar to the mechanism of T1DM (Kumar 2017).

Fructose Metabolism and Development of Metabolic Syndrome

Fructose consumption has increased exponentially starting in the early 1980's and has only recently begun to decrease as shown in figure 7 (USDA, 2019). The consumption of high-fructose corn syrup has been associated with unfavorable health effects, including increased weight gain, IR, and hypertriglyceridemia (Kokubo, 2019). There has been much research exploring how much fructose contributes to obesity and subsequent complications leading to MetS (Taskinen, 2017).

Fructose is an important nutrient that plays a role in normal metabolism. Normal levels of fructose work with glucose in a synergistic manner. Fructose does not exist by itself as a monosaccharide in nature. In plants, fruits, and honey, fructose is in the form of a disaccharide and paired with glucose to form sucrose. When present as a monosaccharide, fructose is not efficiently absorbed in the gut. However, when present as glucose and fructose together in the form of sucrose, glucose assists in the absorption of fructose. Maximal absorption of fructose is in a 1:1 ratio with glucose. While in the liver, fructose catalyzes glucose uptake and storage as glycogen (Laughlin, 2014).

In the gastrointestinal tract, sucrose is absorbed and split by the digestive enzyme sucrase into its monosaccharide components. After entering the blood, glucose travels in systemic circulation and is delivered to all cell types through specialized glucose transporters (GLUT). The human body encodes 14 types of GLUT in the genome.

After being absorbed into the bloodstream, glucose first enters the pancreatic beta cells through GLUT 2 and stimulates the production of insulin. Because the pancreas makes insulin, the pancreas does not require insulin for glucose to enter. Therefore,

GLUT 2 functions as an insulin-independent transporter. When insulin is released into circulation, insulin enters all the body's cells through their respective insulin receptors. When insulin enters a cell, it stimulates the production of other specialized GLUT. For example, muscle and heart cells produce GLUT 4, while the brain's neurons make GLUT 3. Without insulin, GLUT are not synthesized within the cell. Glucose is then unable to enter the cell, starving the cell of its energy source which consequently makes the cell unable to perform its specialized functions.

Fructose is unique amongst the sugars, because most of it is processed only in the liver, whereas glucose can be metabolized for energy by cells in all other organs. Fructose enters the liver through GLUT 2. Other organs have GLUT 2, but since the liver contains unique enzymes to break down fructose, fructose is primarily metabolized by the liver. The liver can convert fructose into glucose or pyruvate, which is also the end product of glycolysis. Pyruvate can enter into the mitochondria of the liver cell to produce ATP; but if energy is not needed, pyruvate will be metabolized into citrate and leave the mitochondria. In the presence of insulin, citrate is metabolized into a triglyceride and leaves the liver via VLDL. In the well-fed state, the VLDL delivers the triglycerides mostly to the adipose tissue in the abdomen for storage. Table 2 summarizes the different types of glucose transporters.

Table 2

Glucose Transporter Types

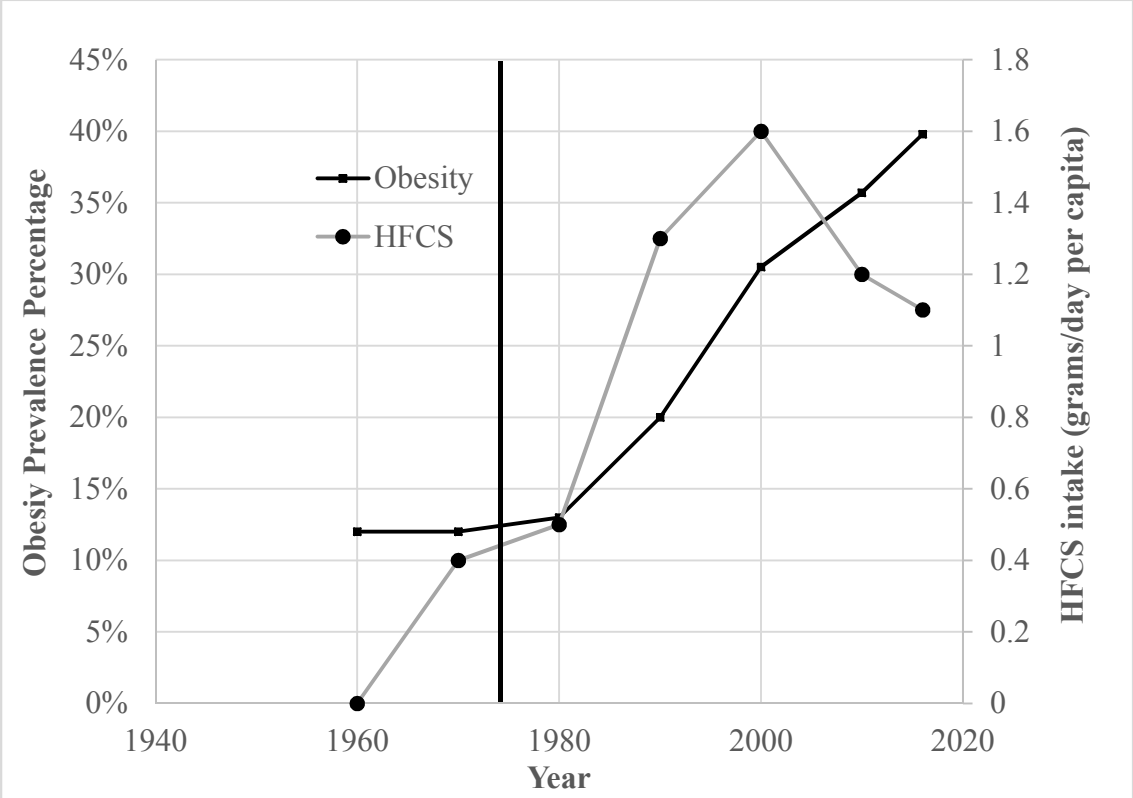
Types	Description
GLUT1	Glucose uptake in blood-brain barrier and red blood cells
GLUT2	Glucose uptake in liver and pancreatic beta cells
GLUT3	Glucose uptake in neurons
GLUT4	Glucose uptake in skeletal muscle and adipose (fat) tissue
GLUT5	Fructose uptake in the liver

Because of this unique metabolism of fructose in the liver, when there is an overabundance of fructose consumption, fat starts to form around the abdominal organs leading to visceral fat (Jenson, 2018). Visceral fat surrounding the liver can lead to what is known as non-alcoholic fatty liver disease (NAFLD). The increased adipose tissue surrounding the liver leads to IR (Hardy, 2014). When the liver cannot efficiently absorb glucose due to IR, glucose remains in circulation leading to hyperglycemia. This forces the pancreatic beta cells to release more insulin which promotes fat storage.

High insulin levels also block leptin signaling to the brain, so there is a constant sensation of hunger when the body does not need the extra food for energy. Increased glucose in circulation for long periods also damages blood vessels and the kidneys which are important organs for blood pressure control. This cycle of IR and increased blood levels of glucose, triglycerides, and insulin continues until all the components of MetS are met: abdominal obesity, hyperglycemia, hypertriglyceridemia, and hypertension.

Figure 7

Obesity Prevalence and HFCS Intake 1960 to 2016



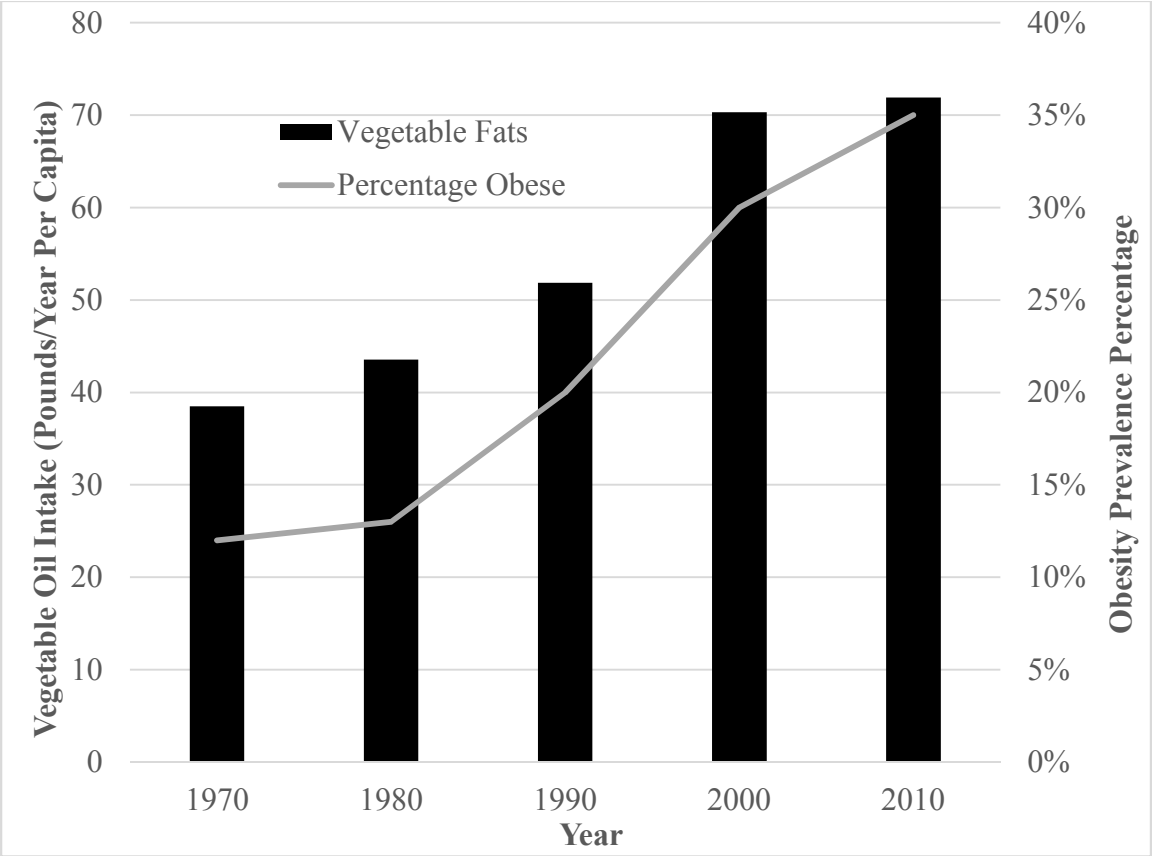
Vegetable Oils' and Omega-6 Fatty Acids' Contribution to Obesity

Though fructose and sugar consumption has been in decline since the beginning of the twenty-first century, obesity rates have continued to increase. The rise in obesity prevalence that parallels the rise of sugar and processed food consumption is also concomitantly seen with the increased consumption of vegetable oils as seen in figure 8. Oils are fats in the form of liquid at room temperature and have many uses in food preparation. Vegetable oils come from the oils extracted from various types of plant seeds and also fruits, grains, and nuts (Bhagavan, 2015). Common types of vegetable oils used

in food products include soybean, canola, corn, cottonseed, and sunflower. Vegetable oils are used as cooking oils for frying and baking. Like sugar, vegetable oils are also used as an ingredient in many processed food products to add flavor and texture, such as salad dressings, margarine, mayonnaise, and cookies (Shanahan, 2017).

Figure 8

Vegetable Oil Consumption Parallels Rise in Obesity in the US

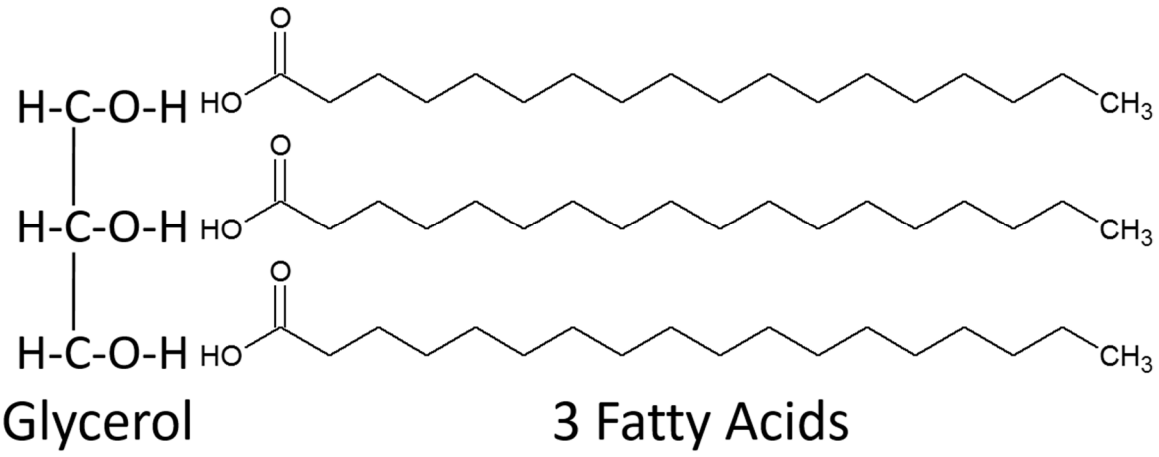


The oils are composed of various forms of triglycerides. As seen in figure 9, a triglyceride is composed of a glycerol head that serves as a backbone to join three fatty acid tails that consist of a chain of carbon atoms connected to hydrogen atoms. Each fatty acid tail may differ in carbon length and degree of hydrogen saturation. Based on the

carbon hydrogen saturation, fatty acids are classified as saturated fats, monounsaturated fats, polyunsaturated fats, and trans-fats. The first carbon atom of the chain is referred to as the alpha carbon, and the last one is the omega carbon. A carbon atom is able to connect to another atom with a maximum of four single bonds, becoming fully saturated. A saturated fatty acid is linear in shape, which gives it stability and makes it remain solid at room temperature.

Figure 9

Example of a Triglyceride, the Storage Form of Fat



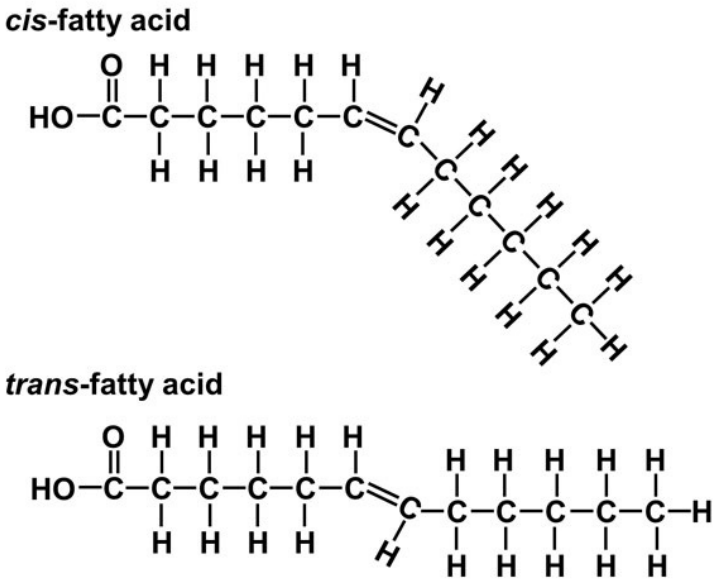
A carbon atom becomes unsaturated when it forms a double bond with another atom. A monounsaturated fat refers to a fatty acid tail that has only one double bond in the carbon chain, with the remaining carbons having single bonds. Polyunsaturated fatty acids (PUFAs) have more than two double bonds. When a double bond forms, the adjacent hydrogen atoms on the two carbon atoms that share a double bond can be on the same side, and this is referred to as a cis configuration. A trans configuration is seen

when the adjacent hydrogen atoms are on the opposite sides of the double bonded carbon atoms. Figure 10 shows an example of the cis and trans forms.

In nature, the cis-fatty acids are more prevalent compared to trans-fatty acids (Bhagavan, 2015). Trans-fats are a type of unsaturated fat that is both found in nature and commercially made. Trans-fats are made from unsaturated fats through a process called hydrogenation whereby cis-fatty acids are rearranged into trans-fatty acids, so that these fats behave more like saturated fats. Figure 10 compares the cis and trans configurations. Unsaturated fats are prone to spoil and become rancid because the double bonds are unstable when exposed to oxygen. Trans-fats were made by the food industry to prevent fats from becoming rancid and to have a longer shelf-life at grocery stores. Trans-fats have been shown to be an unhealthy type of fat as they raise LDL cholesterol, reduce HDL cholesterol and are associated with heart disease (Go, 2014).

Figure 10

Cis and Trans forms of Fatty Acids



Note. Cis and trans configurations based on the hydrogen placement on the double-bonded carbon atoms. Note the greater angle in the double bond in the cis-fatty acid compared to the trans-fatty acid.

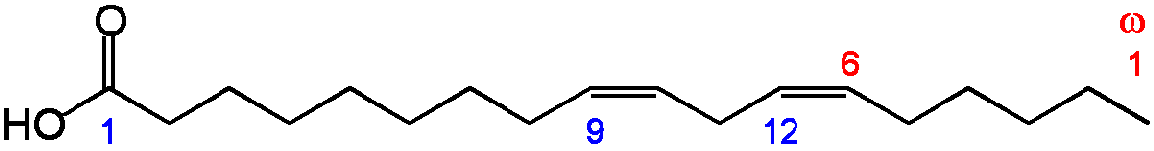
The body's liver can produce the fatty acids it needs using available carbohydrates, fat, or protein, except for two types of PUFAs, linoleic acid and alpha linolenic acid. These are important fatty acids the body needs for the management of the immune response, clot formation, levels of triglycerides, cell membrane components, brain function, and inflammation (Johnson, 2012). Since the body cannot synthesize linoleic acid or alpha linolenic acid, they are known as the essential fatty acids and can only be obtained through diet.

Linoleic acid and alpha linolenic acid are types of omega-6 and omega-3 PUFAs, respectively. Omega-6 fatty acids have a double bond between the sixth and seventh

carbon atoms, counting from the last (omega) carbon atom seen in figure 11 and 12. Similarly, omega-3 fatty acids have a double bond between the third and fourth carbon atoms, counting from the omega carbon seen in figures 13 and 14. Linoleic Acid is found in the oils of plant seeds. Diets that contain high amounts of vegetable oil, seeds, nuts, and whole-grain foods will meet the body's needs for omega-6 fatty acids. Omega-6 fatty acids are converted to arachidonic acid and then further oxidized into a large family of signaling molecules called the eicosanoids, which produce many of the molecules that induce inflammation and thrombosis (Gibson, 2011). Two types of eicosanoids, leukotrienes and thromboxane (TXA), are responsible for inflammation and thrombosis, respectively. Pro-inflammatory eicosanoids are important signaling molecules for the immune response, but when too many of them are produced, they can increase inflammatory diseases.

Figure 11

Linoleic acid structure



Note. Schematic structure of linoleic acid, a polyunsaturated omega-6 fatty acid. The term omega-6 refers to the sixth carbon atom (seen in red) to contain the first double bond starting from the last carbon at the end of the chain.

Figure 12

Configuration of linoleic acid

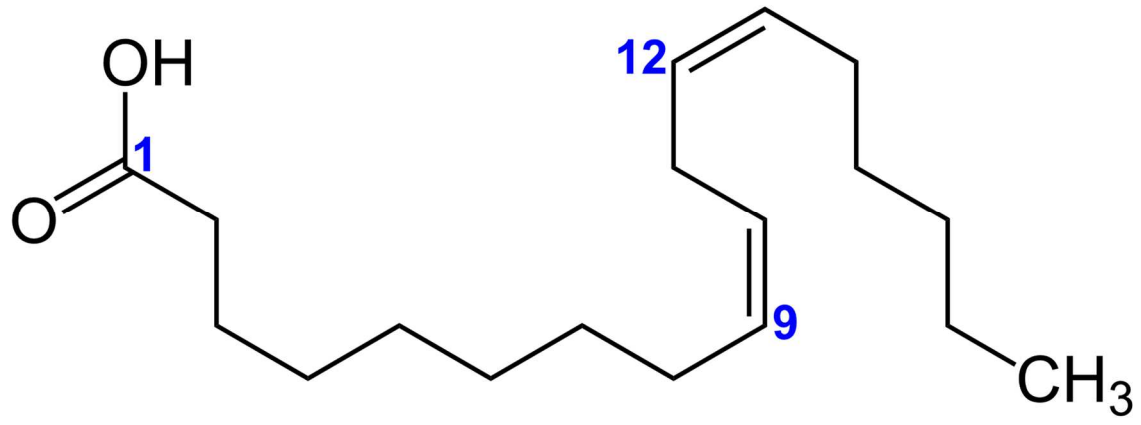
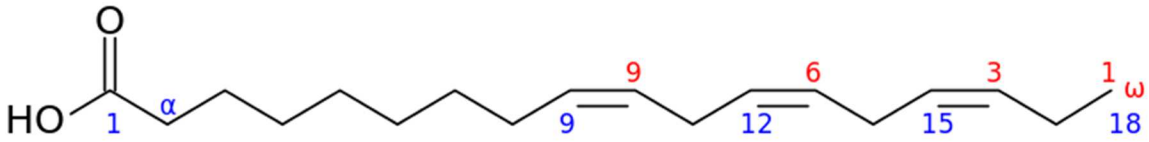


Figure 13

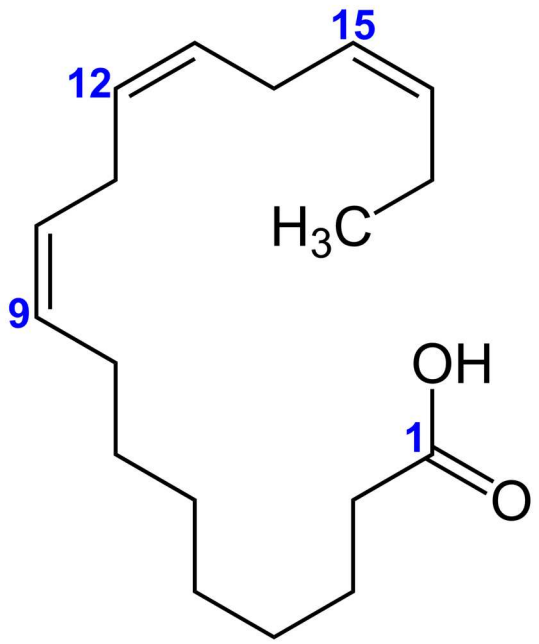
Alpha linoleic acid structure



Note. Schematic structure of alpha linolenic acid, a polyunsaturated omega-3 fatty acid. Note the double bond at the third carbon counting from the last omega carbon.

Figure 14

Configuration of alpha linolenic acid



Alpha linolenic acid as seen in figures 13 and 14, is found primarily in many species of fish and marine mammals, including mackerel, herring, tuna, halibut, salmon, and cod liver and also in whale and seal blubber (Bou, 2017). In the body, alpha linolenic acid is converted into eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). DHA plays a role in brain and eye development in prenatal babies during the last trimester. DHA makes up 40% of the PUFAs in the cerebral cortex and 60% in the retina of the eye and also is present at high levels in the male testis and sperm (Ogundipe, 2018). The health benefits from EPA include prevention of coronary artery disease and reduction of triglycerides. EPA also is used for treating depression, Alzheimer's disease, and attention deficit-hyperactivity disorder (Russel, 2012).

During most of human history, humans have had amounts of omega-6 to omega-3 fatty acids in a 1:1 ratio. The plant and animal foods that were available during the Paleolithic era would not have resulted in a higher ratio, because animal fat contains little omega-6 fatty acids and higher amounts of saturated and monounsaturated fat (Gibson, 2009). In nature, there would have been a balance of both types of fatty acids found in animal meat, wild fish, wild plants, nuts, and berries (Eaton, 1985). However, over the past generation, there has been a shift in the ratio of omega-6 to omega-3 intake from 1:1 during our time as hunter-gatherers to approximately 20:1 or higher due to today's Western diets (Simopoulos, 2013). Largely as a result of recommendations from government agencies, saturated fats have been replaced with plant-based PUFAs in the form of vegetable oil, such as canola and soy oils, which are high in omega-6 fatty acids and low in omega-3 fatty acids.

This ratio increase from 1:1 to 20:1 comes just from the past 30 years, which parallels the obesity epidemic. The derivatives of omega-3 fatty acids, EPA and DHA, act as mediators of the inflammatory and thrombotic effects of omega-6 fatty acids. Populations that have diets rich in omega-3 fatty acids from wild fatty fish, such as the Alaskan Inuit and Icelandic peoples have low incidence of obesity and heart disease (Schraer, 1999). Humans developed their genetic pattern based on a 1:1 ratio during evolution, and this kept the body in a healthy balance, but today's Western diets are deficient in omega-3 fatty acids and have excessive amounts of omega-6 fatty acids (Simopoulos, 2002). Excessive amounts of omega-6 PUFAs with the high omega-

6/omega-3 ratio seen today promote the pathogenesis of diseases seen in MetS and also cancer and inflammatory and autoimmune diseases (Simopoulos, 2016).

High amounts of omega-6 fatty acids from vegetable oils increase the risk of obesity and decrease the health benefits of omega-3 fatty acids due to several mechanisms. Omega-6 fatty acids are metabolized to TXA and Leukotriene B4 (LTB4), which contribute their proinflammatory and prothrombotic effects to atherosclerosis, obesity, and diabetes. Omega-6 fatty acids affect weight gain by increasing cell membrane permeability in fat cells, so triglycerides are more able to enter the fat cell. In contrast, omega-3 fatty acids reduce fat deposition by inhibiting enzymes that convert acetyl CoA into a triglyceride (Ukropec, 2003) and also by activating an enzyme called Peroxisome Proliferator-Activated Receptors (PPAR) that stimulates fat breakdown (Belchior, 2015).

Vegetable oils also contribute to heart disease due to a cascade of events that lead to an accumulation of oxidized LDL (oxLDL) on the endothelial surface of the arteries leading to atherosclerosis (Idris, 2018). When used for cooking foods, the fatty acids in vegetable oils become susceptible to oxidation due to their unstable double bonds during heating, particularly in foods that are deep fried, such as fries and chicken. Oxidation is the removal of an electron from an atom, leaving the atom with an unpaired electron, known as a free radical. Free radicals cause damage, because they continue to remove electrons from neighboring atoms, which creates more free radicals and the cascade continues. Free radical damage distorts the shape of the cell and degrades the entire cell (Shanahan, 2018).

Lipids are a natural component of all cell membranes, and fatty acids provide a source of these membrane lipids, including LDL lipoproteins. LDL lipoproteins becomes oxidized when oxidized fatty acids become part of the LDL cell membrane. The LDL receptors from the liver and other organs that need the cholesterol from the LDL lipoprotein will not be able to recognize the damaged oxLDL (DiNicolantonio, 2018). The oxLDL then degrades and empties its contents into the bloodstream. The degraded oxLDL and oxidized fat drift in the bloodstream until they deposit on the endothelial layer of the arteries, including the coronary arteries, and start the inflammation process that leads to atherosclerosis (Ramji, 2018).

WATE-ON Product for Weight Gain

Omega-6 fatty acids from vegetable oils and sugar increase fat storage through different methods. When taken in large amounts together, they can have a synergistic effect in developing obesity and consequently MetS (Duwaerts, 2019). Sugar intake with vegetable oils were known to cause weight gain since the beginning of the 20th century, and there was a food product marketed for the sole purpose of weight gain. For many decades from the 1920's to the 1960's, a product called WATE-ON was sold to the public. As seen in Figure 15, Hollywood actresses, including Raquel Welch, advertised for WATE-ON. WATE-ON was marketed primarily to women who wanted to gain more weight for a full-figure appearance to appear more attractive (Zimdars, 2016). The product's main ingredients were sugar and vegetable oils, the two sources which the present study argues are the cause of obesity and MetS.

Figure 15

Actress Raquel Welch in 1960's WATE-ON advertisement

Note. Excerpt from the advertisement reads "An attractive feminine figure is a movie star's main requisite. It's the man's way of judging a woman. An undernourished body with no flowing figure-line may spell oblivion to a popular social life." From Kiddie, J. (2018). *Evidence that Refined Carbs with Vegetable Oils Cause Weight Gain*. The Low Carb Healthy Fat Dietian. https://www.lchf-rd.com/2018/06/26/evidence-that-refined-carbohydrate-with-vegetable-oils-cause-weight-gain/.

Development of Atherosclerosis

CVD remains the leading cause of morbidity and mortality worldwide and in the US (CDC, 2018). The underlying cause for most types of cardiovascular deaths is atherosclerosis (Theodorou, 2018). Atherosclerosis is a chronic inflammatory disease of the medium and large vessels of the arteries, the vessels that deliver oxygenated blood and nutrients to cells. The disease is driven by deposits of lipid content and also by inflammatory cytokines which are small proteins. Obesity and hyperglycemia both independently contribute to the development of atherosclerosis by first damaging the inner layer of the coronary arteries, called the endothelium (Tabas, 2015).

One method by which hyperglycemia affects endothelial cells is through a process called glycation. Glycation is when fat or proteins combine with glucose in the bloodstream to form what are known as advanced glycation end products (AGEs) (Forrester, 2018). Glycation can occur on all the body's proteins, whether or not the proteins are in circulation and whether the proteins are extracellular or intracellular. These proteins include hemoglobin, albumin, insulin, immunoglobulins, LDL lipoprotein receptors, and collagen (Fournet, 2018). The kidneys can eliminate AGEs if blood glucose is within a normal range, but if there are continuous high levels of blood glucose, too many AGEs will form, and the body will not be able to eliminate them, which leads to their accumulation.

Glycation of an enzyme that is located on the endothelial surface of arteries called endothelial nitric oxide synthase 3 (eNOS), damages the enzyme and will not be able to perform its function of smooth muscle relaxation. Under normal conditions, eNOS

releases nitric oxide (NO) which relaxes the smooth muscle within the arterial vessel and causes vasodilation. Vasodilation widens the circumference of the vessel, so blood flow is increased and blood pressure is reduced. With the glycation of eNOS in the endothelium, the enzyme is no longer able to produce NO, and vessels will not be able to relax. This contributes to elevated blood pressure (Li, 2015). Glycation can occur anywhere in the circulation, which is why AGEs are also associated with other chronic diseases, such as kidney failure and Alzheimer's disease (Fishman, 2018). When there is normal blood glucose, the kidneys are able to excrete these glycation metabolites, which gives urine its characteristic yellow color (Shanahan, 2016).

Hyperglycemia contributes to inflammation of the endothelium due to the high concentration of glucose in the arterial vessels. Endothelial cells do not need insulin for glucose to enter. With elevated blood glucose, glucose enters the endothelial cell and is metabolized by the mitochondria. A natural by-product of oxidative phosphorylation in the mitochondria is a chemically reactive species called a reactive oxygen species (ROS). ROS contain an unpaired electron and seeks other molecules' electrons to pair with. ROS can damage proteins, DNA, and cell membranes. When ROS react with the cell membranes of the endothelial cells, it removes an electron from one cell, and that cell becomes unpaired and has to seek another electron, starting a chain reaction. This process damages the endothelial layer and directly promotes the inflammatory response and subsequent immune response of the arterial vessels (Ren, 2017).

The contribution of obesity to inflammation and atherosclerosis is from the high concentration of saturated fatty acids and triglyceride-rich LDL cholesterol in circulation.

The lipoproteins deliver the fatty acids to the endothelium and induce endothelial apoptosis (cell destruction) and trigger the proinflammatory cytokine nuclear factor kappa B (NF-kB) (Tampakakis, 2016). NF-kB is a protein complex found inside of cells that, when activated, starts the inflammatory process and attracts immune cells to enter through the endothelial cells by increasing vascular permeability. Monocytes and LDL cholesterol are then able to enter beneath the endothelial layer and accumulate. Monocytes are a type of white blood cell of the immune system that function as a macrophage. Monocytes engulf and digest foreign and invading cells detrimental to the health of the cell in a process called phagocytosis.

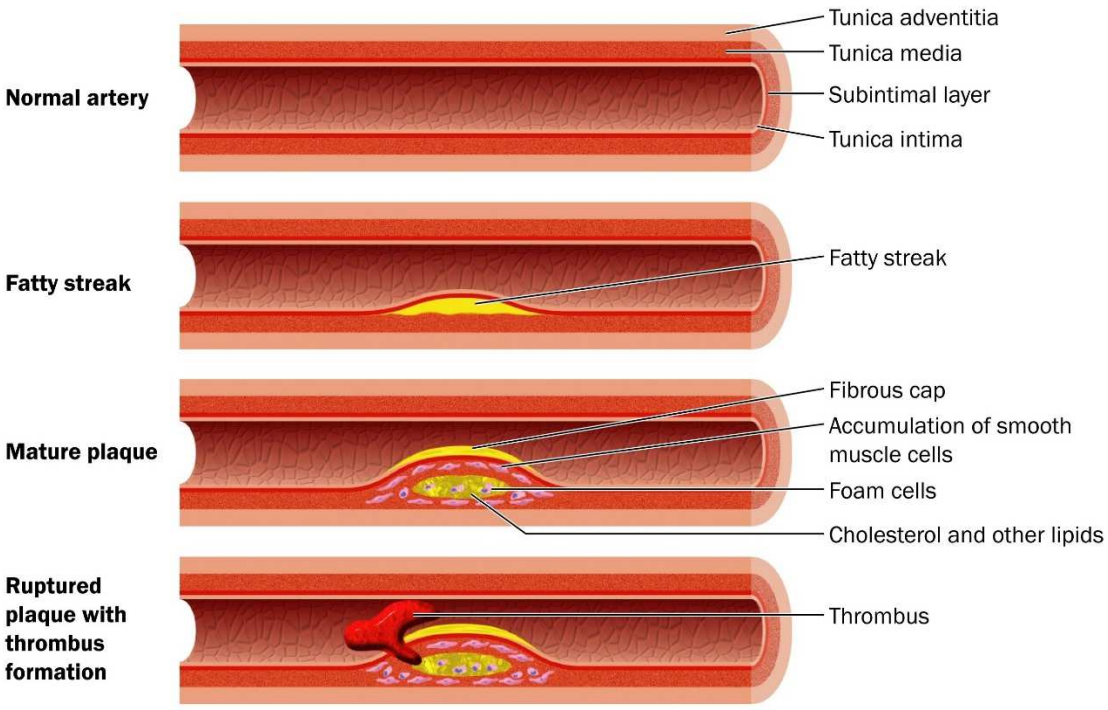
When the monocytes and LDL cholesterol begin to accumulate and meet inside the endothelial cell, the monocytes engulf the LDL cholesterol and transform into what are called foam cells. The monocytes and foam cells further release the inflammatory cytokines, tumor necrosis factor-alpha (TNF-α) and Interleukin-1 (IL-1), and inflammation continues. The foam cells also release growth factor and stimulate the proliferation of smooth muscle towards the endothelial cells. The combination of smooth muscle growth, LDL cholesterol, monocytes, and foam cells forms a fibrous plaque that protrudes into the lumen of the arterial wall.

Later, calcium salts are deposited onto the plaque which leads to calcification of the arterial wall. This later stage of atherosclerosis is what is popularly known as "hardening of the arteries," because the walls are so rigid that they are unable to relax and lose their distensibility and become easily ruptured. When the red blood cells accumulate around the ruptured plaque, a thrombus forms and blocks the flow of blood. If the plaque

completely breaks off from the arterial wall, the traveling blood clot is called an embolism. When either the thrombus or embolism blocks the flow of blood to the heart to the point where the heart cannot function due to lack of oxygenated blood, a myocardial infarction occurs. If blood flow is stopped in the brain, a stroke occurs (Kumar, 2017). Figures 16 shows a summary of the process of plaque development and rupture in atherosclerosis while figure 17 shows how plaque formation can disrupt the normal flow of blood.

Figure 16

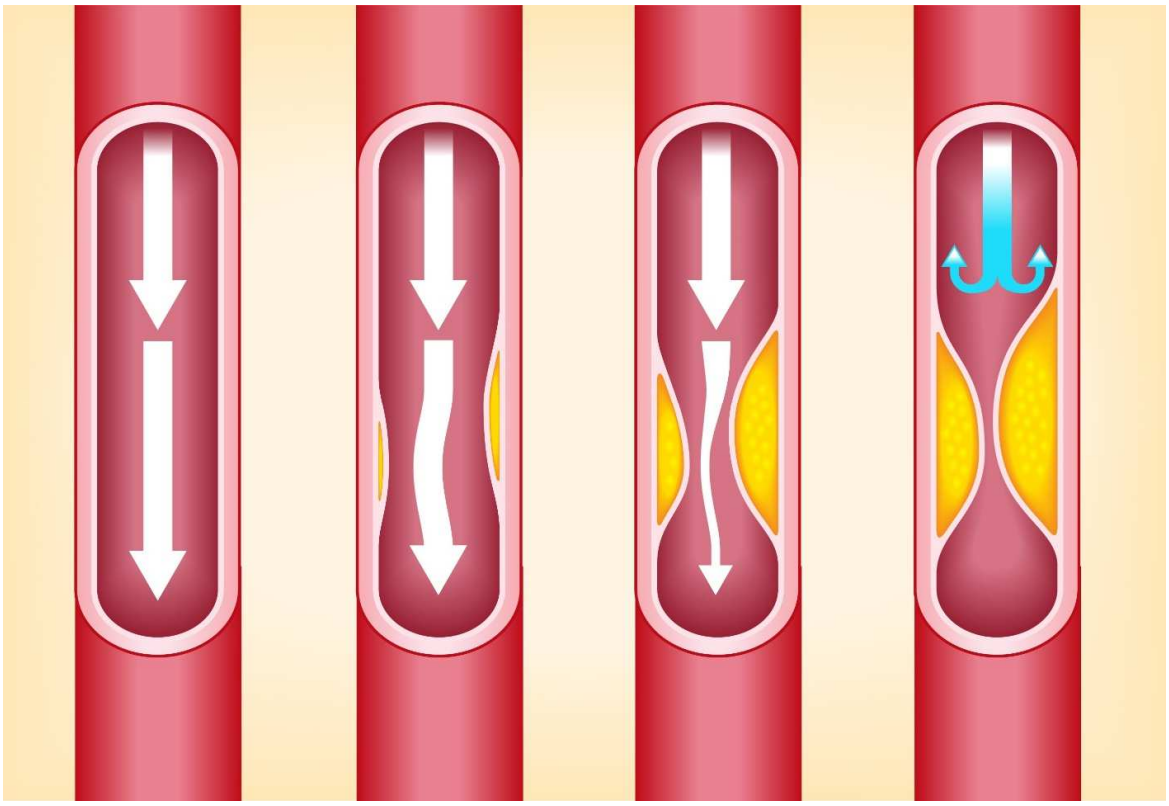
Plaque development and rupture in atherosclerosis



Note. From Grinko, V. (2022). *Plaque formation in artery*. 123RF. https://www.123rf.com/photo_11943433_plaque-formation-in-artery.html?downloaded=1.

Figure 17

Plaque development impeding the flow of blood.



Note. From Grinko, V. (2022). *Human Atherosclerosis*. 123RF. https://www.123rf.com/photo_12186049_vienna-human-atherosclerosisthe-structure-of-a-veins-the-veins-in-the-manifestation-of-the-disease.html?downloaded=1.

Health Status of Modern Hunter-Gatherers

Human life on earth shares only a small portion of time compared to the immense geological and cosmological timescales of the earth and universe. Physicists estimate the universe began approximately 13.7 billion years ago (bya), galaxies and stars formed 10 bya, and our solar system formed 4.6 bya (Reiss, 2019). The earth formed 4.5 bya, and

life began in the oceans approximately 3.8 bya. In the prebiotic earth, six of the 118 elements in the periodic table, carbon, hydrogen, nitrogen, oxygen, phosphorus, and sulfur existed and formed the basis to make proteins, lipids, and carbohydrates. These molecules could then form into the basic unit of life, the cell, and bacteria emerged as the first type of life (LeDoux, 2019). This means that literally everything on earth today, from living and non-living things, whether man-made or natural, arrived cosmically billions of years ago.

The age of the dinosaurs began 230 mya, starting what is known as the Mesozoic Era and ended abruptly 66 mya when an asteroid collided into the earth in the present-day Yucatán Peninsula in the Gulf of Mexico (Gulick, 2019). The impact triggered large-scale geological cataclysms that led to a mass extinction on earth, ending the Mesozoic era and starting the Cenozoic era which continues to the present day. Without predation from the extinct dinosaurs, the start of the Cenozoic era paved the way for the evolution of mammals, including the primates and humans.

Genetic and fossil evidence indicates the human linage separated from its primate relative, the chimpanzee, 4 to 6 mya (Katoh, 2016). There have been several human species within the genus family of homo, all of which have gone extinct except for today's modern human species Homo sapiens. H. sapiens appeared in eastern Africa 300,000 years ago (Rito, 2019). Then approximately 70,000 to 50,000 years ago, H. sapiens traveled out of Africa and migrated to the rest of the continents and continued to evolve into the multiple racial groups seen in the present day.

The humans that lived during the Paleolithic Age, also popularly known as the Stone Age, faced threats to their health that were much different compared to now. This period in prehistory dates from 3.3 mya to 12,000 years ago, before the start of agriculture. The Stone Age covers a time in which hominins and later hunter-gatherer humans obtained their food by hunting wild animals, fishing, and gathering plants using primitive tools. Infection, injuries, and starvation killed humans early in their lives, which prevented many humans from successfully reproducing (Armelagos, 2005). In those humans that did survive, a robust immune system developed to protect against invading microbes and parasites, and they were able to store calories as body fat to be used in times of food scarcity. The daily lifestyle of hunter-gatherers was not at odds with their biological functions for survival.

While there are no longer true hunter-gatherers that live exactly as they once did during the Paleolithic Age, there are still indigenous populations in parts of the world that are able to live within their natural environment by hunting wild game and gathering edible plant-based foods. Two modern day hunter-gatherer populations that have had anthropological studies done on them are the Hazda of Tanzania in Africa and a South American tribe called the Tsimane. Life expectancy at birth for most hunter-gatherer populations is lower compared to industrialized nations due to high rates of infant mortality and infectious diseases in the former. However, those that live to 45 years of age can expect to live at least another 20 years (Gurven, 2007). A 2015 study on the Tsimane found the modal age of death to be 70 years of age (Kaplan, 2017). The researchers attributed this longevity to factors relating to their healthy cardiovascular

state, such as low LDL, low blood pressure, low blood glucose, normal BMI, no smoking, and high levels of physical activity. These indigenous populations are of interest to the public health and medical communities, because even though they do not have access to modern medical care and drugs, they do not suffer from the same pathologies that are most common in industrialized countries, namely obesity, high blood pressure, and heart disease.

With a life expectancy approaching that of industrialized nations and a lifespan of excellent metabolic health, free of chronic diseases, hunter-gatherers can act as models for public health by leading to an understanding of what behaviors contribute to being free of risk factors for heart disease. In this way, their lifestyle can add to public health knowledge by leading to an understanding of the root evolutionary causes of non-communicable diseases. With this knowledge, populations of industrialized nations can live within their technological modernity free of infectious diseases and at the same time, practice dietary and physical behaviors to avoid the risk factors for MetS.

The Tsimane

The Tsimane (pronounced chee-may-nay) are an indigenous tribe that live in the jungles of Bolivia in multiple communities along the Manaqui River, which is a tributary of the Amazon River. As of 2017, their population was approximately 16,000. This population has been studied since 2001 by the Tsimane Health and Life History Project team, as an anthropology project sponsored by the University of New Mexico and University of California, Santa Barbara. Though they live a pre-industrial lifestyle, they are not exclusively hunter-gatherers, as they were introduced to agriculture by Jesuit

missionaries in the late 17th century (Gurven, 2017). Their sustenance is based on a combination of hunting wild game (deer, pigs, armadillos, badgers), foraging plants, and farming (bananas and corn). During occasional poor hunting seasons, the Tsimane get most of their calories from plants and carbohydrates, as farmed plants are a reliable source of food compared to hunting. Their average diet consists of approximately 14% protein, 14% fat, and 72% carbohydrates (Martin, 2012).

A 2017 study showed that despite having chronic inflammation due to infectious parasites, the Tsimane have the lowest prevalence of coronary artery disease of any population recorded to date (Kaplan, 2017). Of the more than 700 Tsimane who participated, 90% had no plaque build-up in their arteries as measured by the coronary artery calcium score (CAC). The study concluded that they are five times less likely to develop atherosclerosis compared to Americans. Only 14% of American adults have CAC scores showing no calcium build-up. In addition to having excellent heart health, they do not suffer from other non-infectious diseases such as obesity, hypertension, hyperglycemia, high cholesterol, all of which are associated with MetS.

Their diet consists of rice, plantain, corn, nuts, bananas, and other fruits. The protein they eat comes mostly from the animal meat they hunt, such as deer, pig, armadillo, and badger meat. This diet is low in fat and high in fiber-rich carbohydrates and omega-3 fatty acids (Martin, 2012). They do not smoke or eat any processed foods. To survive, their lifestyle demands that they remain active throughout most of the day. The adult males walk approximately 7 to 8 miles per day hunting in the daylight hours,

while the women and children harvest plants and prepare meals. They are able to sleep 7 hours at night, which is similar to the amount of time the industrialized populations sleep.

However, since they are devoid of modern housing, good sanitation, running water, and electricity, they suffer from high rates of respiratory and gastrointestinal infectious diseases. Infectious diseases are the primary cause of morbidity and mortality for the Tsimane, unlike in industrialized nations where non-infectious diseases are more common. Most Tsimane have at least one intestinal parasite, namely hookworm or roundworm. The protozoa, Giardia lambia, is also common. Because they live with chronic infections for many years, they also have high levels of inflammatory markers, such as C-reactive protein, white blood cells, erythrocyte sedimentation rate, B-cell antibodies, and natural killer cells compared to Americans at all ages (Blackwell, 2016).

The Hadza and Total Energy Expenditure

The Hadza are a group of hunter-gatherers that live in northern Tanzania in Africa as seen in figures 19, 20, and 21. They live in a savannah-woodland environment and like the Tsimane, the Hadza remain active throughout the daylight hours, hunting and foraging food with bows and arrows, digging sticks, and small axes. In performing these duties, Hadza men will walk up to 8 miles a day while women walk 5 miles a day (Pontzer, 2021).

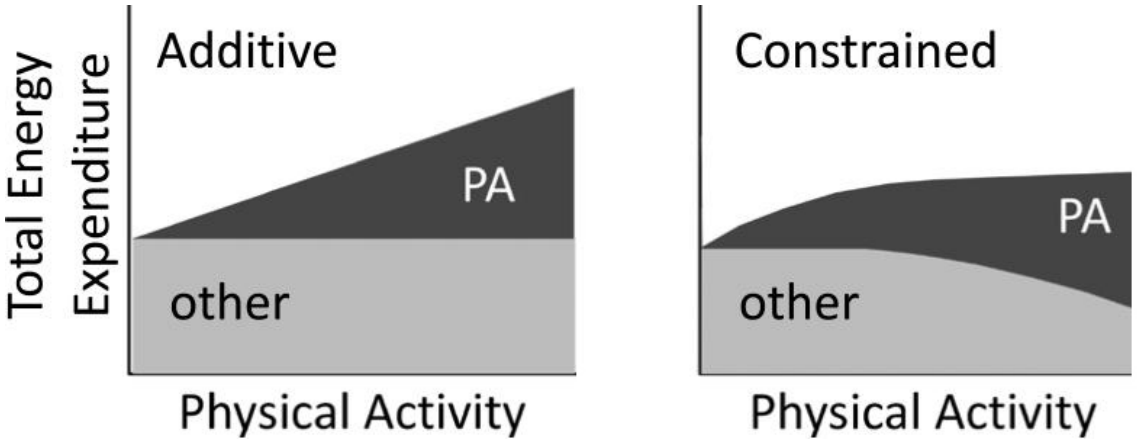
They use no modern electrical tools, guns, or vehicles. Also similar to the Tsimane, obesity is rare, as is CVD. To determine the contributing factors to their good metabolic health, a 2012 study on their caloric intake and total energy expenditure (TEE) was performed. TEE represents the daily summed metabolic activity of all organ systems

in the human body. TEE is measured in calories and is the total amount of calories used per day for basic life processes (basal metabolic rate), to digest and absorb food, and to engage in physical activity (Heydenreich, 2017).

The researchers were under the assumption that since the Hadza hunt and forage most of the day using only hand tools, they would expend more daily energy compared to American adults, who are comparatively more sedentary. This assumption is referred to as the additive total energy expenditure, which means that the more one is physically active, the more calories are used to meet the body's demands. However, the unexpected results showed that their TEE was similar to that of Americans. Despite having a high physical activity level being dependent on wild unprocessed foods, and being lean with low body fat percentage, the TEE for the Hadza was not significantly different from the energy expenditure of Americans. The researchers conducted a power analysis and determined that they had an adequate sample size; the absence of significant results was not due to small samples size (Pontzer, 2016). The researchers' conclusion was that even with vastly different lifestyles, the differences in obesity prevalence between Americans and hunter-gatherers are primarily due to the overconsumption of food rather than levels of physical activity. Studies done thereafter also show that TEE is stable across different populations from Asia, Africa, the US, and the Netherlands, suggesting a common genetic component to how energy is used by the body. Figure 18 shows a schematic graph of how the additive model compares the constrained model of energy use.

Figure 18

Schematic Graphs of the Additive Total Energy Expenditure Model Versus the Constrained Total Energy Expenditure Model.



Note. In the Additive model, total energy expenditure is a linear function of physical activity. This means the more physical activity done, the more calories are used. In the Constrained model, the body adapts to increased physical activity by reducing the energy used on the body's other physiological activity. This maintains total energy expenditure within a set narrow range. From "*Burn"* by H. Pontzer, 2021, Avery.

The average total energy expenditure per day for all adults was found to be between 2,500 and 3,000 kilocalories independent of physical activity level. Since this value for TEE was found to be relatively stable across geographic locations and cultures, TEE is hypothesized to be an evolved physiological trait that is a product of natural selection. However, the mechanisms behind how a stable TEE would be of survival and reproductive benefit to a population are still under investigation (Pontzer, 2018). One hypothesis how a stable TEE would be beneficial in humans is that in times of famine, a

stable TEE would keep energy demands low while utilizing stored fat as an energy reserve (Pontzer, 2021).

Figure 19

Hadza tribesman hunting with a bow and arrow

Note. Adult Hadza men regularly walk up to 8 miles per day hunting for food. From *Hadza Stock Photos and Images.* 123RF. https://www.123rf.com/stock-photo/Hadza.html?sti=o50d3jfa9ndeyzyyb3|&oriSearch=Hadza.

Figure 20

Hadza tribesman kills a bird with an arrow

From *Hadza Stock Photos and Images.* 123RF. https://www.123rf.com/stock-photo/Hadza.html?sti=o50d3jfa9ndeyzyyb3|&oriSearch=Hadza.

Figure 21

Group of Hadza dancing

From *Hadza Stock Photos and Images.* 123RF. https://www.123rf.com/stock-photo/Hadza.html?sti=o50d3jfa9ndeyzyyb3|&oriSearch=Hadza.

Benefits of Resistance Training

Though food intake has a more direct effect on weight change compared to physical activity, there are still many health benefits to exercise. The health benefit of resistance training is to gain muscle mass and strength. Like adipocytes, the number of muscle cells called myocytes does not change after birth but either grows or shrinks depending on the level of muscle use (Yang, 2014). Resistance training of the lower and upper extremities through lifting weights can increase the size of the skeletal myocytes. Weight training strengthens not only the muscles but also bones, ligaments, and tendons

(Baar, 2017). There is also increased insulin sensitivity and better lipid profiles associated with resistance training (Vinet, 2015). Having adequate muscle mass in seniors can help prevent joint injuries and allows for greater functional independence (Vilaca, 2013). Being able to walk and perform tasks without the aid of others or devices offers more autonomy.

Skeletal muscle is the largest source of glucose to be utilized as fuel for muscle contraction, so having increased muscle mass provides a source for blood glucose to be metabolized rather than remaining in the vessels (Gamboa, 2011). Because skeletal muscle is the organ most used by glucose, increasing muscle mass can either lower the risk of developing T2DM or help to manage the condition. This is due to the increased number of mitochondria that are created from increased physical activity through a process called mitochondrial biogenesis, which is the growth and division of pre-existing mitochondria (Jornayvaz, 2010). GLUT 4 also is increased with more muscle mass, allowing more glucose to be transported into muscle tissue (Chavanelle, 2017).

Aging is associated with sarcopenia, the loss of muscle mass, along with the strength to walk and perform tasks. Therefore, performing resistance training to gain muscle mass would be beneficial for seniors with obesity or MetS. Studies on seniors have shown that with increased muscle mass, there is less need for the common diabetes medication, Metformin (Agnera, 2018). Reduced usage of Metformin to maintain normal levels of blood glucose indicates metabolic improvement and also minimizes the gastrointestinal side effects of Metformin (Scheen, 2013).

Summary and Transition

This chapter was a literature review of the events that led to the rise of the obesity epidemic in the US and the causes of MetS and heart disease. Heart disease began to rise in the 1950's, and prominent researchers during the time investigated whether fats or sugar was the primary cause of blood vessel damage leading to heart disease. Nutritionist Ancel Keys became well-known for arguing that a diet high in saturated fats was the cause of heart disease. Harvard nutritionists also published research citing saturated fats as the cause of heart disease. The US government relied on these conclusions to make the first official USDA dietary recommendations. The food pyramid diagram that was created suggested a healthy diet consists of low fat and moderate complex carbohydrates. Food companies then started to reduce fat in their products and to increase taste palpability, added sugars to their foods and sodas, including HFCS. Then starting in the early 1980's, obesity prevalence in the US began to rise exponentially. Chronic obesity led to the components of MetS and over time, became a strong risk factor for heart disease, which is the leading cause of mortality in the US.

To understand how chronic disease develops, recent anthropological research has shown how modern-day hunter- gatherers in South America and Africa live their daily lives. These populations of indigenous tribes have two of the lowest prevalence rates of heart disease and obesity in the world. Their diet consists of carbohydrates, fats, and proteins from their cultivated plants and wild animals caught through hunting. These are the same types of foods Americans eat, except that hunter-gatherers have no processed foods or refined sugars in their diet and do not overconsume food to become overweight.

All their traditional food is either captured or cultivated. Even though they have much lower rates of non-communicable chronic diseases compared to industrialized countries, they suffer from chronic inflammation from parasitic infections for many years of their lives.

The health statuses of hunter-gatherers and Americans illustrate that it is possible for industrialized populations to have a high QoL without suffering from either chronic noninfectious or infectious diseases if they live in sanitary environments, reduce the consumption of processed foods and sugary foods, and maintain a minimum level of physical activity for muscle growth. Chapter 3 will discuss the research methodology, data collection, sample, study design, and statistical analysis that were used for this study.

Chapter 3: Research Method

The purpose of the present study was to identify risk factors that would significantly predict MetS status and to also identify which demographic groups are at increased risk of developing MetS. Chapter 3 discusses the research design and rationale, sample population, data collection, operationalization of variables, data analysis plan, and threats to validity.

Research Design and Rationale

For over 50 years, the NHANES has assessed the health and nutritional status of noninstitutionalized adults and children in the United States. The NHANES program is part of the National Center for Health Statistics (NCHS), which is also a part of the CDC. The CDC produces health statistics for the nation based on NHANES results. NHANES uses a combination of interviews, lab work, and physical examinations to capture the health status of Americans every year (CDC, 2020c). The participants are not followed through in time, so my dissertation used a cross-sectional design. The data had already been collected by NHANES, was screened and had been made available to the public as secondary data. The data were analyzed using quantitative methods.

The entire dataset is available to download on the CDC website. I chose the relevant variables for my study. These included variables that would make it possible to calculate the prevalence of MetS, and variables that have been identified as risk factors for MetS based on past literature. All these variables were then merged into one dataset and analyzed. There were no deletions or changes to any values or cases. The present study assumed that all the data collected were valid and reliable. Approval from the

Institutional Review Board (IRB) for the present study was given after committee approval of the study's proposal. IRB number was 12-15-20-0334945.

Methodology

The goal of this study was to identify the significant risk factors of MetS across different age groups of different sex and ethnicities. A cross-sectional design examines multiple exposures (risk factors) in relation to a disease at a moment in time. A disadvantage of a cross-sectional study is that it is unable to determine the temporal sequence of disease and exposure. The design cannot tell which came first, the exposure or the disease. However, a cross-sectional study can assess the current disease prevalence in relation to the current exposure level. An advantage of a cross-sectional design is that if the study is based on a sample from the general population, as is the case for this NHANES study, the results are highly generalizable (Aschengrau, 2018). The appropriate magnitude of effect for a cross-sectional study is the odds ratio. The odds ratio value in this study signified how much more likely one is to have MetS versus not having MetS based on the risk factor variables (Howell, 2011).

Population

To assess the health status of Americans, NHANES examines a nationally representative sample of approximately 5,000 noninstitutionalized Americans of all ages every year across the country. To capture an accurate assessment of minorities in the present study, NHANES oversampled Hispanics, Asians, and African Americans. Additionally, the creators of NHANES recognized the growing prevalence of seniors in the US population, and this group has therefore also been oversampled. The health status

of older Americans will need to be assessed because the aging population will play a significant role in health care needs, public policy, and research priorities in the United States. Middle-aged to older seniors played a significant role in this study, as these age groups are most susceptible to metabolic disorders.

Sampling and Sampling Procedures

The 2015-2016 NHANES had a total sample of 9,254 participants from age 0 to 80. There were 3,398 minors under the age of 18 and 5,856 adults. I only analyzed the adult population. Of the total adult participants, 2,972 underwent laboratory tests and the physical examination required to diagnose MetS status. For analysis, demographic variables were merged with the MetS risk factor variables into one dataset. The variables from the NHANES dataset that were used as predictors for MetS were chosen based on past literature describing the risk factors for MetS.

The 46 predictors for MetS that were tested for significance in the present study were:

- Amount of sugar (grams/day)
- Total protein (grams/day)
- Amount of alcohol (grams/day)
- Amount of fiber (grams/day)
- Saturated fats (grams/day)
- Unsaturated fats (grams/day)
- Total cholesterol (mg/day)
- Sodium (mg/day)

- Potassium (mg/day)
- Vitamin B12 (mcg /day)
- Vitamin D (mcg/day)
- Vitamin C (mg/day)
- Insulin
- Triglyceride:HDL ratio
- Eicosapentaenoic acid (grams/day)
- Docosahexaenoic acid (grams/day)
- Albumin, urine (ug/mL)
- Creatinine, urine (mg/dL)
- Apolipoprotein (B) (mg/dL)
- Chlamydia – Urine
- HDL cholesterol
- LDL cholesterol
- Hepatitis B surface antibody
- Hepatitis C RNA
- Herpes Types I and II
- HIV Antibody
- Testosterone
- Health insurance coverage
- Alcohol intake over past year
- Money spent at supermarket/grocery store

- Money spent on eating out
- Inability to afford balanced meals
- Hep A immunization
- Hep B immunization
- Usual amount of sleep time on weekdays
- Average number of cigarettes smoked /day during past 30 days
- Ever been told you have asthma
- Ever been told you have coronary heart disease
- Ever been told you have congestive heart failure
- Ever been told you have thyroid problems
- Ever been told you have cancer or malignancy
- Vigorous recreational activities
- Number of days of vigorous work per week
- Moderate recreational activities
- How much time spent walking on a typical day
- Minutes sedentary activity per day

A general problem for researchers is determining an adequate sample size to avoid Type I and II errors (Yenipinar, 2019). For the present study, G-power was used to determine sample size. G-power is a downloadable program that calculates sample sizes for a variety of statistical tests commonly used in social and behavioral research. For a logistic regression test, an alpha level of .05, power of 95%, and odds ratio of 1.5, the

sample size needed was 1,312. Therefore, the sample size available from the NHANES dataset was more than sufficient to meet these requirements.

Instrumentation and Operationalization of Constructs

The definition for MetS for the present study was based on meeting the following three out of five criteria: abdominal obesity as measured by a waist circumference greater than 40 inches in men and greater than 35 inches in women, high blood pressure as measured by systolic blood pressure greater than 130 mm Hg, elevated triglycerides greater than 150mg/dL, reduced high-density lipoprotein less than 40mg/dL in men and less than 50mg/dL in women, and hyperglycemia as measured by a fasting glucose level of 100 mg/dL or greater (American Heart Association, 2019).

The dietary and behavioral variables used as predictors of MetS were recorded by NHANES staff during in-person interviews at the participants' homes. The participants' health measurements were made and specimens collected by physicians and health technicians in specially designed and equipped mobile trailers.

Data Analysis Plan

The data were analyzed using SPSS ver.25. The raw data were downloaded from the NHANES website and converted into SPSS data files. The outcome variable was Mets status. MetS status is a dichotomous variable with two outcomes, having MetS or not having MetS. There were41 risk factor variables that were used to predict MetS status. These 41 predictors are a combination of categorical and continuous variables. A logistic regression analysis was performed to answer research question 1. After

identifying the significant risk factors for MetS, an odds ratio was calculated to measure the likelihood of having MetS based on each of those significant risk factors.

Research question 1 was as follows:

Research Question 1: Will any of the following health and behavioral variables significantly predict MetS status: alcohol use, cardiovascular health, hormone levels, consumer behavior, recreational drug use, food security, insurance, immunizations, income, medical conditions, medications, physical activity, smoking, sleep, and diet?

$H_0$1: None of the health and behavioral variables will significantly predict MetS status.

H_a1: Some or all of the health and behavioral variables will significantly predict MetS status.

After the significant risk factors were identified using logistic regression, the risk factors were stratified based on age groups, sex, and race. The significant risk factors were both nominal and continuous variables and are presented in the appropriate tables and graphs.

The second research question was as follows:

Research Question 2: Do the significant predictors of MetS differ among age groups, sex, and ethnicity?

$H_0$2: The significant predictors of MetS do not differ among age groups, sex, and ethnicity.

H_a2: The significant predictors for MetS will differ among age groups and/or ethnicity.

Threats to Validity

This study utilized secondary data previously collected and published online by the CDC. The conclusions made from this study were intended to be generalizable to the greater US population. The integrity of the data collection process and the ability of the data to accurately represent the health status of all Americans were crucial for both internal and external validity. If there were errors in the data collection process that produced inaccuracies in measurements from physical examinations and of lab values, then internal validity would be threatened. If the sample weighting was insufficient, then external validity would be threatened. I had no involvement in the collection of the NHANES data, and I did not make any changes to the values in the dataset post download, so I will assume that the data were properly collected, and that the participants are a representative sample of the US population.

Summary

This quantitative study identified significant risk factors for MetS using a logistic regression analysis, which produced odds ratio values which indicated the likelihood of having MetS based on the risk factors. Tables and graphs were created to showcase the differences in MetS status stratified by the demographic variables, age, sex, and ethnicity. Secondary data was used for this study, and it will be assumed that these data were collected without error and with proper sampling so the results will be valid for generalizability to the US population.

Chapter 4: Results

The purpose of the present study was to find significant predictors of MetS from data taken from the 2015-2016 NHANES survey. The research questions were:

Research Question 1: Will any of the following health and behavioral variables significantly predict MetS status: alcohol use, cardiovascular health, hormone levels, consumer behavior, recreational drug use, food security, insurance, immunizations, income, medical conditions, medications, physical activity, smoking, sleep, and diet?

$H_0$1: None of the health and behavioral variables will significantly predict MetS status.

H_a1: Some or all of the health and behavioral variables will significantly predict MetS status.

Research Question 2: Do the significant predictors of MetS differ among age groups, sex, and ethnicity?

$H_0$2: The significant predictors of MetS do not differ among age groups, sex, and ethnicity.

H_a2: The significant predictors for MetS will differ among age groups, sex, and/or ethnicity.

In this study, age groups were most associated with differences in the four predictors of MetS, so the null hypothesis was rejected, and the alternate hypothesis was accepted. MetS prevalence was low in the youngest age group and consistently increased to the highest age group for both men and women of all races.

This chapter presents the results of the data analysis. Descriptive analysis of MetS status amongst the age, race, and sex will first be presented. Then the results of the logistic regression test will show what variables were significant predictors of MetS. These predictors were tested for significant differences amongst age and race groups in a series of both ANOVA and chi-square tests. Due to physiological differences in sex, men and women have separate ANOVA and chi-square tests performed.

Since 1971, NHANES has assessed the health and nutritional status of noninstitutionalized adults and children in the United States annually. The data for the present study was collected for the 2015-2016 assessment. The data used for the present study had already been collected, screened and collection techniques were reviewed by an ethics review board. The 2015-2016 data is available to the public as secondary data on the CDC's website.

In this quantitative analysis of the 2015-2016 NHANES, there were a total of 2,303 cases that either met the requirement for MetS or not. In the present study, 28% (636) were classified as having MetS and 72% (1,667) did not have MetS. Both men and women had similar MetS prevalence values at 26.90% and 28.32%, respectively. However, MetS prevalence varied over different age groups and races. Table 3 summarizes the overall results of MetS status by sex and Table 4 summarizes the overall results of MetS status by age group and race.

Table 3

MetS Statuses for All Participants by Sex

		MetS Status			
		Has MetS	Does not have MetS	*n*	Percentage with MetS
Sex	Male	308	837	1,145	26.90%
	Female	328	830	1,158	28.32%
	Total	636	1,667	2,303	27.62%

Table 4

MetS Statuses for All Participants by Race and Age Group

Race	Age Group	Has MetS	Does not have MetS	Total
Non-Hispanic White	18-29	9	114	123
	30-49	52	170	222
	50-69	98	160	258
	>70	68	113	181
Black	18-29	3	97	100
	30-49	35	107	142
	50-69	61	110	171
	>70	18	27	45
Hispanic	18-29	14	131	145
	30-49	53	167	220
	50-69	120	142	262
	>70	50	44	94
Asian	18-29	4	56	60
	30-49	11	95	106
	50-69	12	59	71
	>70	7	12	19
Other	18-29	4	18	22
	30-49	6	32	38
	50-69	7	10	17
	>70	4	3	7
All Races	All ages	636 (28%)	1667 (72%)	2,303

Table 5 summarizes MetS status in men based on age group and race and Figure 22 displays a histogram of MetS status in men. There was a continual increase in MetS

prevalence in males from the 18 to 29 age group to the 50 to 69 age group for all races. MetS prevalence in males had a range from 2% to 18% in the 18 to 29 age group. Then the prevalence range increased to 11% to 30% for the 30 to 49 age group and then increased again to 15% to 46% for the 50 to 69 age group. Asian males had the lowest overall prevalence at 13%, and Hispanic males had the highest at 31%. Hispanic males in the 50 to 69 age group were the single group with highest MetS prevalence at 46%.

Table 5

MetS Statuses for Male Participants by Race and Age Group

Race	Age Group	Has MetS	Does not have MetS	Total	Percentage with MetS	Without MetS Percentage
White	18-29	7	48	55	13%	87%
	30-49	29	88	117	25%	75%
	50-69	46	85	131	35%	65%
	>70	38	64	102	37%	63%
	Total	120	285	405	30%	70%
Black	18-29	1	42	43	2%	98%
	30-49	19	45	64	30%	70%
	50-69	28	56	84	33%	67%
	>70	5	15	20	25%	75%
	Total	53	158	211	25%	75%
Hispanic	18-29	8	68	76	11%	89%
	30-49	25	81	106	24%	76%
	50-69	56	67	123	46%	54%
	>70	18	27	45	40%	60%
	Total	107	243	350	31%	69%
Asian	18-29	3	31	34	9%	91%
	30-49	6	47	53	11%	89%
	50-69	6	33	39	15%	85%
	>70	2	7	9	22%	78%
	Total	17	118	135	13%	87%
Other/ Mixed Race	18-29	2	9	11	18%	82%
	30-49	4	15	19	21%	79%
	50-69	4	7	11	36%	64%
	>70	1	2	3	33%	67%
	Total	11	33	44	25%	75%

Figure 22

Histogram of MetS Statuses in Males by Age Group and Race

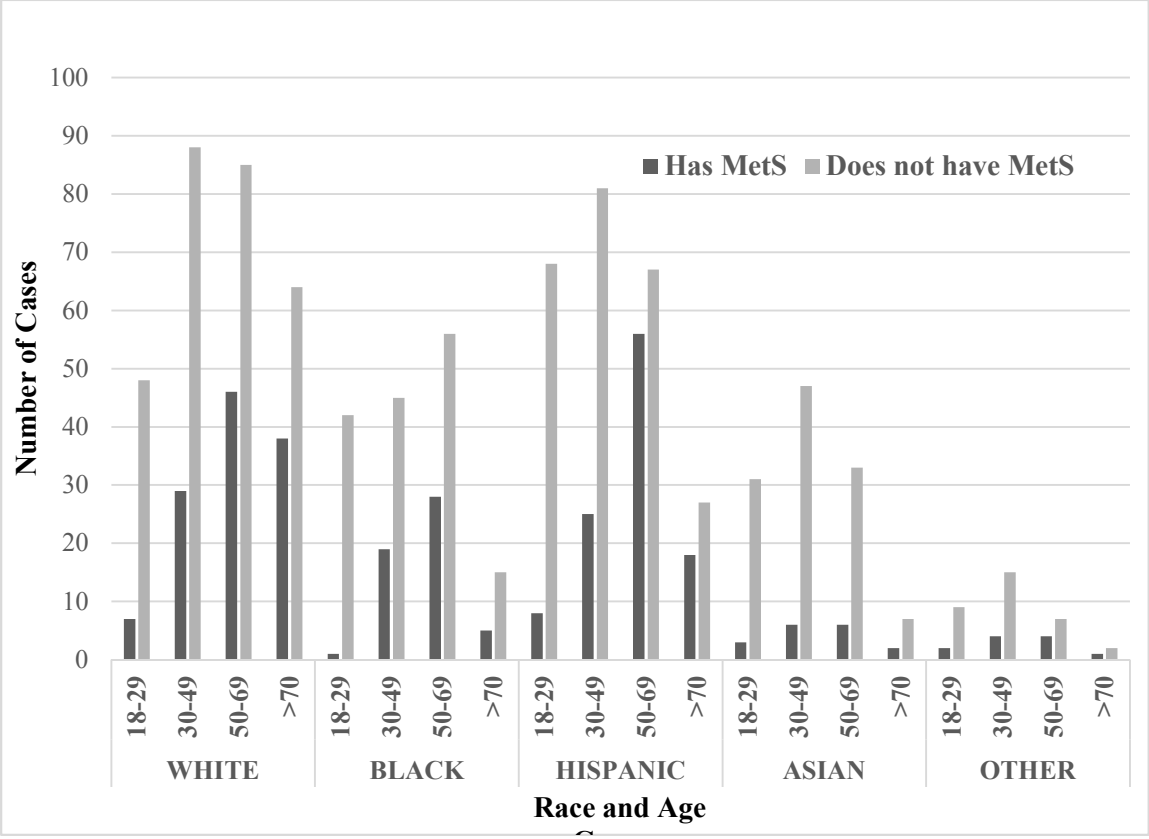


Table 6 summarizes MetS status in women based on age group and race and Figure 23 displays a histogram of MetS status in women. There was a continual increase in MetS prevalence in females from the 18 to 29 age group to the 50 to 69 age group for the White, Black, Hispanic, and Asian races. MetS prevalence in females had a range from 3% to 18% in the 18 to 29 age group. Then the prevalence range increased to 9% to 25% for the 30 to 49 age group and then increased again to 19% to 50% for the 50 to 69 age group. Asian females had the lowest overall prevalence at 15%, and Hispanic females

had the highest at 35%. Hispanic females over age 70 was the single group with the highest MetS prevalence at 65%.

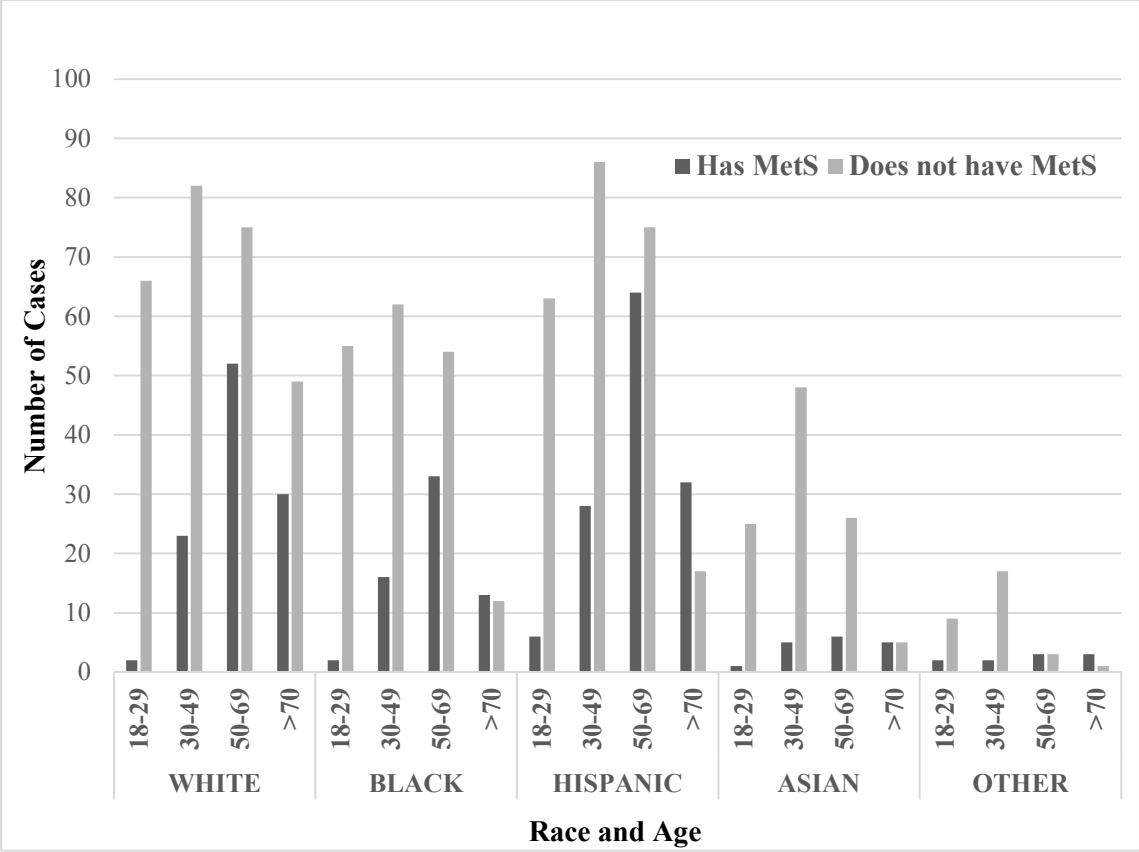
Table 6

MetS Statuses for Female Participants by Race and Age Group

Race	Age Group	Has MetS	Does not have MetS	Total	Percentage with MetS	Without MetS Percentage
White	18-29	2	66	68	3%	97%
	30-49	23	82	105	22%	78%
	50-69	52	75	127	41%	59%
	>70	30	49	79	38%	62%
	Total	107	272	379	28%	72%
Black	18-29	2	55	57	4%	96%
	30-49	16	62	78	21%	79%
	50-69	33	54	87	38%	62%
	>70	13	12	25	52%	48%
	Total	64	183	247	26%	74%
Hispanic	18-29	6	63	69	9%	91%
	30-49	28	86	114	25%	75%
	50-69	64	75	139	46%	54%
	>70	32	17	49	65%	35%
	Total	130	241	371	35%	65%
Asian	18-29	1	25	26	4%	96%
	30-49	5	48	53	9%	91%
	50-69	6	26	32	19%	81%
	>70	5	5	10	50%	50%
	Total	17	104	121	14%	86%
Other/ Mixed Race	18-29	2	9	11	18%	82%
	30-49	2	17	19	11%	89%
	50-69	3	3	6	50%	50%
	>70	3	1	4	75%	25%
	Total	10	30	40	25%	75%

Figure 23

Histogram of MetS Statuses in Females by Age Group and Race



Logistic Regression

Logistic regression was performed separately on each of the predictors. The assumptions of a logistic regression test are that the dependent variable be binary, each observation is independent of each other, minimal or no multicollinearity among the predictor variables, there is linearity of the predictors and log odds, and that there be a sufficient sample size. Since this is secondary data collected by the CDC, I am assuming that the dataset was screened for errors and that each case is valid and the assumptions were met. No change or deletion in the dataset was made.

Of the 46 predictors, only four were found to be significant predictors of MetS. The four predictors were: TG:HDL ratio, Insulin levels, Testosterone levels, and vigorous recreational activities. Tables 7 summarizes the classification results, and table 8 summarizes the logistic regression results.

Table 7

Classification Results from Logistic Regression

			Predicted		
			MetS Status		
			Has MetS	Does not have MetS	Percentage Correct
Observed	MetS Status	Has MetS	235*	367**	39%
		Does not have MetS	84**	1,433*	95%
			Total Percentage Correct		79%

Note. * = values are correctly classified.

** = values classified incorrectly.

The logistic regression model correctly classified 95% of the cases where the participants did not have MetS and 39% of the cases who had MetS. The model had an overall rate of 79% correct.

Table 8

Logistic Regression Summary

Source	B	*SE*	Wald	*p*	*OR*	95% CI *OR*
TG:HDL Ratio	-.464	.033	198.003	0.000	0.629	[.590,.671]
Insulin levels	-.033	.005	99.526	0.000	0.967	[.958, .977]
Testosterone levels	0.001	.000	30.065	0.000	1.001	[1.000, 1.002]
Vigorous recreational activities	.823	.156	27.830	0.000	2.277	[1.677, 3.092]
Constant	2.126	.122	305.954	0.000	8.384	

The logistic regression test is based on how well the model correctly predicts participants having membership in the "not having MetS" group. The chi-square test value was significant at $\chi^2(4) = 554.456$, $p<.05$. This means that the model with the four predictors entered simultaneously was significantly different from the null model where no predictors were entered. TG:HDL ratio, Insulin levels, Testosterone levels, and Vigorous recreational activities were all significant at $p<.001$. The logistic regression model was $log\left(\frac{p}{1-p}\right) = -.464_{\text{TG:HDL}} \quad -0.033_{\text{Insulin}} + 0.001_{\text{Testosterone}} + .823_{\text{Vigorous Recreational Activity}} + 2.126$, where p is the probability of not having Mets.

The odds-ratio value refers to the change in probability of belonging to one of the two groups in the dichotomous dependent variable when there is an incremental change in the predictor variable. An odds-ratio value of 1.00 means that any incremental change in the predictor variable has no effect on membership in MetS status. In the present study,

an odds-ratio value more than 1.0 increased the probability of group membership in the "not having MetS" group, and a value less than 1.0 decreased the probability of membership in the "not having MetS group."

The negative beta coefficient and odds-ratio value less than one for the TG:HDL ratio means that as the TG:HDL ratio rose, there was a less likely probability of being classified as "not having MetS." One minus the odds-ratio value of 0.629 is 0.371, which is 37%. This means that as the TG:HDL ratio increased incrementally, the odds of being in the "does not have MetS" group decreased by 37%.

The negative beta coefficient and odds-ratio value less than one for insulin levels means that as insulin levels rose, there was a less likely probability of being classified as "not having MetS." One minus the odds-ratio value of 0.967 is 0.033, which is 3.3%. This means that as insulin levels rose incrementally, the odds of being in the "does not have MetS" group decreased by 3.3%.

The positive beta coefficient and odds-ratio value of 1.001 for testosterone levels means that a participant was 1.001 times as likely to not have MetS with higher levels of testosterone. However, the value of 1.001 is close to the null value of 1.0, where the predictor would have no effect on the likelihood of group membership. An analysis of the testosterone levels in the different age groups, sex and races is necessary to explain how testosterone levels is a significant predictor for MetS status.

The question asked to the participants for the predictor vigorous recreational activities was: "In a typical week do you do any vigorous-intensity sports, fitness, or recreational activities that cause large increases in breathing or heart rate like running or

basketball for at least 10 minutes continuously?" The response was either Yes or No. The odds-ratio for vigorous recreational activities was 2.27 which means that a participant was 2.27 times as likely to be in the "does not have MetS" group if he/she answered yes to that question.

Although there were no significant differences between sexes for MetS Status, the analyses of the 4 predictors were separated by sex, because there are physiological differences in the levels of insulin, triglycerides, and testosterone in men and women.

The Triglyceride:HDL Ratio

The TG:HDL ratio is the ratio between the level of triglycerides in circulation and the level of HDL in circulation. A high ratio value does not cause MetS; rather it is a biomarker that is representative of a prothrombotic, proinflammatory state and increased insulin resistance (Nur, 2019). Primary hypertriglyceridemia is the result of genetic disorders, while secondary hypertriglyceridemia is acquired and results from obesity, excessive alcohol intake, and hyperglycemia. Hypertriglyceridemia is also associated with insulin resistance, non-alcoholic fatty liver disease, and MetS. Secondary causes of hypertriglyceridemia are more common than primary causes, and this study assumed that more cases of hypertriglyceridemia are due to poor dieting compared to genetic inheritance. The higher the TG:HDL ratio, the higher the risk for heart disease. There is no official cut-off point as to what the ratio value should be to represent a healthy state. Literature on the subject suggests that a TG:HDL ratio below 2.5 is healthy, while higher values indicate increased risk for heart disease (Quispe, 2015).

A high TG:HDL ratio is the result of too much triglycerides in circulation, and increased levels of VLDL produced by the liver. HDL is the cardioprotective lipoprotein that functions to remove cholesterol from vessels and bring it back to the liver to be transported for elimination through a process called reverse cholesterol transport (RCT). The process of RCT occurs through two pathways, the direct and indirect pathways. In the direct pathway, the liver produces HDL particles which are then released into circulation. HDL removes cholesterol plaque build-up from the walls of vessels, including the coronary arteries of the heart. The HDL particles then travel back to the liver and release their stored cholesterol and then travel back into circulation for the process to begin again (Ferrier, 2017). The indirect pathway involves a protein called the cholesterol ester transfer protein (CETP). In circulation, the role of CETP is to transfer cholesterol from HDL to VLDL particles and, in exchange, to transfer triglycerides from VLDL to HDL particles. This results in smaller HDL particles that have become cholesterol depleted but dense with triglycerides. Then, when the triglycerides are removed from the HDL particles in the liver, the liver degrades these smaller HDL particles which are then excreted through the kidneys (Sultani, 2020). This results in fewer HDL particles available for RCT activity.

A TG:HDL ratio under 2.5 would indicate normal levels of triglycerides in circulation, and normal levels and size of HDL. Values above 2.5 would indicate increased triglycerides in circulation and smaller sized HDL in lower levels. The higher the TG:HDL ratio, the more severe the risk for heart disease. Obesity and increased visceral adipose tissue surrounding the internal organs promotes the development of

insulin resistance and hypertriglyceridemia. Hypertriglyceridemia stimulates the activity of CETP, which results in a higher TG:HDL ratio through the indirect process of RCT (Wu, 2014). Tables 9 and 10 show the mean TG:HDL ratios for men and women based on age groups and race categories.

Table 9

TG:HDL Mean Ratio Values in Men Based on Age Group and Race Categories

			TG:HDL Ratio (SD)	**Sample Size**	**Normal or High**
White	Has MetS	18-29 years of age	4.88(2.95)	6	High
		30-49 years of age	5.34(3.81)	27	High
		50-69 years of age	4.82(2.93)	46	High
		70 years of age and above	3.68(2.74)	37	High
	Does not have MetS	18-29 years of age	2.11(1.45)	43	Normal
		30-49 years of age	2.38(1.99)	81	Normal
		50-69 years of age	2.07(2.03)	79	Normal
		70 years of age and above	1.67(0.98)	57	Normal
Hispanic	Has MetS	18-29 years of age	4.11(3.14)	8	High
		30-49 years of age	6.12(3.02)	25	High
		50-69 years of age	6.98(12.80)	55	High
		70 years of age and above	4.68(6.20)	16	High
	Does not have MetS	18-29 years of age	2.15(1.54)	66	Normal
		30-49 years of age	3.06(3.94)	72	High
		50-69 years of age	2.6(3.56)	67	High
		70 years of age and above	1.56(0.67)	20	Normal
Black	Has MetS	18-29 years of age	3.72	1	High
		30-49 years of age	5.05(6.88)	19	High
		50-69 years of age	3.6(3.72)	26	High
		70 years of age and above	2.39(2.11)	4	Normal
	Does not have MetS	18-29 years of age	1.33(0.97)	38	Normal
		30-49 years of age	2.45(2.53)	37	Normal
		50-69 years of age	1.45(1.09)	50	Normal
		70 years of age and above	0.94(0.52)	13	Normal

Asian	Has MetS	18-29 years of age	4.66(1.53)	3	High
		30-49 years of age	8.84(8.03)	6	High
		50-69 years of age	7.93(7.83)	6	High
		70 years of age and above	0.98	1	Normal
	Does not have MetS	18-29 years of age	1.58(0.84)	31	Normal
		30-49 years of age	3.15(2.57)	43	High
		50-69 years of age	2.59(2.07)	31	High
		70 years of age and above	2.7(2.14)	6	High
Other Race	Has MetS	18-29 years of age	2.18(1.01)	2	Normal
		30-49 years of age	10.12(14.40)	4	High
		50-69 years of age	8.80(7.09)	4	High
		70 years of age and above	2.78	1	High
	Does not have MetS	18-29 years of age	1.50(0.64)	9	Normal
		30-49 years of age	2.56(2.02)	15	High
		50-69 years of age	1.79(0.97)	6	Normal
		70 years of age and above	2.78(1.13)	2	High

Table 10

TG:HDL Mean Ratio Values in Women Based on Age Group and Race Categories

			TG:HDL Ratio	Sample Size	Normal Or High
White	Has MetS	18-29 years of age	4.10(1.20)	2	High
		30-49 years of age	4.03(2.13)	23	High
		50-69 years of age	3.82(2.59)	52	High
		70 years of age and above	2.36(1.34)	25	Normal
	Does not have MetS	18-29 years of age	1.53(1.08)	58	Normal
		30-49 years of age	1.70(0.93)	82	Normal
		50-69 years of age	1.76(1.25)	74	Normal
		70 years of age and above	1.61(0.59)	17	Normal
Hispanic	Has MetS	18-29 years of age	3.83(3.13)	6	High
		30-49 years of age	6.64(2.12)	27	High
		50-69 years of age	3.78(2.43)	62	High
		70 years of age and above	3.35(3.07)	28	High
	Does not have MetS	18-29 years of age	1.53(1.08)	58	Normal
		30-49 years of age	1.70(0.93)	82	Normal
		50-69 years of age	1.76(1.25)	74	Normal
		70 years of age and above	1.61(0.59)	17	Normal
Black	Has MetS	18-29 years of age	1.86(0.68)	2	Normal
		30-49 years of age	2.35(1.44)	15	Normal
		50-69 years of age	2.12(1.64)	33	Normal
		70 years of age and above	1.58(1.18)	12	Normal
	Does not have MetS	18-29 years of age	0.92(0.46)	52	Normal
		30-49 years of age	1.13(0.61)	57	Normal
		50-69 years of age	1.17(0.62)	51	Normal
		70 years of age and above	1.02(0.48)	9	Normal
Asian	Has MetS	18-29 years of age	4.56	1	High
		30-49 years of age	10.37(10.74)	5	High
		50-69 years of age	4.13(2.94)	5	High
		71 years of age and above	2.34(0.72)	5	Normal
	Does not have MetS	18-29 years of age	1.66(1.46)	23	Normal
		30-49 years of age	1.19(0.74)	44	Normal
		50-69 years of age	1.48(1.03)	25	Normal
		71 years of age and above	1.74(0.66)	4	Normal

Other Race	Has MetS	18-29 years of age	7.25(1.92)	2	High
		30-49 years of age	6.11(4.12)	2	High
		50-69 years of age	2.30(1.01)	3	Normal
		72 years of age and above	2.62(1.61)	3	High
	Does not have MetS	18-29 years of age	1.67(0.78)	7	Normal
		30-49 years of age	1.51(0.77)	16	Normal
		50-69 years of age	1.15(0.58)	3	Normal
		72 years of age and above	0.89	1	Normal

ANOVA Tests for TG:HDL Ratio in Men for Age Group and MetS Statuses

Assumptions for factorial ANOVA are that the dependent variables be continuous, there is normality in scores, there is homogeneity of variance in scores, and there is no multicollinearity amongst the independent variables. I am assuming that the dataset was screened for errors and that each case is valid and the assumptions were met. No change or deletion in the dataset was made.

The TG:HDL ratio was the strongest predictor for MetS in the logistic regression. A 2 by 4 two-way factorial ANOVA test was done individually for men and women with MetS status and age group as the two factors, and the TG:HDL ratio as the dependent variable. The descriptive and ANOVA results for men are summarized in Tables 11 and 12. The main effect for MetS status was significant at $F(1,1,055) = 69.57$, $p<.05$. The mean value for the TG:HDL ratio in men with MetS was 4.93, which was significantly higher than the mean of 2.09 in men without MetS.

Age group was also significant at $F(3,1,055) = 5.93$, $p<.05$. Post hoc tests using the Scheffe test showed the ratio value of 3.03 in the 18-29 age group was significantly lower compared to the ratios of 4.37 and 3.93 for the 30-49 group and 50-69 age group, respectively. However, the Beta-squared value for the interaction was low at .02.

Table 11

TG:HDL Ratio for MetS Statuses and Age Group in Men (N=1,063)

MetS Status	Mean(SD)	Age Group	Mean (SD)
Has MetS	4.93(0.30)	18-29	3.03(0.48)
Does not have MetS	2.09(0.16)	30-49	4.37(0.26)
		50-69	3.93(0.22)
		Over 70	2.72(0.34)

Table 12

ANOVA summary for TG:HDL Ratio in MetS Statuses and Age Groups in Men (N=1,063)

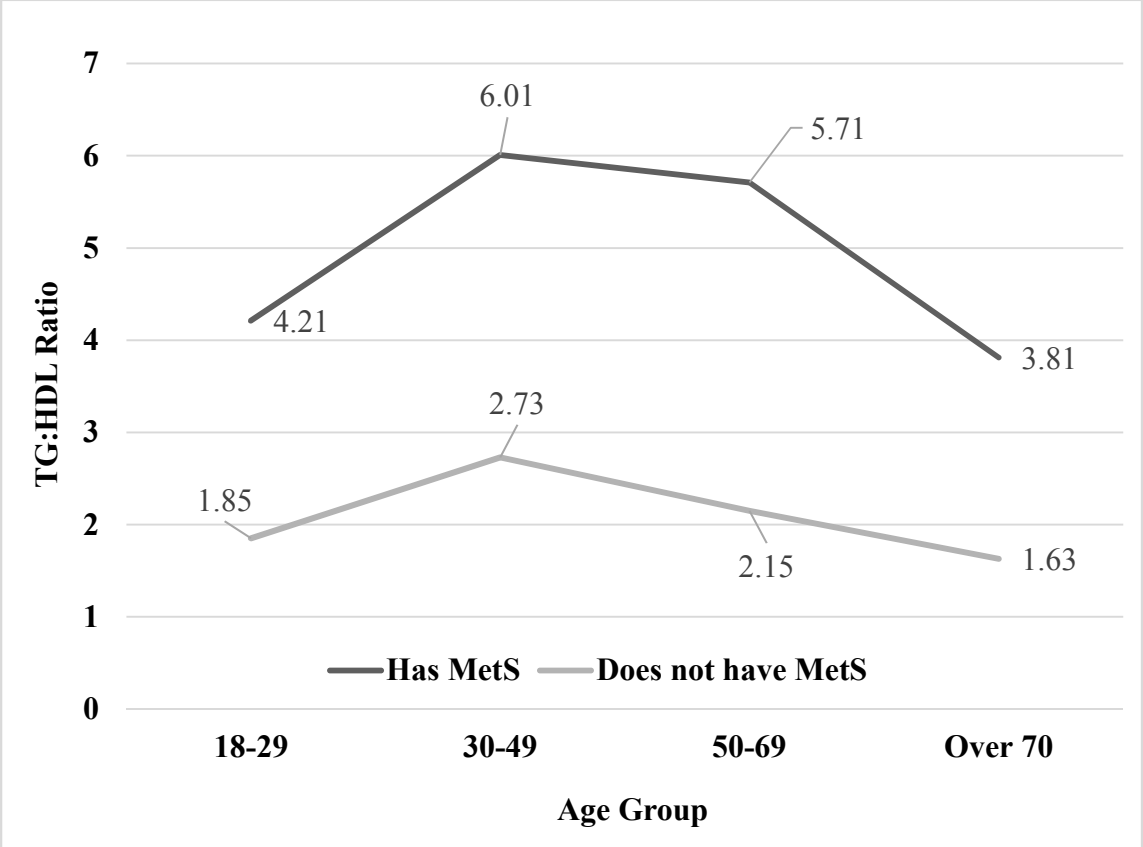
Source	F-ratio	d/f	p	η2
MetS Status	*69.57	1	0.000	0.06
Age Groups	*5.93	3	0.001	0.20
MetS by Age Groups	1.22	3	0.301	0.00

Note. *Significant *at p*<.05.

Figure 24 shows how the TG:HDL ratio was higher in the "has MetS" group compared to the "does not have MetS" group across all four age groups. Using an adjusted Bonferroni correction, simple effects testing showed that each difference in ratio values between the MetS status groups was significantly different for each age group. All subsequent simple effects testing for multiple comparisons used an adjusted Bonferroni correction.

Figure 24

TG:HDL Ratio in MetS Statuses and Age Groups in Men



Note. Simple effects testing using an adjusted Bonferroni value showed that at every age group, the TG:HDL ratio was significantly higher in the MetS group compared to those who did not have MetS.

ANOVA Tests for TG:HDL Ratio in Men for Race and MetS Status

A 2 by 5 two-way factorial ANOVA was done with MetS status and race as the two factors and the TG:HDL ratio as the dependent variable. Descriptive and ANOVA summary results are seen in Tables 13 and 14. The main effect from MetS status was significant at $F(1,053) = 84.14$, $p<.05$, with an eta-squared value of .07. The main effect

from race was significant at F(4,1,053) = 5.83, p<.05, with a low eta-squared value of .02. The Scheffe post hoc test showed that the mean ratio value of 4.36 in Hispanics was significantly higher than the mean ratio value of 2.85 in Blacks. The interaction between MetS status and age group was non-significant at F(4,1,053) = 2.20, p>.05.

Table 13

TG:HDL Ratio for MetS Statuses and Race in Men (N=1,063)

MetS Status	**Mean(SD)**	**Race**	**Mean (SD)**
Has MetS	5.92(.36)	White	3.33(.23)
Does not have MetS	2.18(.19)	Black	2.85(.34)
		Hispanic	4.36(.24)
		Asian	4.88(.55)
		Other	4.83(.72)

Table 14

ANOVA summary for TG:HDL Ratio in MetS Statuses and Race in Men (N=1,063)

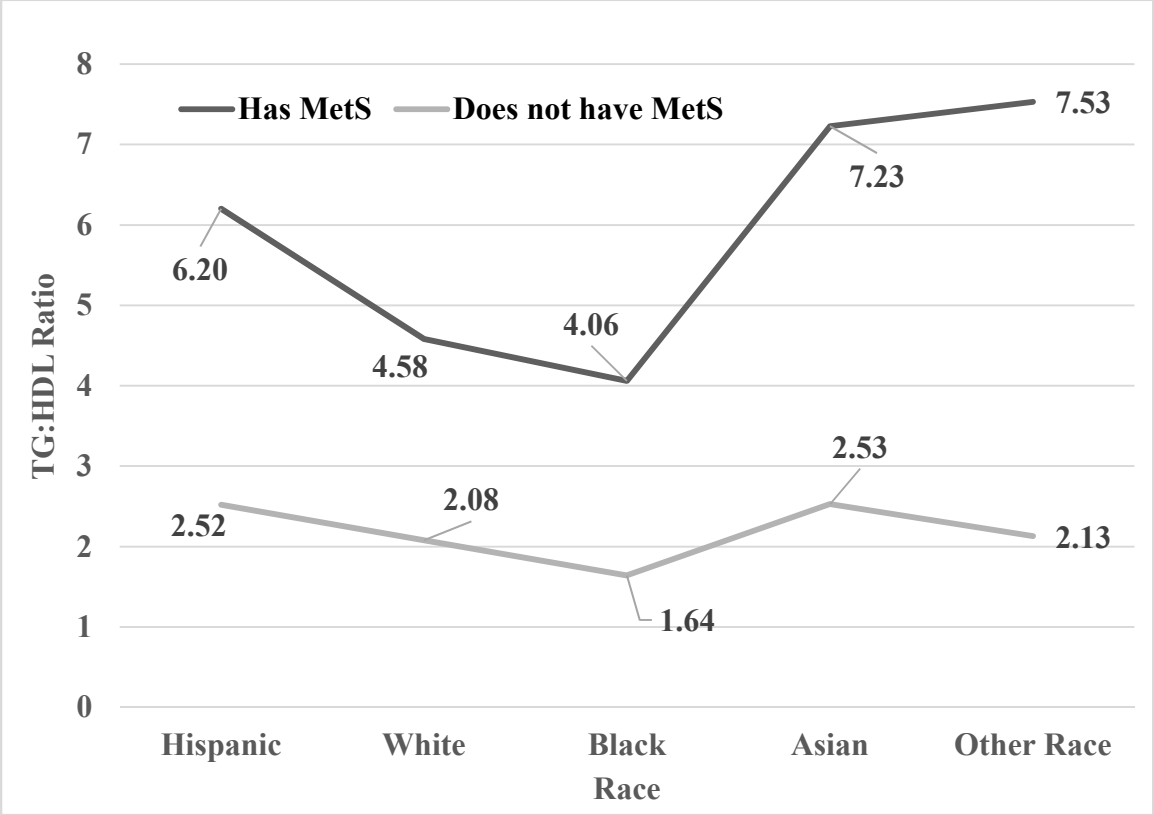
Source	**F-ratio**	**d/f**	**p**	**η2**
MetS Status	*84.14	1	0.000	0.07
Race	*5.83	4	0.000	0.02
MetS by Age Groups	2.20	4	0.070	0.00

Note. *Significant *at p*<.05.

Figure 25 shows how the TG:HDL ratio was higher in the "has MetS" group compared to the "does not have MetS" group across all race groups. Simple effects testing showed that each difference in ratio values between the MetS status groups was significantly different across all race categories.

Figure 25

TG:HDL Ratio in MetS Statuses and Race in Men



Note. Simple effects testing showed that for every race category, the TG:HDL ratio was significantly higher in the MetS group compared to those who did not have MetS.

ANOVA Tests for TG:HDL Ratio in Women for Age Group and MetS Status

The descriptive and ANOVA results for men are summarized in Tables 15 and 16. The main effect for MetS status was significant at $F(1,1,077) = 186.54$, $p<.05$. The mean value for the TG:HDL ratio in women with MetS was 3.57, which was significantly higher than the mean of 1.45 in women without MetS. Age group was also significant at $F(3,1,077) = 5.27$, $p<.05$.

Post hoc test showed that the ratio of 2.06 in the over 70 age group was significantly lower compared to the three other age groups. However, the Beta-squared value for the interaction was low at .01. The interaction between MetS status and age groups was significant at F(3,1077) = 6.96 but had a low Beta square value of .01.

Table 15

TG:HDL Ratio for MetS Statuses and Age Group in Women (N=1,085)

MetS Status	**Mean(SD)**	**Race**	**Mean (SD)**
Has MetS	3.57(.14)	18-29	2.74(.24)
Does not have MetS	1.45(.07)	30-49	2.73(.11)
		50-69	2.51(.09)
		Over 70	2.06(.14)

Table 16

ANOVA summary for TG:HDL Ratio in MetS Statuses and Age Groups in Women (N=1,085)

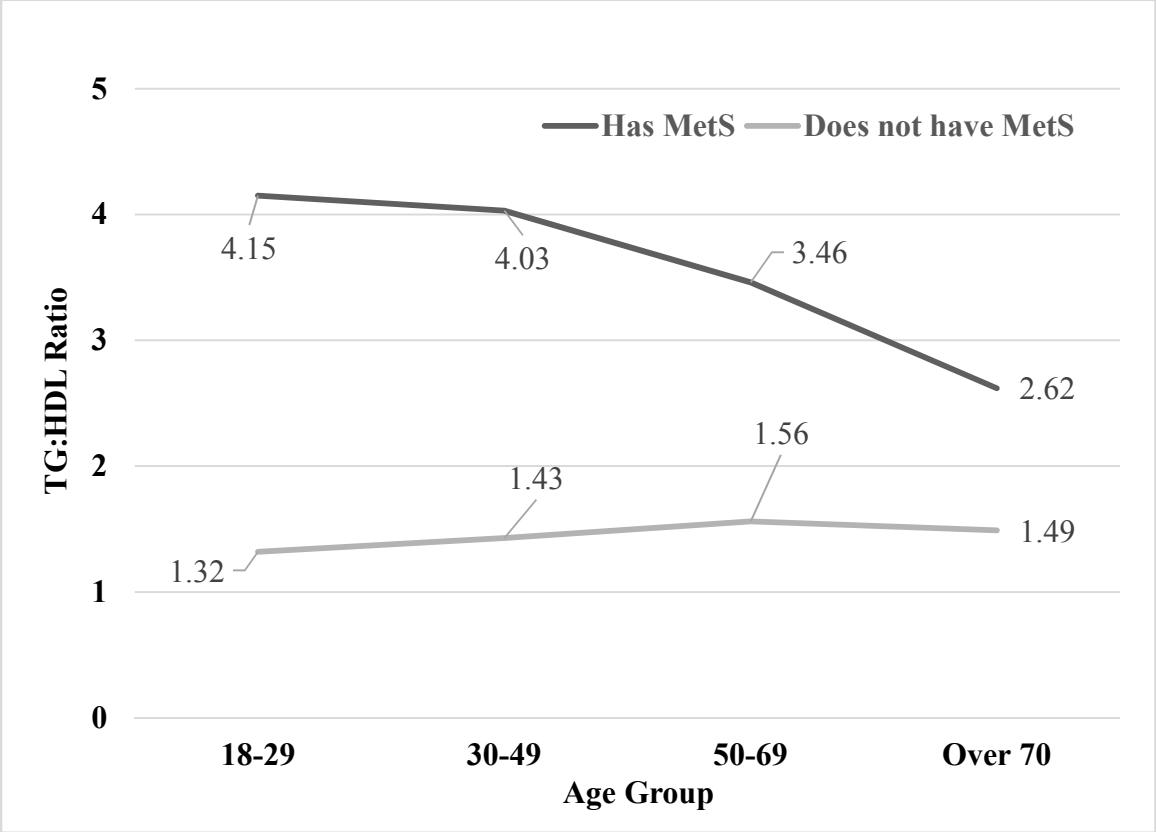
Source	**F-ratio**	**d/f**	**p**	**η2**
MetS Status	*186.54	1	0.000	0.15
Age Groups	*5.27	3	0.001	0.01
MetS by Age Groups	*6.96	3	0.000	0.01

Note. *Significant *at p*<.05.

Figure 26 shows how the TG:HDL ratio was higher in the "has MetS" group compared to the "does not have MetS" group across all four age groups. Simple effects testing showed that each difference in ratio values between the MetS status groups was significantly different for each age group.

Figure 26

TG:HDL Ratio in MetS Statuses and Age Groups in Women



Note. Simple effects testing showed that for every age group, the TG:HDL ratio was significantly higher in the MetS group compared to those who did not have MetS.

ANOVA Tests for TG:HDL Ratio in Women for Race and MetS Status

Descriptive and ANOVA summary results are seen in Tables 17 and 18. The main effect from MetS status was significant at $F(1,075) = 204.01$, $p<.05$, with an eta-squared value of .16. The main effect from race was significant at $F(4,1,075) = 20.83$, $p<.05$, with an eta-squared value of .07. The Scheffe post hoc test showed that the mean ratio of 1.57 in Blacks was significantly lower compared to the mean ratio of the remaining race groups.

The interaction between MetS status and age group was significant at $F(4,1,075) = 10.53$, $p<.05$. The difference in the TG:HDL ratio values between MetS status was the lowest for Blacks, while Asians had the highest difference. However, simple effects testing showed that all differences were significant across racial categories.

Table 17

TG:HDL Ratio for MetS Statuses and Race in Women (N=1,085)

MetS Status	**Mean(SD)**	**Race**	**Mean (SD)**
Has MetS	3.79(.15)	White	2.51(.09)
Does not have MetS	1.43(.08)	Black	1.57(.12)
		Hispanic	2.69(.09)
		Asian	3.48(.22)
		Other	2.82(.30)

Table 18

ANOVA summary for TG:HDL Ratio in MetS Statuses and Race in Women (N=1,085)

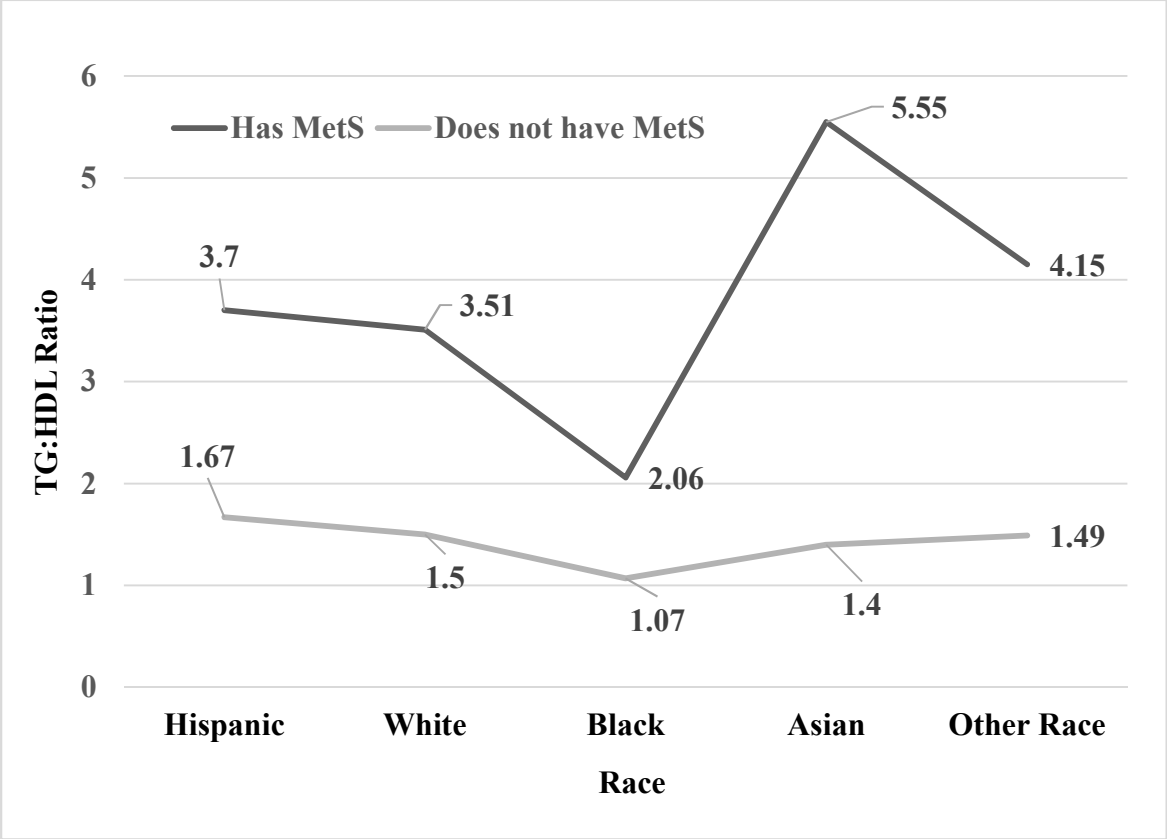
Source	F-ratio	d/f	p	η2
MetS Status	*204.01	1	0.000	0.16
Race	*20.83	4	0.000	0.07
MetS by Age Groups	*10.53	4	0.000	0.04

Note. *Significant *at p*<.05.

Figure 27 shows how the TG:HDL ratio was higher in the "has MetS" group compared to the "does not have MetS" group across all race categories.

Figure 27

TG:HDL Ratio in MetS Statuses and Race in Women



Note. Simple effects testing showed that for every race category, the TG:HDL ratio was significantly higher in the MetS group compared to those who did not have MetS.

Insulin Levels

ANOVA Tests for Insulin Levels in Men for Age Group and MetS Status

The descriptive and ANOVA results are summarized in Tables 19 and 20. The main effect for MetS status was significant at $F(1,1,125) = 109.39$, $p<.05$. The mean score for insulin levels in men with MetS was 25.92 μU/mL, which was significantly different from the mean score of 10.67 μU/mL in men without MetS. Age groups was also significant at $F(3,1,125) = 4.32$, $p<.05$. However using the conservative Scheffe test for post hoc multiple comparisons, there were no significant differences amongst the different age groups. The eta-squared value for the main effect in age groups was also low at .01. The interaction between the two factors was significant but also with a low eta-squared value of .01.

Figure 28 shows how insulin levels in the "has MetS" group were consistently higher compared to the "does not have MetS" group across all of the four age groups. Using an adjusted Bonferroni correction, simple effects testing showed that each difference in insulin scores between the MetS groups was significantly different for each age group.

Table 19

Insulin Mean Levels for MetS Statuses and Age Groups in Men (N=1,133)

MetS Status	**Mean(SD)**	**Age Groups**	**Mean (SD)**
Has MetS	25.92(1.3)	18-29	23.93(2.07)
Does not have MetS	10.67(.66)	30-49	17.44(17.44)
		50-69	16.27(0.96)
		Over 70	15.52(1.42)

Table 20

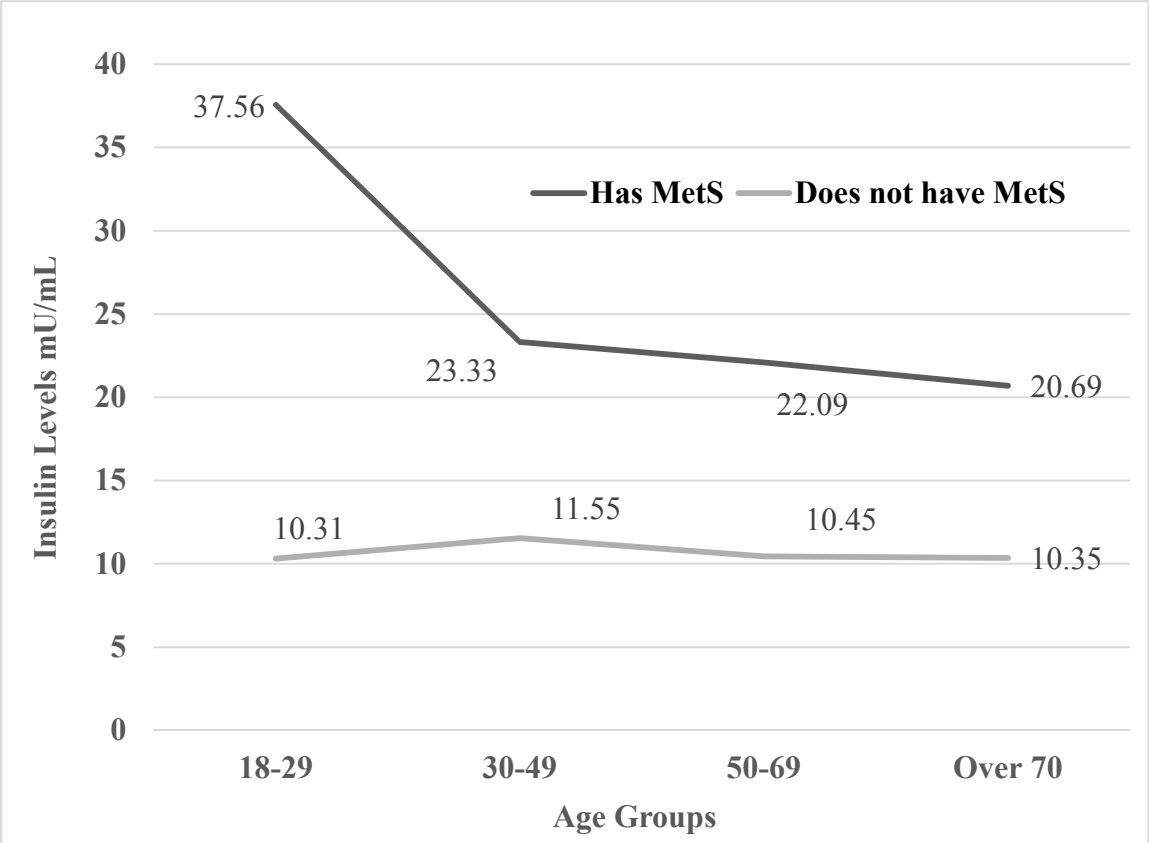
ANOVA summary for Insulin Levels in MetS Statuses and Age Groups in Men (N=1,333)

Source	F-ratio	d/f	p	η2
MetS Status	*109.39	1	0.000	0.09
Age Groups	*4.32	3	0.005	0.01
MetS by Age Groups	*4.50	3	0.004	0.01

Note. *Significant *at p*<.05.

Figure 28

Insulin Levels in MetS Statuses and Age Groups in Men



Note. Simple effects testing showed that for every age group, insulin levels was significantly higher in the MetS group compared to those who did not have MetS.

Insulin Levels and HOMA-IR

As discussed previously, insulin is a hormone that is secreted by the beta cells of the pancreas to maintain blood glucose levels within a normal range. The pancreas is stimulated to release insulin by glucose, so there is an insulin spike after a high carbohydrate meal. A high increase in insulin forces the body to make use of the blood sugar either by cells for energy, such as muscles during exercise, or by being stored away as fat if the body is not physically active. Though the exact causes of insulin resistance (IR) remain unknown, IR is associated with high caloric diets and obesity (Youssef, 2021). IR starts to develop when the cells that need glucose for energy have become resistant to the effects of insulin, and glucose is prevented from entering the cells that need it for energy. The pancreas then has to produce more insulin than previously in order to maintain normal blood glucose levels. With increasing IR, the pancreas reaches its maximum capability to produce insulin, and this leads to hyperglycemia and eventually type 2 diabetes (Lu, 2021).

Normal fasting insulin levels should be under 25 μU/mL, but a more accurate assessment of IR and insulin sensitivity is the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) value. HOMA-IR was formulated in 1985 and represents the relationship between pancreatic beta cell function and the ability to maintain adequate glycemic levels. As seen in Figure 29, HOMA-IR is calculated by multiplying fasting glucose levels by fasting insulin levels and then dividing by 405 (Mathews, 1985, Sanchez-Garcia, 2020). An accepted general guideline for cutoffs is as follows: under 2.0 is optimal and indicates high insulin sensitivity, values between 2.0 and 2.9 indicate signs

of early insulin resistance, and values over 3.0 indicate insulin resistance (Horakova, 2019). Tables 21 and 22 shows the summary of IR based on age groups and race in men and women, respectively.

Figure 29

Homeostatic Model Assessment of Insulin Resistance Equation

$$HOMA - IR = \frac{Fasting\ Glucose\ \left(\frac{mg}{dL}\right) \times Fasting\ Insulin\ \left(\frac{\mu U}{mL}\right)}{405}$$

Table 21

HOMA-IR Values in Men

			HOMA-IR Value (SD)	Sample Size	HOMA-IR Grade
Non-Hispanic White	Has MetS	18-29 years of age	20.05(15.85)	7	Insulin Resistant
		30-49 years of age	5.93(5.93)	28	Insulin Resistant
		50-69 years of age	7.9(5.90)	46	Insulin Resistant
		70 years of age and above	9.33(20.27)	37	Insulin Resistant
	Does not have MetS	18-29 years of age	2.4(1.88)	48	At Risk for IR
		30-49 years of age	3.38(7.10)	88	Insulin Resistant
		50-69 years of age	2.83(2.73)	84	At Risk for IR
		70 years of age and above	2.69(1.99)	64	At Risk for IR
Hispanic	Has MetS	18-29 years of age	8.02(4.75)	8	Insulin Resistant
		30-49 years of age	7.62(8.64)	25	Insulin Resistant
		50-69 years of age	6.65(7.16)	55	Insulin Resistant
		70 years of age and above	5.55(4.53)	17	Insulin Resistant
	Does not have MetS	18-29 years of age	3.08(4.11)	68	Insulin Resistant
		30-49 years of age	2.88(2.93)	80	At Risk for IR
		50-69 years of age	2.71(1.29)	66	At Risk for IR
		70 years of age and above	4.49(8.08)	27	Insulin Resistant
Black	Has MetS	18-29 years of age	3.13	1	Insulin Resistant
		30-49 years of age	12.04(24.31)	19	Insulin Resistant
		50-69 years of age	13.8(26.40)	28	Insulin Resistant
		70 years of age and above	6.05(4.74)	5	Insulin Resistant
	Does not have MetS	18-29 years of age	2.44(3.38)	42	At Risk for IR
		30-49 years of age	3.65(4.80)	44	Insulin Resistant
		50-69 years of age	4.18(11.42)	54	Insulin Resistant
		70 years of age and above	1.77(1.15)	15	Insulin Sensitive

Asian	Has MetS	18-29 years of age	5.36(4.06)	3	Insulin Resistant
		30-49 years of age	4.44(3.25)	6	Insulin Resistant
		50-69 years of age	4.19(3.76)	6	Insulin Resistant
		70 years of age and above	2.83(2.49)	2	At Risk for IR
	Does not have MetS	18-29 years of age	2.19(1.17)	31	At Risk for IR
		30-49 years of age	3.21(3.18)	46	Insulin Resistant
		50-69 years of age	2.42(1.27)	33	At Risk for IR
		70 years of age and above	1.94(1.09)	7	Insulin Sensitive
Other Race	Has MetS	18-29 years of age	4.65(3.10)	2	Insulin Resistant
		30-49 years of age	5.13(2.60)	4	Insulin Resistant
		50-69 years of age	6.85(1.45)	4	Insulin Resistant
		70 years of age and above	3.5	1	Insulin Resistant
	Does not have MetS	18-29 years of age	1.39(0.89)	9	Insulin Sensitive
		30-49 years of age	3.4(4.68)	14	Insulin Resistant
		50-69 years of age	3.23(2.31)	7	Insulin Resistant
		70 years of age and above	3.1(2.52)	2	Insulin Resistant

Table 22

HOMA-IR Values in Women

			HOMA-IR Value (SD)	Sample Size	HOMA-IR Grade
Non-Hispanic White	Has MetS	18-29 years of age	3.16(1.66)	2	Insulin Resistant
		30-49 years of age	4.75(3.20)	22	Insulin Resistant
		50-69 years of age	7.60(13.46)	51	Insulin Resistant
		70 years of age and above	6.10(10.07)	29	Insulin Resistant
	Does not have MetS	18-29 years of age	2.89(3.89)	65	At Risk for IR
		30-49 years of age	2.03(1.51)	80	At Risk for IR
		50-69 years of age	1.97(1.29)	73	Insulin Sensitive
		70 years of age and above	2.48(2.38)	49	At Risk for IR
Hispanic	Has MetS	18-29 years of age	6.15(4.08)	5	Insulin Resistant
		30-49 years of age	8.98(15.74)	27	Insulin Resistant
		50-69 years of age	8.09(11.86)	64	Insulin Resistant
		70 years of age and above	10.85(22.23)	32	Insulin Resistant
	Does not have MetS	18-29 years of age	3.19(2.74)	62	Insulin Resistant
		30-49 years of age	3.35(5.67)	86	Insulin Resistant
		50-69 years of age	3.96(8.27)	75	Insulin Resistant
		70 years of age and above	2.38(1.56)	17	At Risk for IR
Black	Has MetS	18-29 years of age	5.64(0.13)	2	Insulin Resistant
		30-49 years of age	11.63(15.21)	16	Insulin Resistant
		50-69 years of age	6.73(11.76)	33	Insulin Resistant
		70 years of age and above	4.11(2.59)	13	Insulin Resistant
	Does not have MetS	18-29 years of age	3.04(2.06)	55	Insulin Resistant
		30-49 years of age	3.04(3.36)	62	Insulin Resistant
		50-69 years of age	2.79(2.21)	53	At Risk for IR
		70 years of age and above	2.64(0.96)	12	At Risk for IR
Asian	Has MetS	18-29 years of age	5.90	1	Insulin Resistant
		30-49 years of age	3.10(1.99)	5	Insulin Resistant
		50-69 years of age	4.04(1.64)	6	Insulin Resistant
		70 years of age and above	3.85(2.23)	5	Insulin Resistant
	Does not have MetS	18-29 years of age	2.52(2.91)	25	At Risk for IR
		30-49 years of age	2.43(2.35)	46	At Risk for IR
		50-69 years of age	2.14(1.76)	25	At Risk for IR
		70 years of age and above	1.99(1.97)	4	Insulin Sensitive

Other Race	Has MetS	18-29 years of age	5.46(2.68)	2	Insulin Resistant
		30-49 years of age	6.26(3.24)	2	Insulin Resistant
		50-69 years of age	5.77(2.17)	3	Insulin Resistant
		70 years of age and above	4.02(3.33)	3	Insulin Resistant
	Does not have MetS	18-29 years of age	2.28(1.22)	9	At Risk for IR
		30-49 years of age	4.15(6.04)	16	Insulin Resistant
		50-69 years of age	3.22(1.88)	3	Insulin Resistant
		70 years of age and above	2.88	1	At Risk for IR

ANOVA Tests for Insulin Levels in Men in Race and MetS Status

A 2 by 5 two-way factorial ANOVA was done with MetS status and race as the two factors. Descriptive and ANOVA summary results are seen in Tables 23 and 24. The main effect from MetS status was significant at $F(1,1,123) = 38.78$, $p<.05$, with an eta-squared value of .03. The main effect from race was significant at $F(4,1,123) = 3.85$, $p<.05$. However the Scheffe post hoc test showed no significant differences amongst the different race groups. The eta-squared value was also low at .01. The interaction was significant at $F(4,1,123) = 2.96$, $p<.05$ with a low eta-squared value of .01.

Table 23

Insulin Mean Levels for MetS Statuses and Race in Men (N=1,133)

MetS Status	Mean(SD)	Race	Mean (SD)
Has MetS	21.76(1.56)	White	17.30(.99)
Does not have MetS	10.75(.84)	Black	21.18(1.43)
		Hispanic	15.58(1.05)
		Asian	11.94(2.34)
		Other	15.28(3.15)

Table 24

ANOVA summary for Insulin Levels in MetS Statuses and Race in Men (N=1,333)

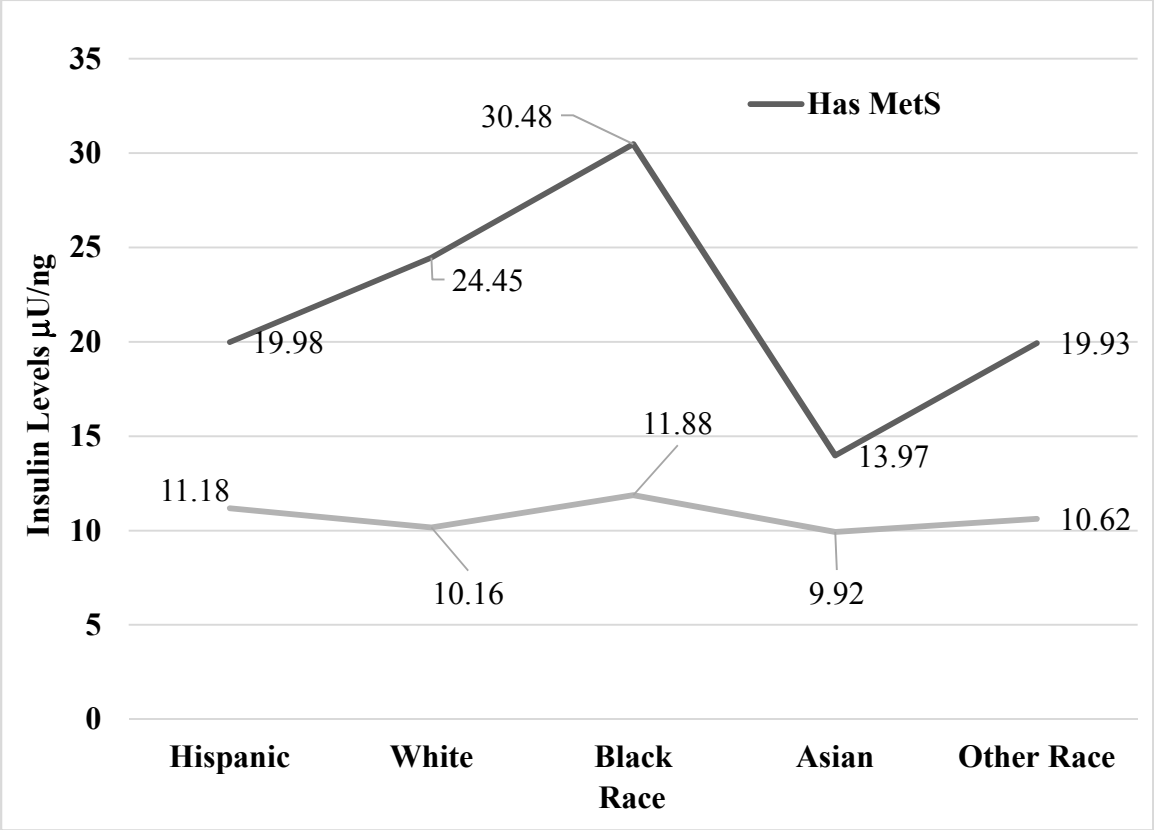
Source	F-ratio	d/f	p	η2
MetS Status	*38.78	1	0.000	0.03
Race	*3.85	4	0.004	0.01
MetS by Age Groups	*2.96	4	0.018	0.01

Note. *Significant *at p*<.05.

Figure 30 shows how insulin levels in the "has MetS" group were consistently higher compared to the "does not have MetS" group across all race groups. The difference was greatest for Blacks and lowest for Asians. Simple effects testing showed that each difference in insulin scores between the MetS groups was significantly different for each race group, except for Asians.

Figure 30

Insulin Levels in MetS Statuses and Race in Men



Note. Simple effects testing showed that insulin levels were significantly higher in the MetS group compared to those who did not have MetS in Hispanic, White, Black and Other Race groups, but not for Asians.

ANOVA Tests for Insulin Levels in Women for Age Group and MetS Status

Descriptive and ANOVA summary results are seen in Tables 25 and 26. Similar to the insulin levels in men's results, the main effect for MetS status was significant at $F(1,1,33) = 37.17$, $p<.05$. The mean insulin level of 20.96 µU/mL was significantly higher in the MetS group compared to the "does not have MetS" group at 10.62 µU/mL.

The main effect for age group and the interaction between the two factors were not significant at p>.05.

Table 25

Insulin Mean Levels for MetS Statuses and Age Groups in Women (N=1,141)

MetS Status	Mean(SD)	Age Groups	Mean (SD)
Has MetS	20.96(1.54)	18-29	16.07(2.68)
Does not have MetS	10.62(0.71)	30-49	16.69(1.19)
		50-69	15.07(0.94)
		Over 70	15.36(1.41)

Table 26

ANOVA summary for Insulin Levels in MetS Statuses and Age Groups in Women (N=1,141)

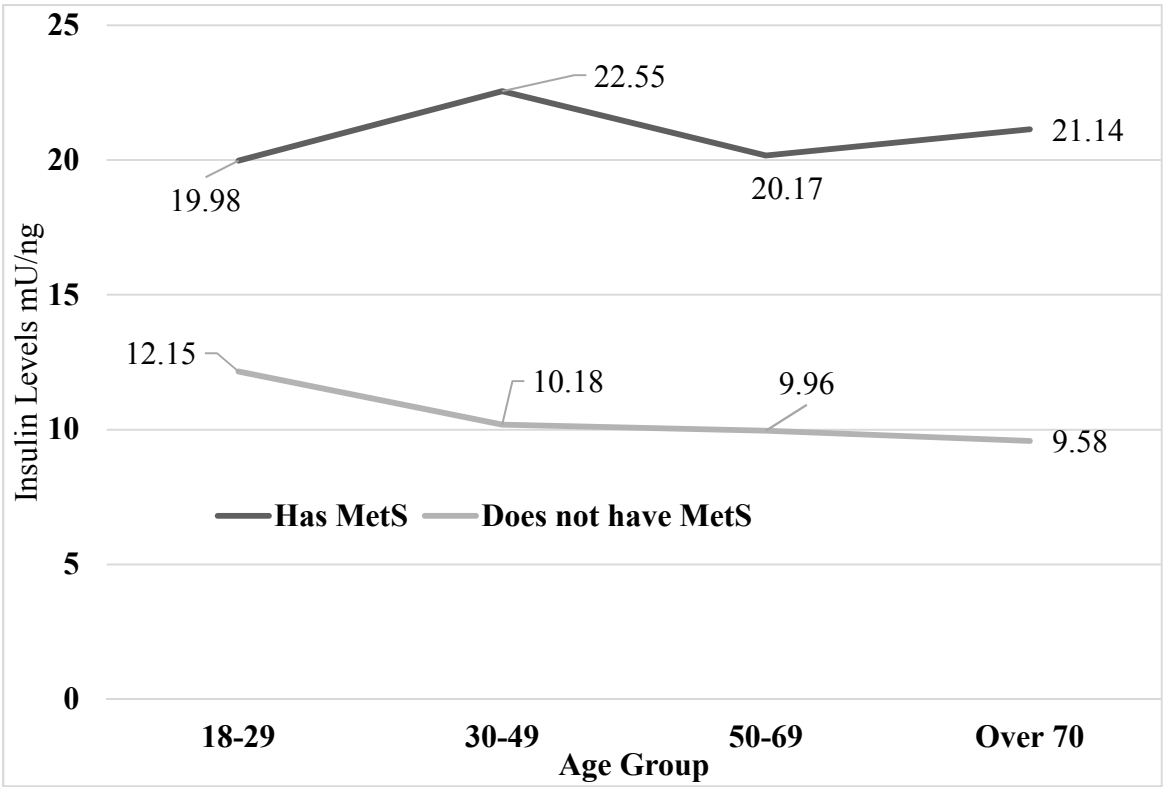
Source	F-ratio	d/f	p	η2
MetS Status	*37.17	1	0.000	0.03
Age Groups	.40	3	0.75	0.00
MetS by Age Groups	.209	3	0.004	0.00

Note. *Significant *at p*<.05.

Figure 31 shows how insulin levels in the "has MetS" group was consistently higher compared to the "does not have MetS" group across all age groups. Simple effects showed that the difference was not significant in the 18 to 29 age group but was significant for the remaining age groups.

Figure 31

Insulin Levels in MetS Statuses and Age Groups in Women



Note. Simple effects testing showed that insulin levels were not significantly higher in the 18-29 MetS group, but the differences were significant for the remaining age groups.

ANOVA Tests for Insulin Levels in Women for Race and MetS Status

Descriptive and ANOVA summary results are seen in Tables 27 and 28. The main effect for MetS status was significant at $F(1,1,131) = 19.68$, $p<.05$. The mean insulin level of 19.02 µU/mL was significantly higher in the MetS group compared to the "does not have MetS" group at 11.04 µU/mL. The main effect for race was significant at $F(4,1,131) = 3.93$, but the eta-squared value was low at .01. The Scheffe post hoc tests

showed that insulin levels in Hispanics were significantly different from Whites and Asians. The interaction between the two factors was not significant at p>.05.

Figure 32 shows that Insulin levels were higher across all race groups, but simple effects testing showed significant differences only in the White, Hispanic, and Black race groups and not in Asians and Other Race groups.

Table 27

Insulin Mean Levels for MetS Statuses and Race in Women (N=1,141)

MetS Status	**Mean(SD)**	**Race**	**Mean (SD)**
Has MetS	19.02(1.58)	White	13.74(1.04)
Does not have MetS	11.04(0.87)	Black	15.66(1.31)
		Hispanic	18.62(0.98)
		Asian	11.31(2.36)
		Other	15.84(3.30)

Table 28

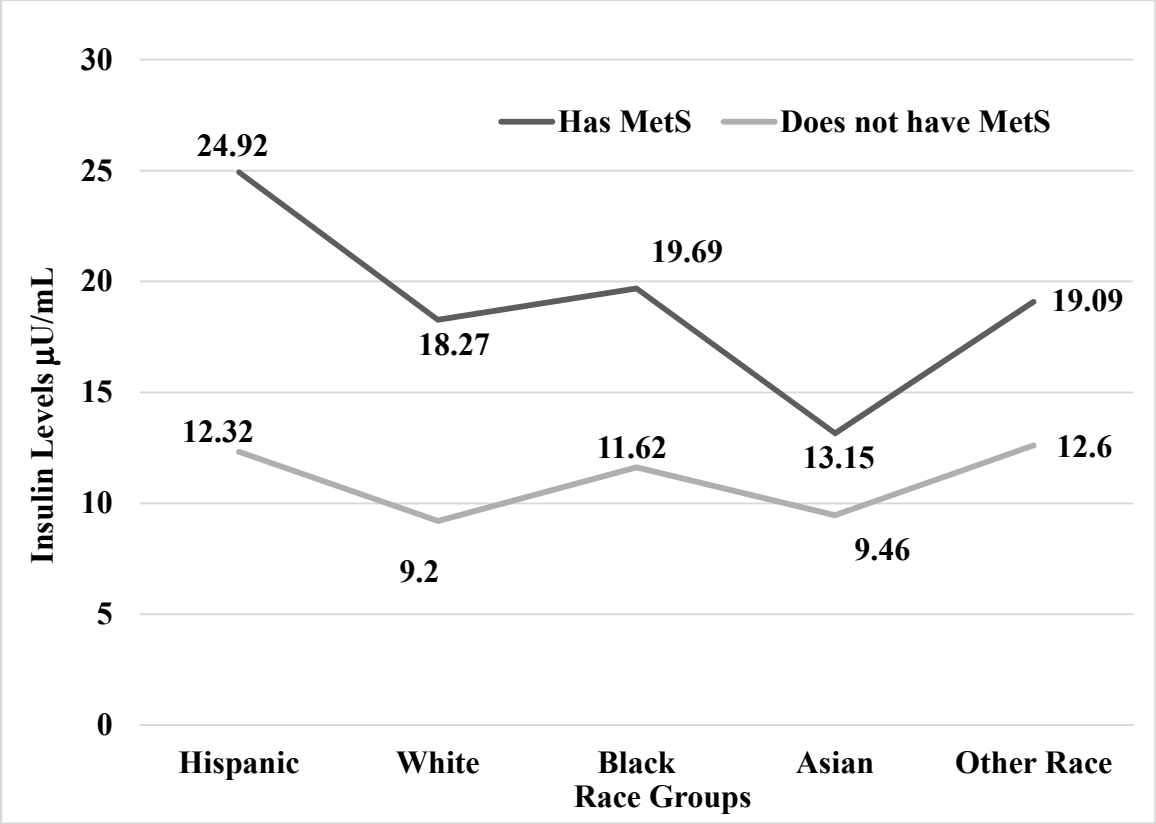
ANOVA summary for Insulin Levels in MetS Statuses and Race in Women (N=1,141)

Source	**F-ratio**	**d/f**	**p**	**η2**
MetS Status	*19.68	1	0.000	0.2
Race	*3.93	4	0.004	0.01
MetS by Age Groups	1.13	4	0.343	0.00

Note. *Significant *at p*<.05.

Figure 32

Insulin Levels in MetS Statuses and Race in Women



Note. Simple effects testing showed that insulin levels between the MetS groups were significantly different in the Hispanic, White, and Black race groups but not significantly different in Asian and Other Race groups.

Testosterone Levels

Testosterone levels in Age Groups and Race Categories for Men

Testosterone is an androgen sex hormone present in both men and women but is normally at much higher levels in males. Testosterone in males is produced in the testes and is responsible for the development of secondary sex characteristics, such as increased muscle growth, bone mass, hair growth, sex drive, and height. Metabolism is also influenced by testosterone, which decreases insulin resistance and activates the breakdown of adipose tissue called lipolysis. Testosterone also has anti-inflammatory effects. Testosterone naturally decreases with age, and the normal range of testosterone in adult men is from 264 ng/dL to 916 ng/dL (Travison, 2017).

Low plasma testosterone levels are associated with MetS symptoms, such as obesity, IR and heart disease. As explained in the obesity development section, adipocytes are the fat cells that store triglycerides. Adipocytes also release inflammatory cytokines, such as TNA-alpha, IL-6, and Il-1. Testosterone has a direct inhibiting effect on the release of these inflammatory cell signaling proteins (Bianchi, 2018). Without testosterone, levels of these inflammatory cytokines increase. Testosterone also reduces IR by increasing insulin responsiveness to GLUT 4 skeletal muscle cells, so glucose molecules in circulation are able to enter the myocytes and then be used for energy (Pal, 2019).

Obesity affects testosterone levels indirectly by increasing the amount of adipocytes. When adipocytes are inflamed and in an IR state, they release an enzyme called aromatase which converts testosterone to estradiol (E2), the active form of

estrogen. The more adipose tissue that is present, as in marked obesity, the more of this conversion will occur (Fui, 2014). Estrogen in men is normally under 40 pg/ml, but when there are higher levels of estrogen in circulation, estrogen inhibits the hypothalamus in the brain from releasing gonadotropin releasing hormone (GnRH) due to negative feedback. GnRH normally stimulates the pituitary to release luteinizing hormone (LH) and follicle stimulating hormone (FSH), which stimulate the testis to produce testosterone. This negative feedback cycle continues as long as obesity is present and results in less than adequate testosterone levels and too high estrogen levels. In men, testosterone and estradiol should be in balance with a testosterone:estradiol ratio (T:E2) of 10:1. For a given value of estrogen, there should be ten times as much testosterone (Abouroab, 2021).

In this study, testosterone level was a significant predictor of MetS status in men only. Testosterone levels in women were low and not significantly different in both MetS and non-MetS cases. There were also no statistical differences in women's testosterone levels between age groups and race categories. In both MetS and non-MetS groups, T:E2 declined with age for each race category. The T:E2 ratio was consistently lower in the MetS group than in the non-MetS group. Table 29 shows the mean testosterone levels in men by age group and race categories.

Table 29

Testosterone Levels in Men Based on Race and Age Group

			T:E2 Ratio (SD)	Sample Size
White	Has MetS	18-29 years of age	379.29(123.44)	7
		30-49 years of age	379.79(161.05)	29
		50-69 years of age	399.09(161.46)	46
		70 years of age and above	336.59(262.20)	37
	Does not have MetS	18-29 years of age	519.00(183.46)	48
		30-49 years of age	454.91(190.80)	87
		50-69 years of age	526.95(206.51)	84
		70 years of age and above	422.94(174.27)	64
Hispanic	Has MetS	18-29 years of age	330.50(79.63)	8
		30-49 years of age	395.58(134.68)	24
		50-69 years of age	357.36(144.74)	55
		70 years of age and above	395.79(138.42)	18
	Does not have MetS	18-29 years of age	509.84(182.70)	68
		30-49 years of age	478.43(170.23)	80
		50-69 years of age	475.77(190.32)	67
		70 years of age and above	414.24(205.19)	27
Black	Has MetS	18-29 years of age	16.30	1
		30-49 years of age	317.43(151.77)	19
		50-69 years of age	370.84(191.44)	28
		70 years of age and above	327.00(91.49)	5
	Does not have MetS	18-29 years of age	634.90(219.93)	42
		30-49 years of age	534.55(303.13)	44
		50-69 years of age	477.50(262.95)	54
		70 years of age and above	418.75(220.09)	15
Asian	Has MetS	18-29 years of age	358.67(129.52)	3
		30-49 years of age	373.83(134.15)	6
		50-69 years of age	373.17(125.37)	6
		70 years of age and above	537.00(183.85)	2
	Does not have MetS	18-29 years of age	590.58(173.70)	31
		30-49 years of age	479.89(156.46)	47
		50-69 years of age	506.13(230.88)	32
		70 years of age and above	518.71(348.18)	7

Other Race	Has MetS	18-29 years of age	733.50(150.61)	2
		30-49 years of age	283.75(34.28)	4
		50-69 years of age	328.00(144.49)	4
		70 years of age and above	525.00	1
	Does not have MetS	18-29 years of age	672.44(166.49)	9
		30-49 years of age	514.40(235.98)	15
		50-69 years of age	422.14(228.78)	7
		70 years of age and above	396.50(169)	2

ANOVA Tests for Testosterone Levels in Men for Age Group and MetS Status

Descriptive and ANOVA summary results are seen in Tables 30 and 31. Unlike MetS status in insulin levels, higher testosterone levels are associated with not having MetS, and lower levels are associated with having MetS. The main effect for MetS status was significant at $F(1,1,127) = 65.93$, $p<.05$. The mean testosterone level of 361.57 ng/dL was significantly lower in the "has MetS group" compared to the "does not have MetS" group at 491.07 ng/dL. The main effect for age group was significant at $F(3,1,127) = 4.26$, but the eta-squared value was low at .01. The Scheffe post hoc tests showed that the mean testosterone level of 466.41 ng/dL in the 18-29 age group was significantly higher compared to all the other age groups. The mean of 379.58 in the over 70 group was significantly lower compared to all the other age groups. The interaction between factors was not significant at $p>.05$.

Figure 33 shows that testosterone levels were higher across all age groups in the "does not have MetS" group compared to the "has MetS" group. Simple effects testing showed that MetS status was significantly different for each age group.

Table 30

Testosterone Mean Levels for MetS Statuses and Age Groups in Men (N=1,135)

MetS Status	Mean(SD)	Age Group	Mean (SD)
Has MetS	361.57(14.25)	18-29	466.41(22.71)
Does not have MetS	491.07(7.26)	30-49	424.31(12.46)
		50-69	434.70(10.52)
		Over 70	379.58(15.51)

Table 31

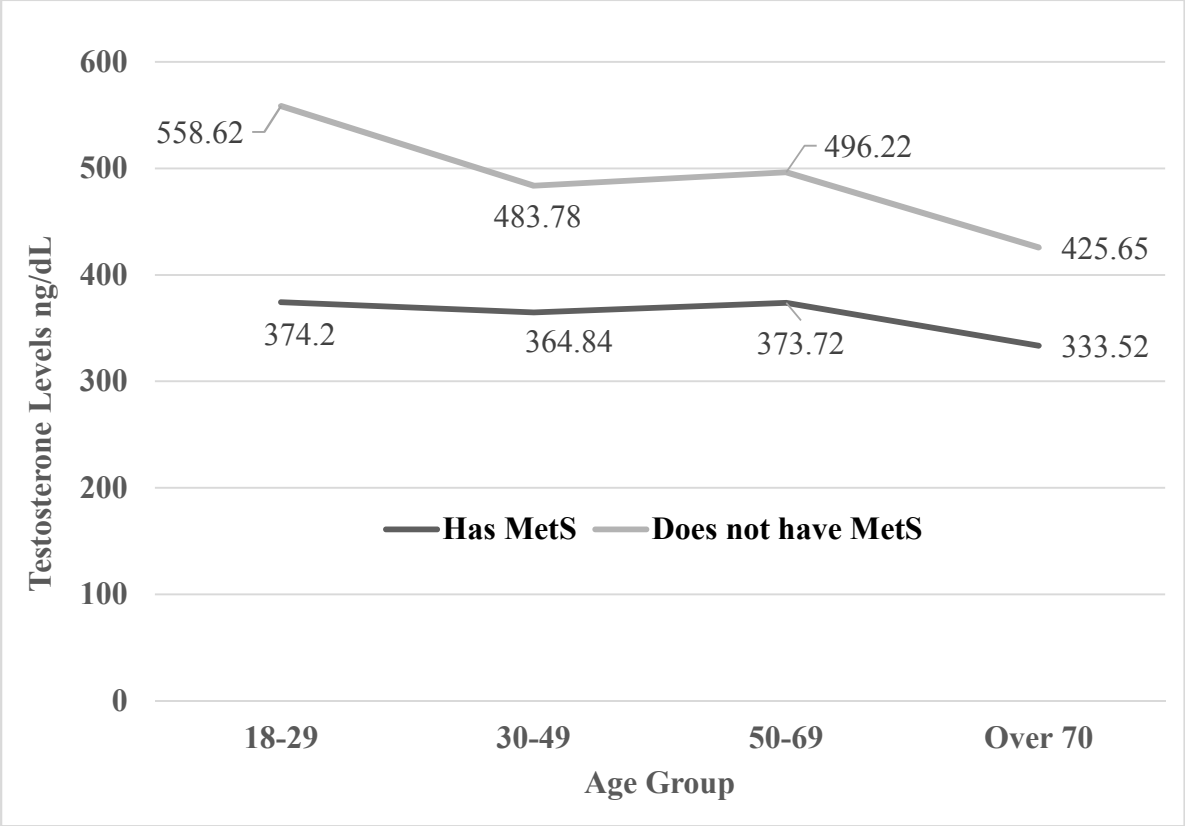
ANOVA summary for Testosterone Levels in MetS Statuses and Age Groups in Men (1,135)

Source	F-ratio	d/f	p	η2
MetS Status	*65.93	1	0.000	0.06
Age Groups	*4.26	3	0.005	0.01
MetS by Age Groups	.942	3	0.420	0.00

Note. *Significant *at p*<.05.

Figure 33

Testosterone Levels in MetS Statuses and Age Groups in Men



Note. Simple effects testing showed that for every age group, testosterone levels was significantly lower in the MetS group compared to those who did not have MetS.

ANOVA Tests for Testosterone Levels in Men for Race and MetS Status

Descriptive and ANOVA summary results are seen in Tables 32 and 33. The main effect for MetS status was significant at $F(1,1,125) = 49.60$, $p<.05$. The mean testosterone level of 372.36 ng/dL was significantly lower in the "has Mets group" compared to the "does not have MetS" group at 510.35 ng/dL. The main effect for race was not significant at $F(4,1,125) = .983$, $p>.05$. The interaction between factors also was not significant at $p>.05$.

Figure 34 shows that testosterone levels were higher across all race groups in the "does not have MetS" group compared to the "has MetS" group. Simple effects testing showed that MetS status was significantly different for Whites, Hispanics, and Blacks but not for Asians or Other.

Table 32

Testosterone Mean Levels for MetS Statuses and Race in Men (N=1,135)

MetS Status	**Mean(SD)**	**Age Group**	**Mean (SD)**
Has MetS	372.36(17.29)	Hispanic	416.48(11.70)
Does not have MetS	510.35(9.21)	White	426.86(10.94)
		Black	435.74(15.93)
		Asian	454.42(25.98)
		Other	473.30(34.85)

Table 33

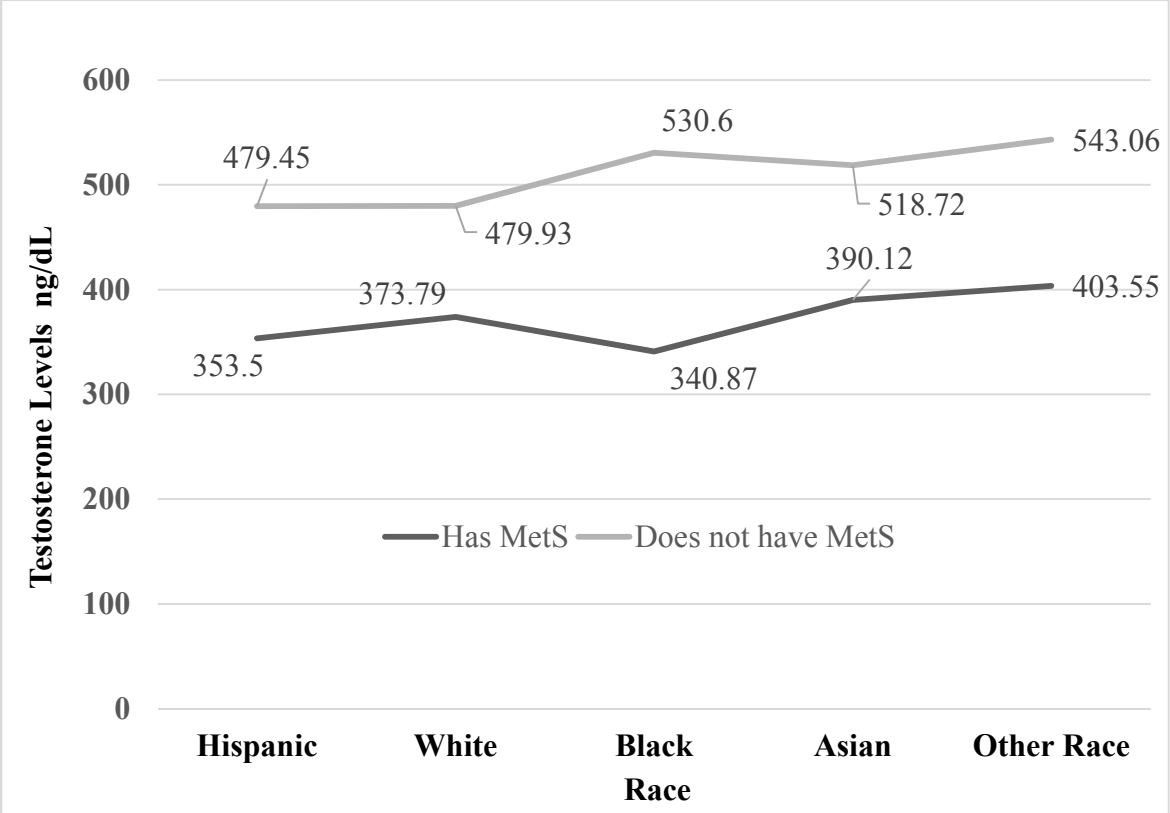
ANOVA summary for Testosterone Levels in MetS Statuses and Race in Men (1,135)

Source	F-ratio	d/f	p	η2
MetS Status	*49.60	1	0.000	0.04
Race	.983	3	0.415	0.03
MetS by Race	1.189	3	0.314	0.04

Note. *Significant *at p*<.05.

Figure 34

Testosterone Levels in MetS Statuses and Race in Men



Note. Simple effects testing showed that testosterone levels were significantly lower in the "has MetS" group compared to the "does not have MetS" group for the Hispanic, White, and Black race groups but not significantly lower for Asians and Other race groups.

ANOVA Tests for Testosterone Levels in Women for Age Group and MetS Status

Descriptive and ANOVA summary results are seen in Tables 34 and 35. Testosterone levels for age groups and race were not as large compared to men, which explains why the logistic regression test did not show as strong an effect for testosterone levels compared to insulin levels. The main effects for age and MetS status and their interaction were not significant at $p>.05$. Figure 35 shows that testosterone levels were higher across all age groups in the "does not have MetS" group compared to the "has MetS" group, but simple effects testing showed that MetS status was not significantly different across all age groups.

Table 34

Testosterone Mean Levels for MetS Statuses and Age Groups in Women (N=1,151)

MetS Status	**Mean(SD)**	**Age Group**	**Mean (SD)**
Has MetS	23.61(2.47)	18-29	33.73(4.26)
Does not have MetS	27.62(1.16)	30-49	23.81(1.95)
		50-69	21.98(1.54)
		Over 70	22.94(2.33)

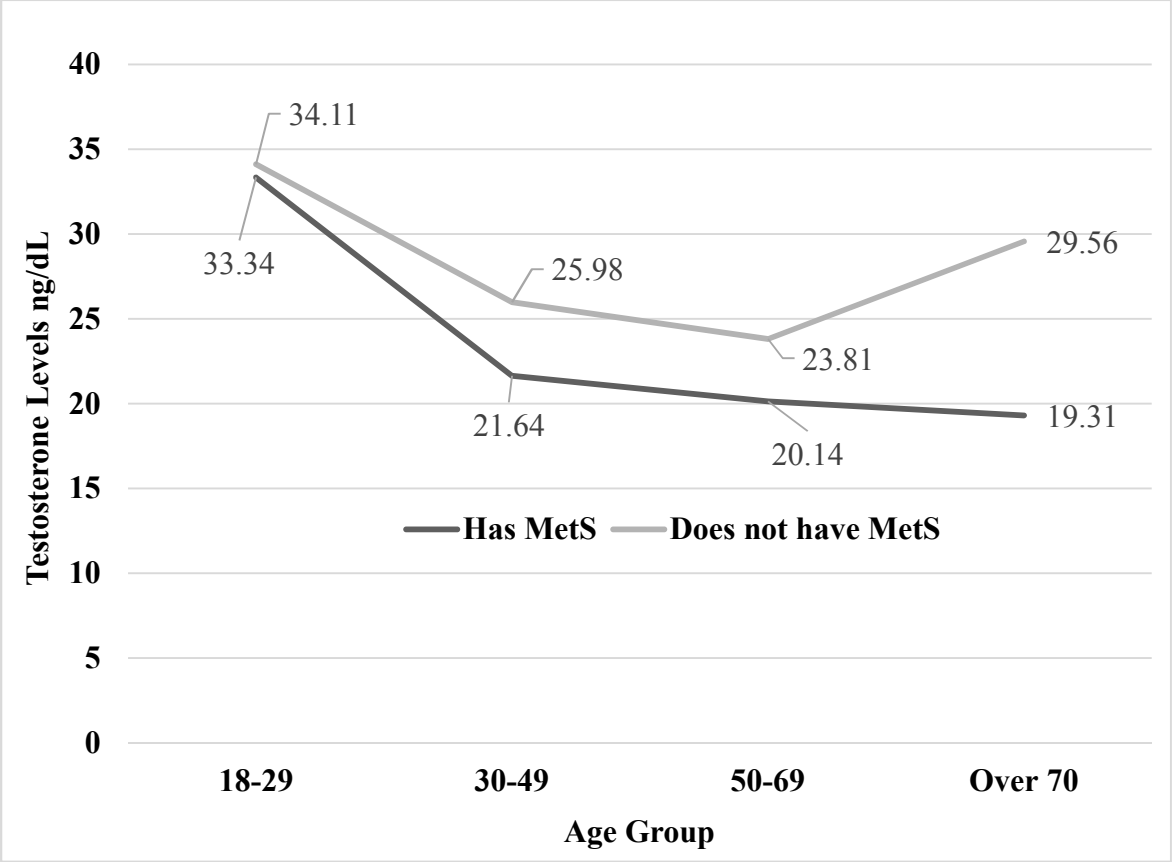
Table 35

ANOVA summary for Testosterone Levels in MetS Statuses and Age Groups in Women (1,151)

Source	**F-ratio**	**d/f**	**p**	**η2**
MetS Status	2.16	1	0.142	0.02
Age Groups	2.28	3	0.078	0.01
MetS by Age Groups	.942	3	0.204	0.01

Figure 35

Testosterone Levels in MetS Statuses and Age Groups in Women



Note. Though testosterone levels for women were consistently higher in the "does not have MetS" group, the interaction between MetS Status and age group was non-significant, and simple effects tests showed that the differences in MetS status across age groups was also non-significant.

ANOVA Tests for Testosterone Levels in Women for Race and MetS Status

Descriptive and ANOVA summary results are seen in Tables 36 and 37. The main effects for age and race and their interaction were not significant at p>.05. Figure 36 shows that testosterone levels were higher across all race groups in the "does not have MetS" group compared to the "has MetS" group, but simple effects testing showed that MetS status was not significantly different across all race groups.

Table 36

Testosterone Mean Levels for MetS Statuses and Races in Women (N=1,151)

MetS Status	**Mean(SD)**	**Race**	**Mean (SD)**
Has MetS	21.51(2.63)	White	23.06(1.72)
Does not have MetS	26.94(1.43)	Black	25.19(2.20)
		Hispanic	25.37(1.64)
		Asian	22.59(3.93)
		Other	24.90(5.48)

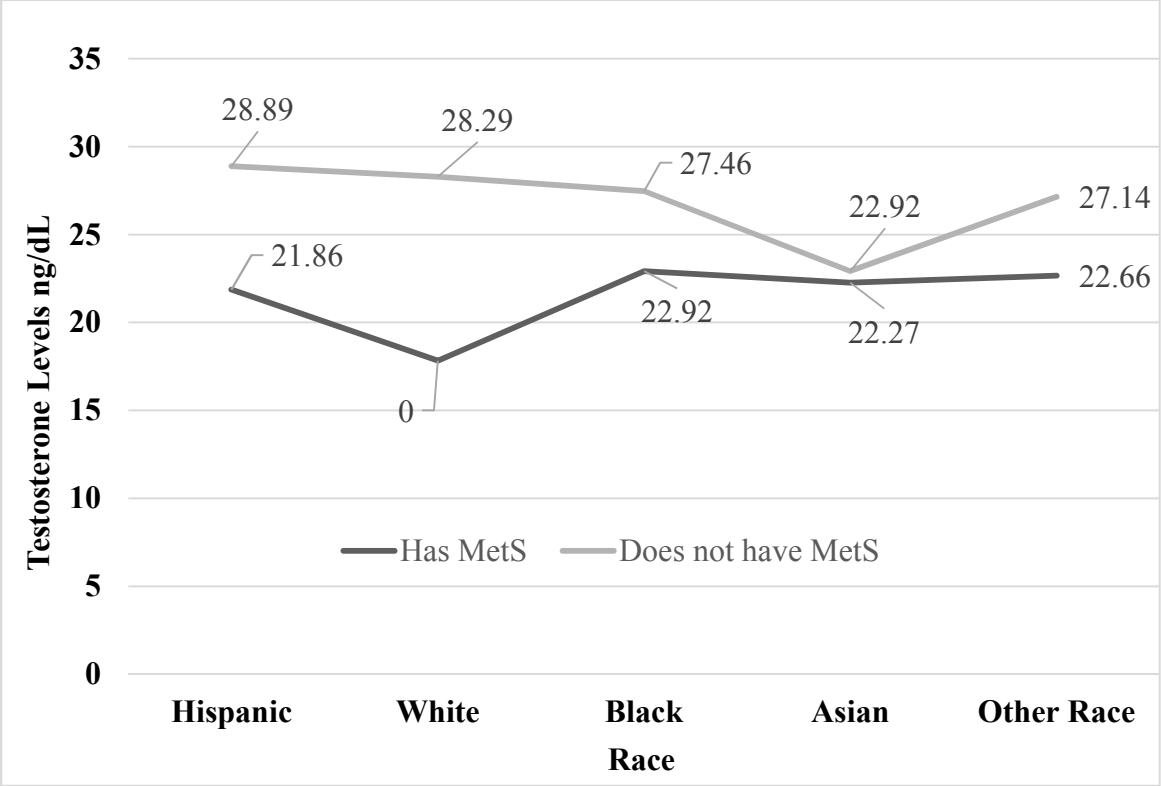
Table 37

ANOVA summary for Testosterone Levels in MetS Status and Race in Women (N=1,151)

Source	**F-ratio**	**d/f**	**p**	**η2**
MetS Status	3.30	1	0.07	0.00
Race	.33	4	0.86	0.00
MetS by Age Groups	.51	4	0.73	0.00

Figure 36

Testosterone Levels in MetS Statuses and Race in Women



Note. The interaction between MetS Status and age group was non-significant, and simple effects tests showed that the differences in MetS status across the race groups was also non-significant.

Vigorous Recreational Activities

Chi-Square Tests for Vigorous Recreational Activities in Men

Since Vigorous Recreational Activities was a dichotomous variable with responses yes or no, a chi-square test was done to test if there was a significant relationship between MetS status and vigorous recreational activities. One chi-square test

was performed for each sex. Figure 37 shows a histogram of the overall observed counts for this predictor.

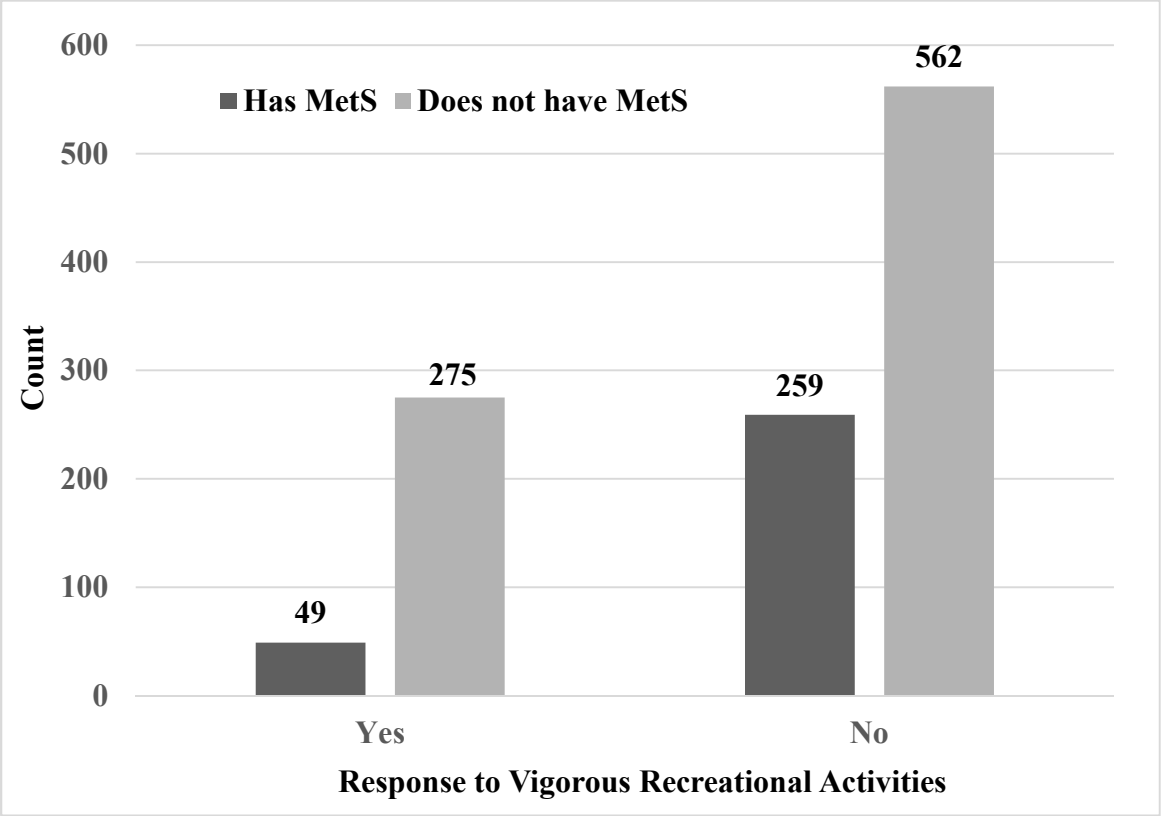
The assumptions for a chi-square test are that the observations be independent of each other and that there is sufficient sample size. I am assuming that the dataset was screened for errors and that each case is valid and the assumptions were met. No change or deletion in the dataset was made.

The chi-square test for all men was significant at $\chi^2(1, N=1{,}145) = 31.87$, $p<.05$. The phi value was -.17, which suggests a weak relationship between MetS status and vigorous recreational activities. The negative phi value means that those who responded yes to participating in vigorous recreational activities were more likely to fall into the "does not have MetS" group. There were 49 cases where participants responded yes to vigorous recreational activities and did not have MetS, versus 259 cases where participants said no and had MetS.

The odds ratio was calculated as OR = (275*259)/562*49) = 2.6. This means that men who participated in any vigorous-intensity sports, fitness, or recreational activities that cause large increases in breathing or heart rate for at least 10 minutes continuously were 2.6 times as likely not to have MetS.

Figure 37

Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status in Men



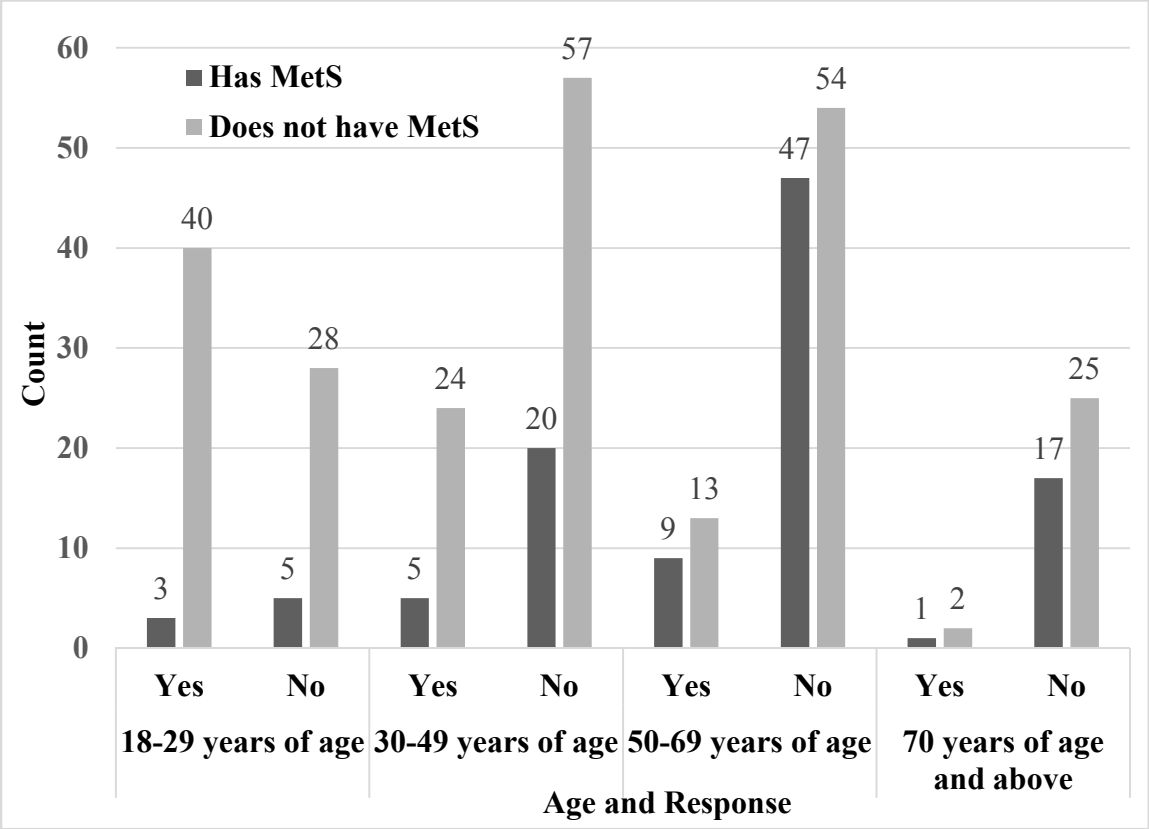
Note. Overall results of men who participated in vigorous recreational activities were 2.6 times as likely to not have MetS.

Histograms for Race and Vigorous Recreational Activities in Men

Figures 38 through 42 shows the histogram results for each race category. In the Hispanic, White, and Black race categories, the discrepancy in count between the yes and no replies for MetS statuses was greatest in the 50 to 69 age group. Asians had the lowest numbers of having MetS in all race and age groups. The sample size in the Other race group was low and may not accurately represent this predictor.

Figure 38

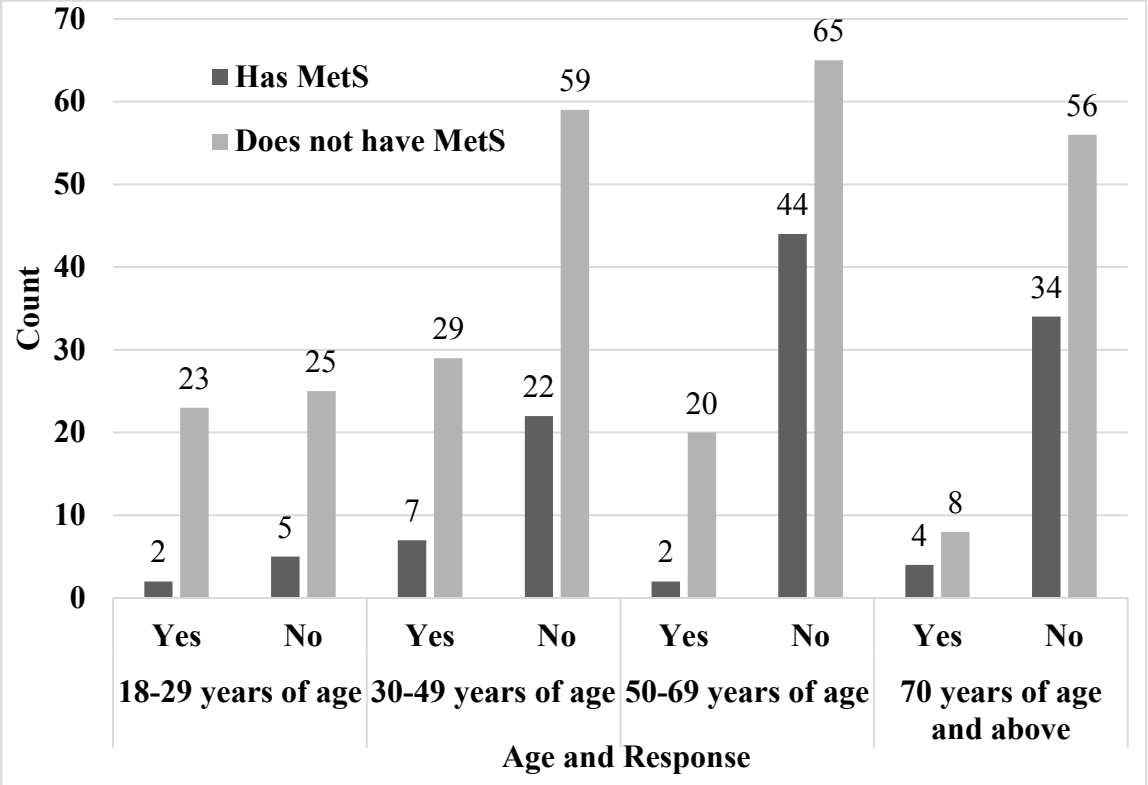
Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for Hispanic Men



Note. The 50-69 age group had the greatest MetS status discrepancy. There were 38 less "has MetS" cases in the Yes respondents compared to No respondents. The OR for the 50 to 69 age group was 1.3. A Hispanic male in the 50 to 69 age group was 1.3 times as likely to not have MetS if he participated in vigorous recreational activities.

Figure 39

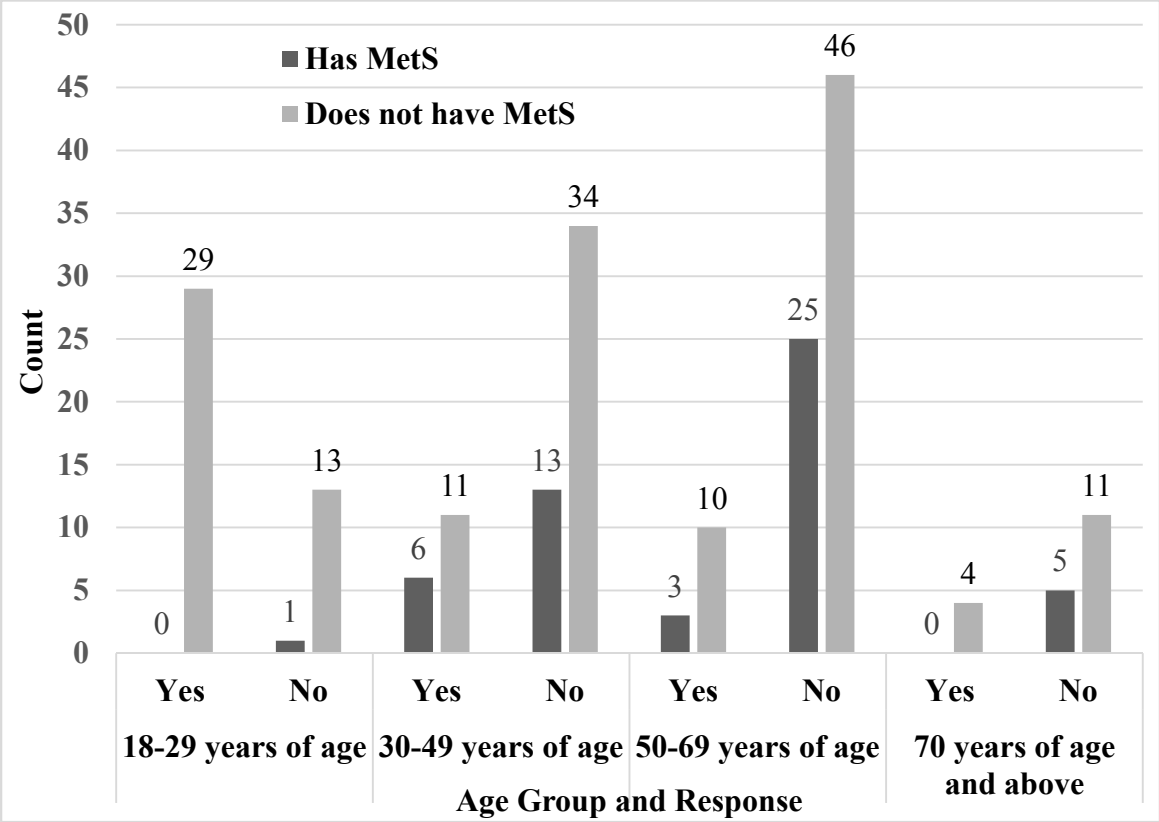
Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for White Men



Note. The 50-69 age group had the greatest MetS status discrepancy. There were 42 less "has MetS" cases in the Yes respondents compared to No respondents. The OR for the 50 to 69 age group was 6.8. A White male in the 50 to 69 age group was 6.8 times as likely to not have MetS if he participated in vigorous recreational activities.

Figure 40

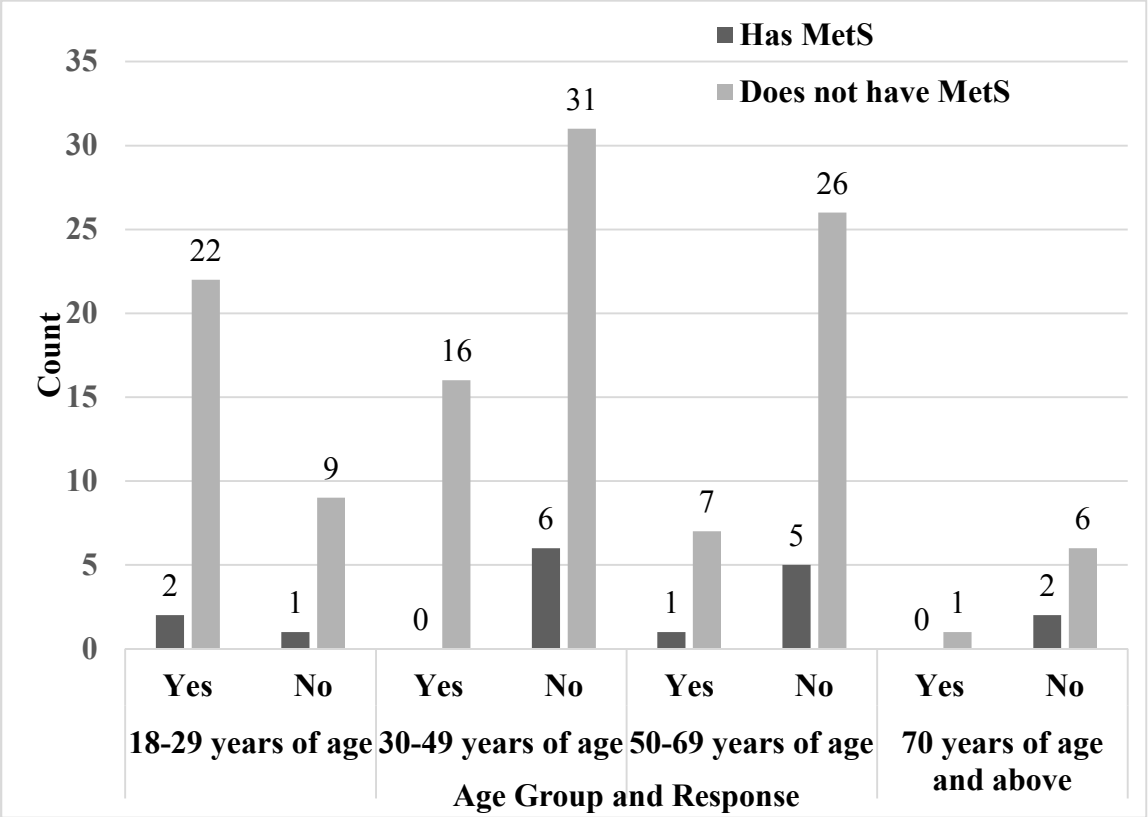
Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for Black Men



Note. The 50-69 age group had the greatest MetS status discrepancy. There were 22 less "has MetS" cases in the Yes respondents compared to No respondents. The OR for the 50 to 69 age group was 1.8. A Black male in the 50 to 69 age group was 1.8 times as likely to not have MetS if he participated in vigorous recreational activities.

Figure 41

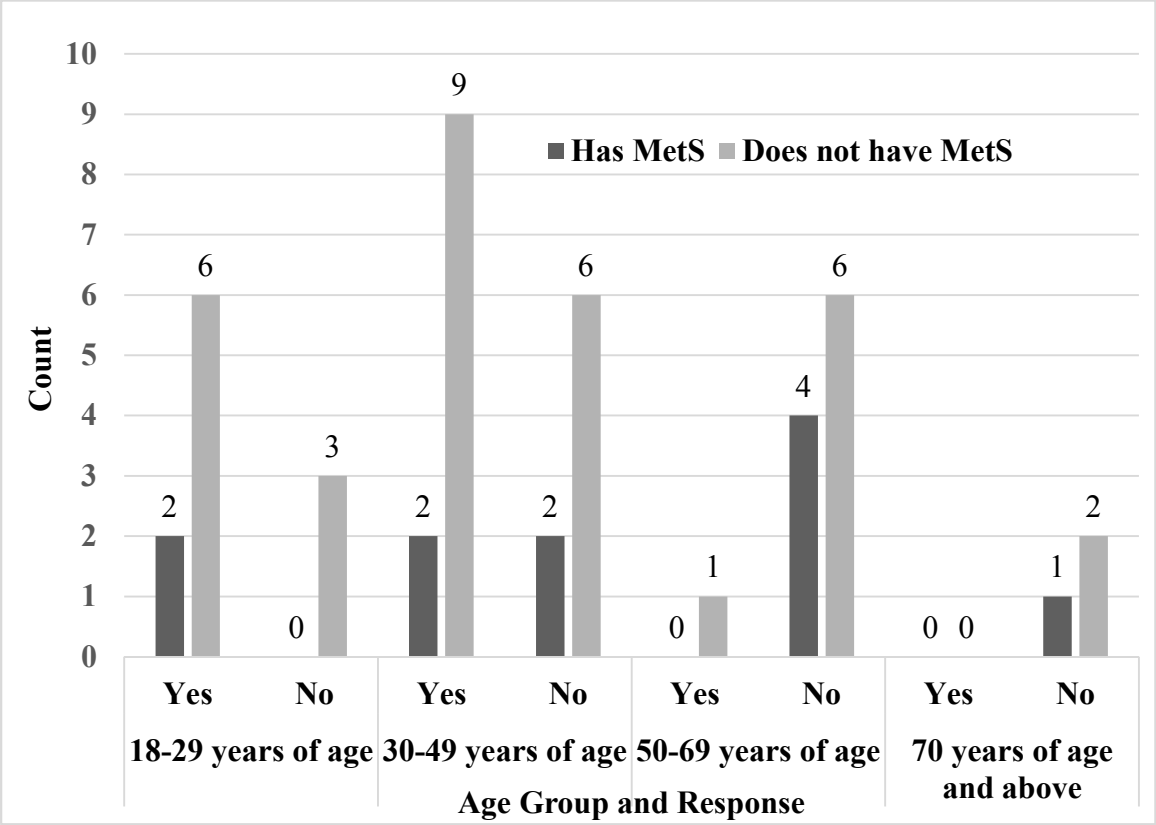
Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for Asian Men



Note. Asian men had the lowest rates of having MetS among the male race categories.

Figure 42

Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for Other Race Men



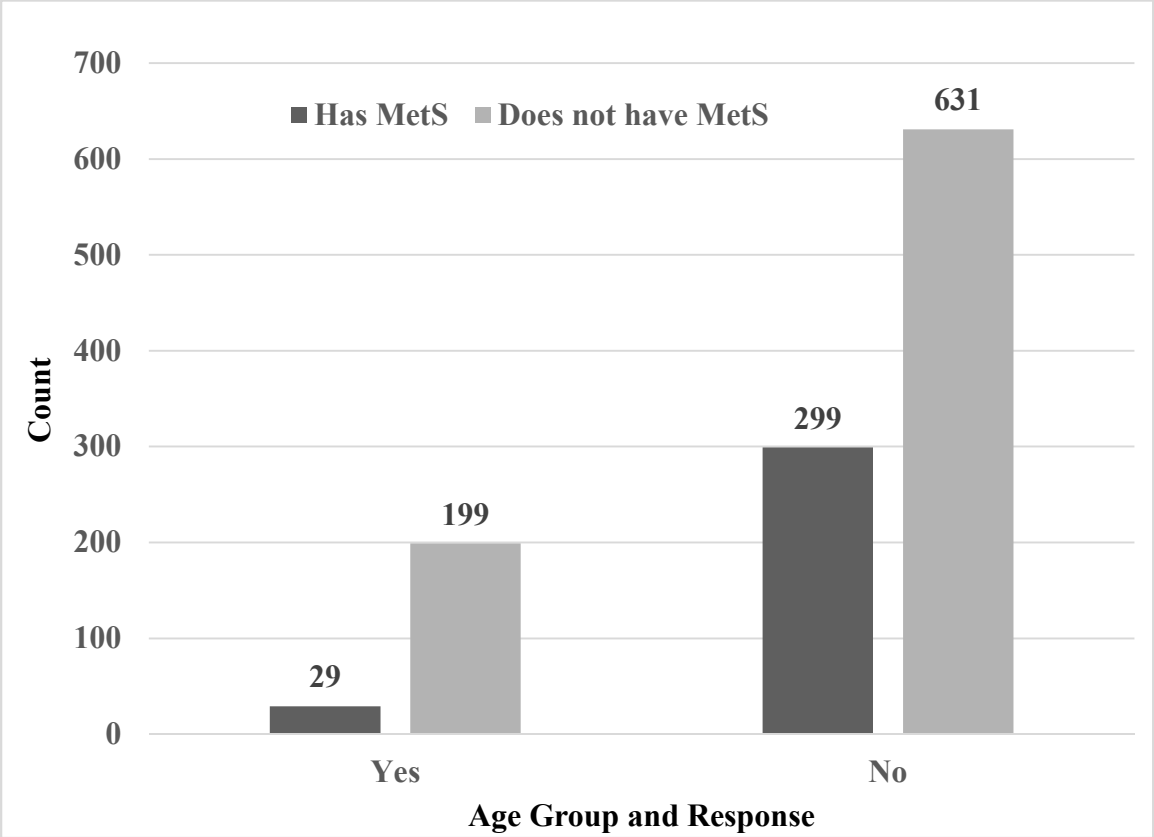
Note. There were low sample sizes in the other race category for men, so the results may not accurately represent how vigorous recreational activities affected MetS status in males.

Chi-Square Tests for Vigorous Recreational Activities in Women

Figure 43 shows a histogram of the overall observed counts for this predictor. The chi-square test for all women was significant at $\chi^2(1, N=1{,}158) = 34.06$, $p<.05$. The phi value was .17 which suggests a weak relationship between MetS status and vigorous recreational activities. The negative phi value means that those who responded yes to participating in vigorous recreational activities were more likely to fall into the "does not have MetS" group. There were 29 cases where participants responded yes to vigorous recreational activities and did not have MetS, versus 299 cases where participants said no and had MetS. The odds ratio was calculated as OR = (199*299)/631*29) = 3.3. This means that women who participated in any vigorous-intensity sports, fitness, or recreational activities that cause large increases in breathing or heart rate for at least 10 minutes continuously were 3.3 times as likely not to have MetS.

Figure 43

Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status in Women



Note. Overall results of women who participated in vigorous recreational activities were 3.3 times more likely to not have MetS.

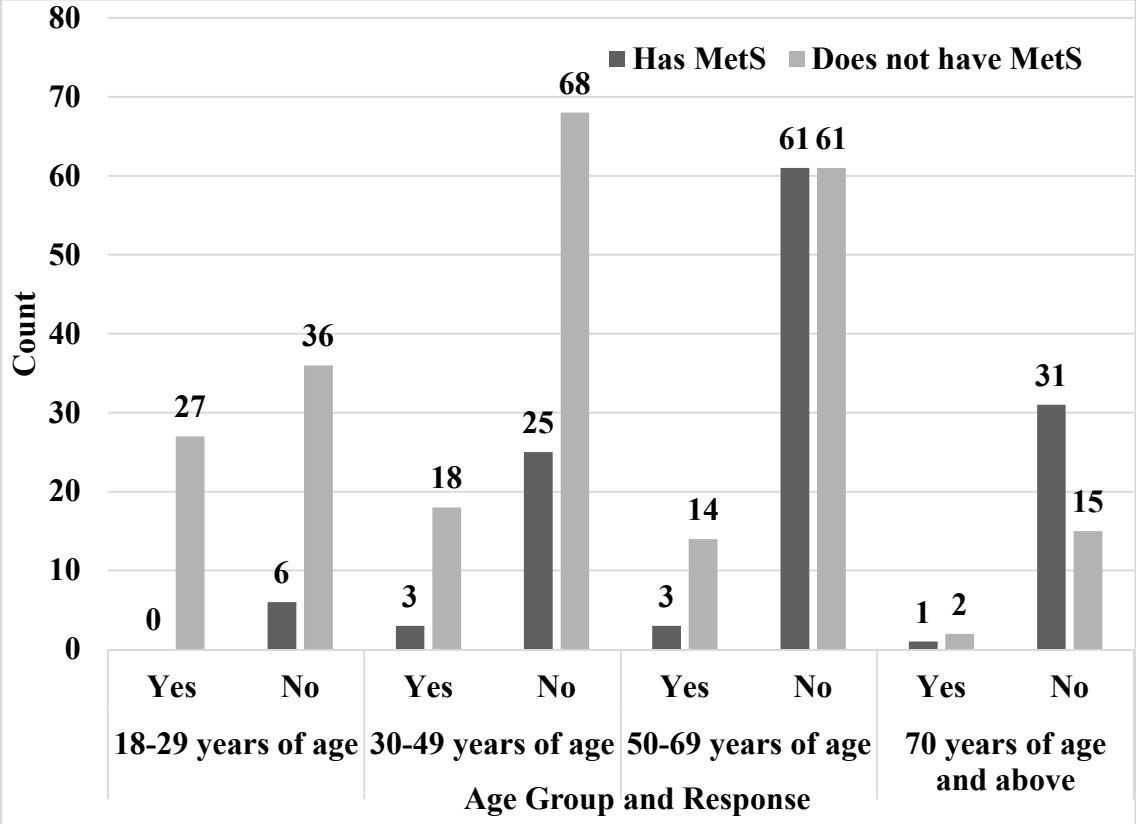
Histograms for Race and Vigorous Recreational Activities in Women

Figures 44 through 48 shows the histogram results for each race category. The results were similar to the men's findings. In the Hispanic, White, and Black race categories, the discrepancy in count between the yes and no replies for MetS statuses was greatest in the 50 to 69 age group. Asians had the lowest numbers of having MetS in all

race and age groups. The sample size in the Other race group was low and may not accurately represent this predictor.

Figure 44

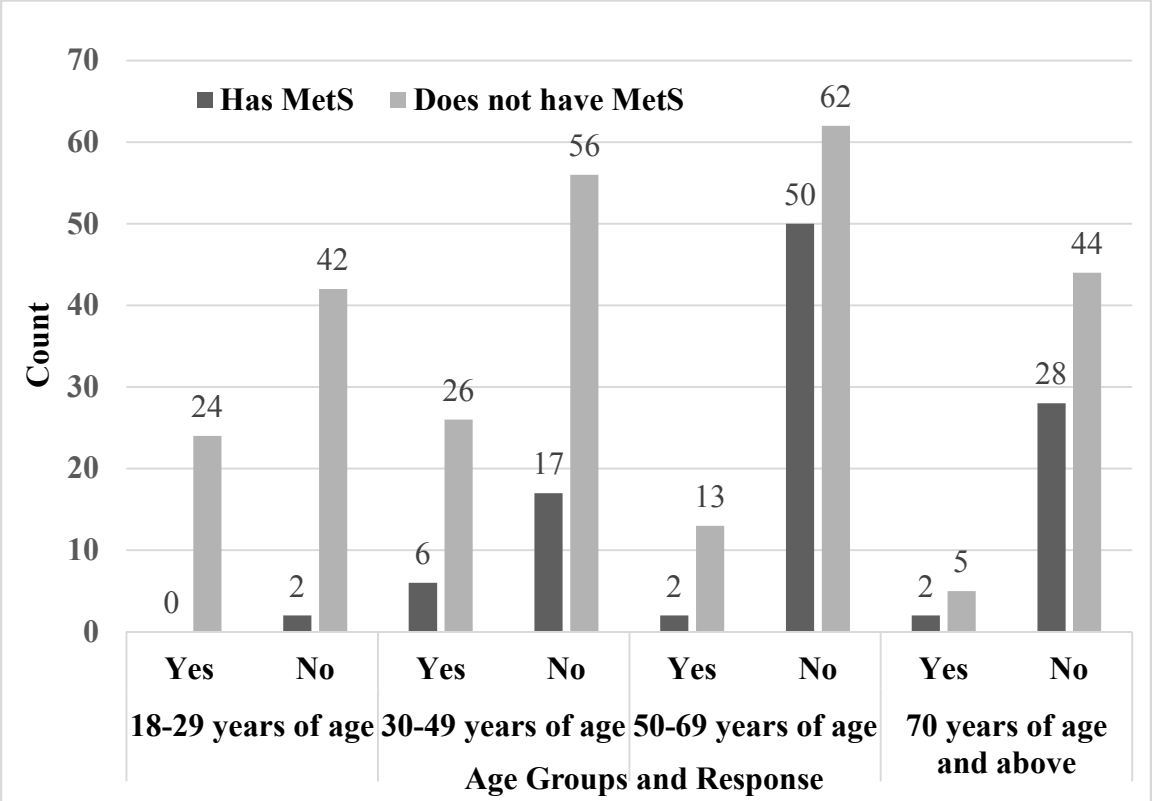
Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for Hispanic Women



Note. The 50-69 age group had the greatest MetS status discrepancy. There were 58 less "has MetS" cases in the Yes respondents compared to No respondents. The OR for the 50-69 group was 4.7, which means a Hispanic female in the 50-69 age group was 4.7 times as likely to not have MetS if she participated in vigorous recreational activities.

Figure 45

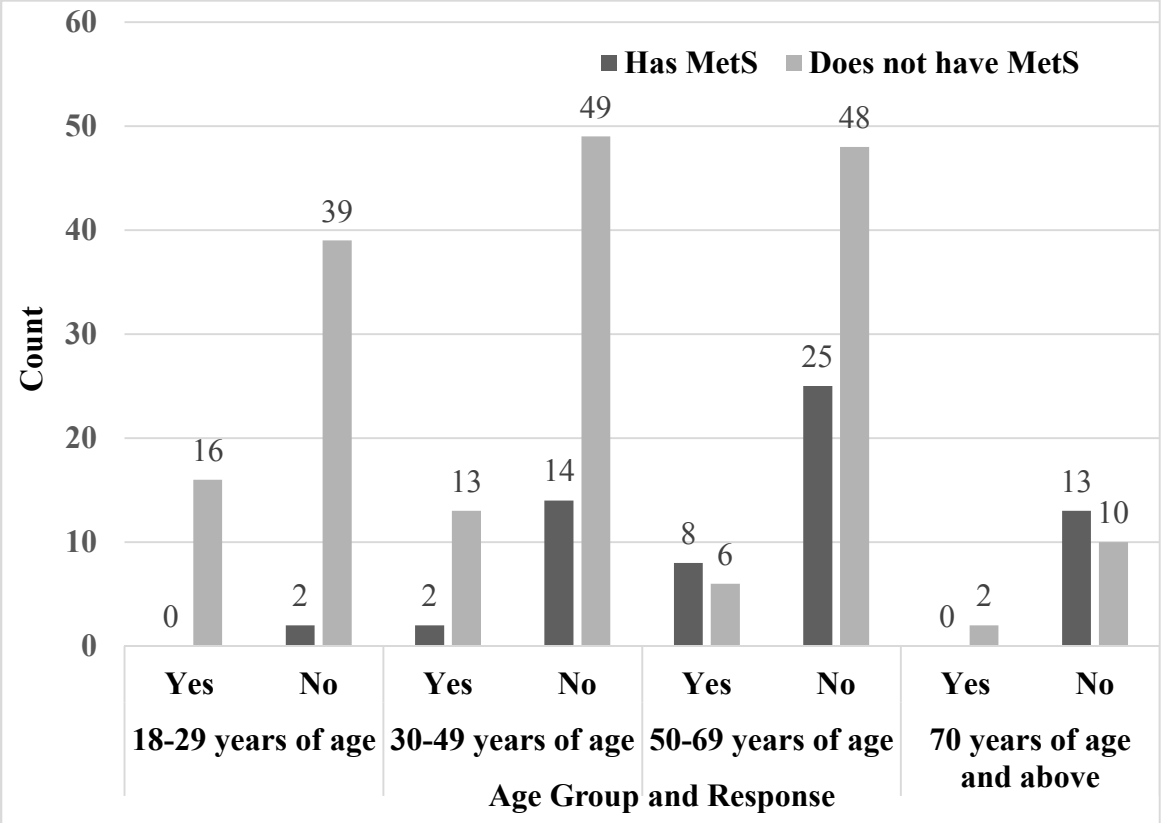
Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for White Women



Note. The 50-69 age group had the greatest MetS status discrepancy. There were 48 less "has MetS" cases in the Yes respondents compared to No respondents. The OR for the 50-69 group was 4.8, which means a White female in the 50-69 age group was 4.8 times as likely to not have MetS if she participated in vigorous recreational activities.

Figure 46

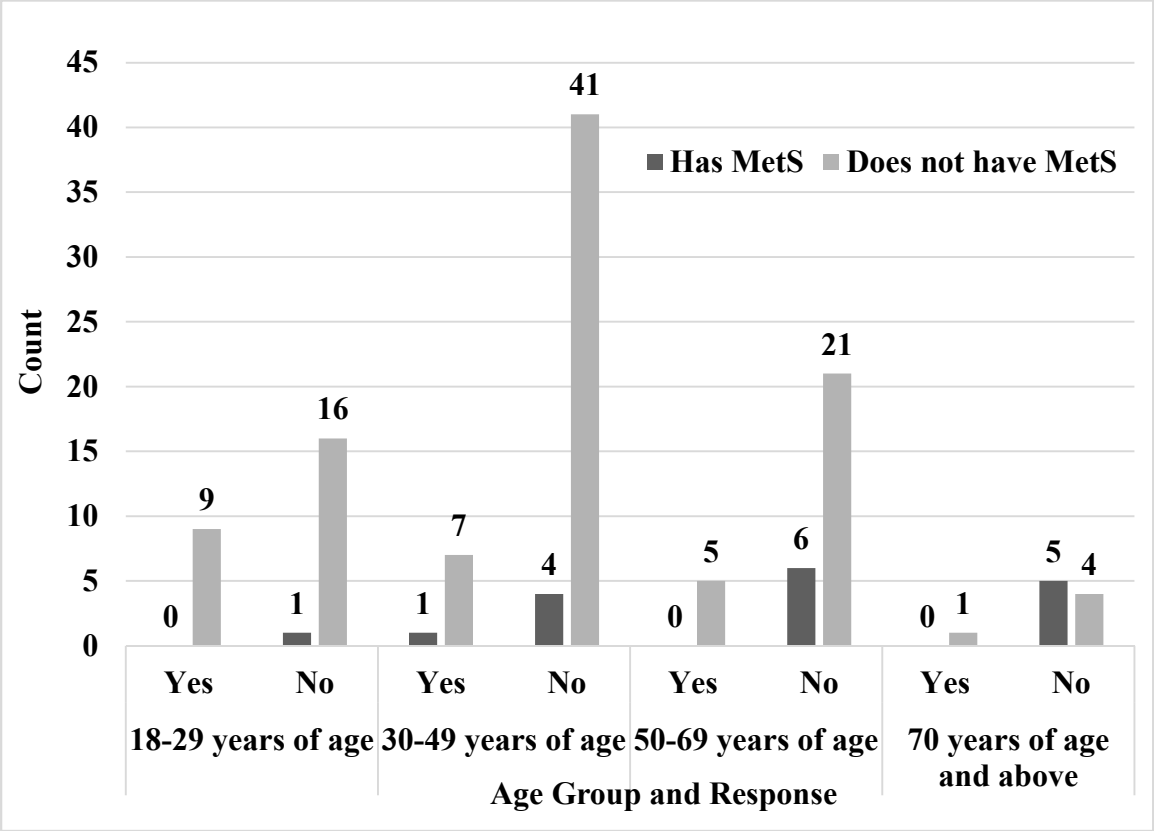
Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for Black Women



Note. The 50-69 age group had the greatest MetS status discrepancy. There were 17 less "has MetS" cases in the Yes respondents compared to No respondents. The OR for the 50-69 group was 2.6, which means a Black female in the 50-69 age group was 2.6 times as likely to not have MetS if she participated in vigorous recreational activities.

Figure 47

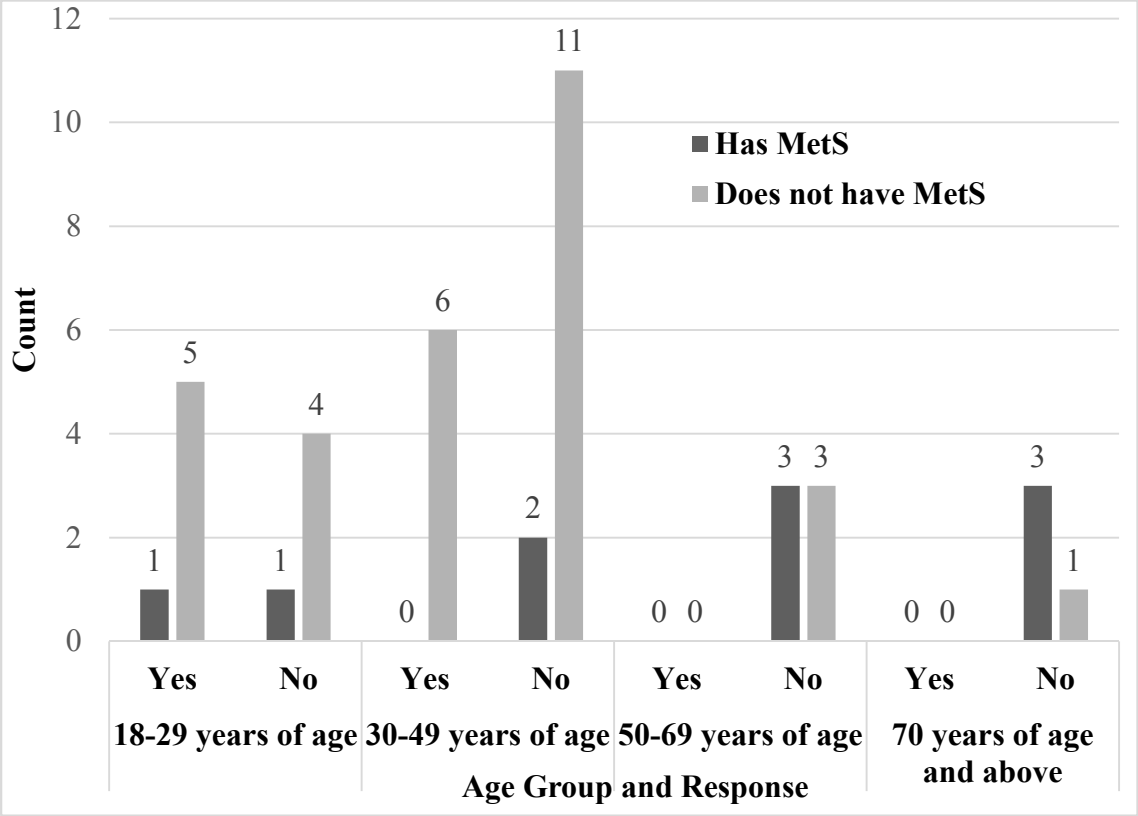
Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for Asian Women



Note. Asian women had the lowest rates of having MetS among the female race categories.

Figure 48

Histogram of Observed Counts for Vigorous Recreational Activities and MetS Status for Other Race Women



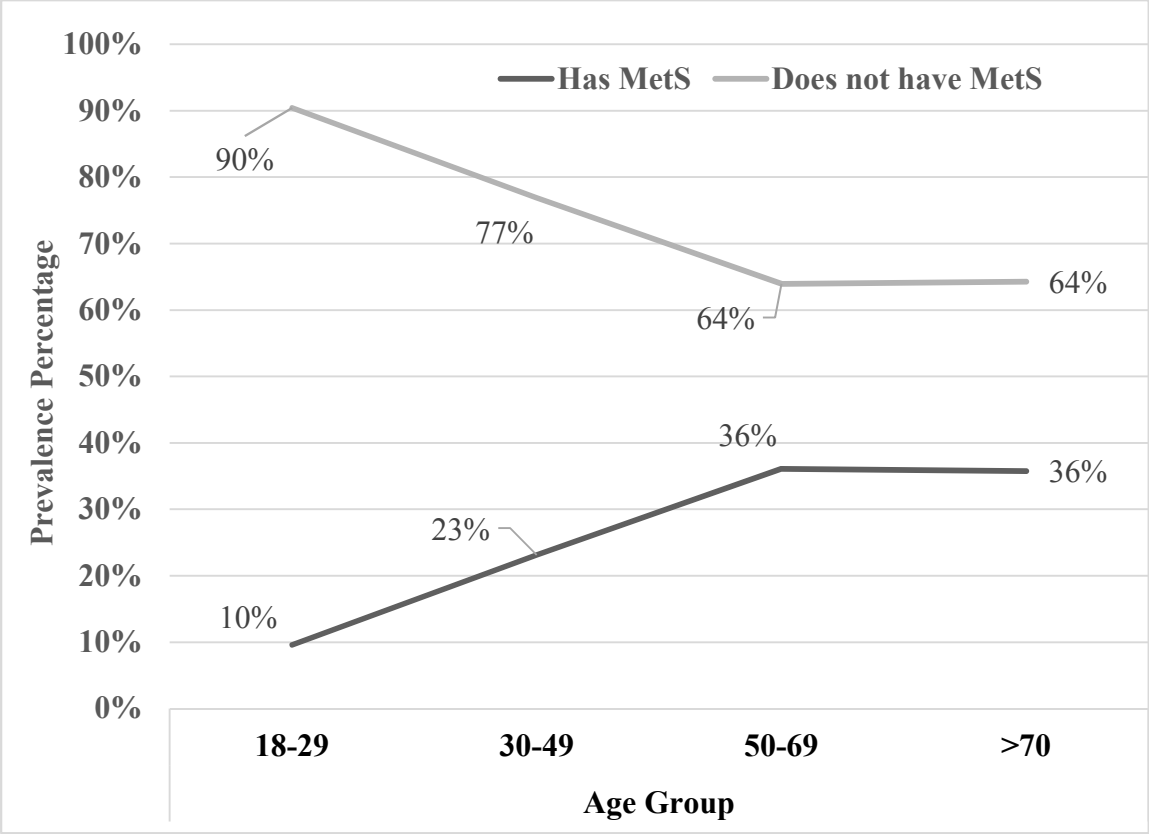
Note. There were low sample sizes in the Other race category for women, so the results may not accurately represent how vigorous recreational activities affect MetS status in females.

MetS Prevalence Based on Age Groups

In men, there is a linear increase in the percentage of MetS prevalence between the first two age group intervals. There is a 13% increase in MetS from the 18 to 29 age group to the 30 to 49 age group and then another 13% increase to the 50 to 69 age group. Then the prevalence of MetS remains the same at 36% after age 70. Figure 49 displays the rise in prevalence and then the plateau.

Figure 49

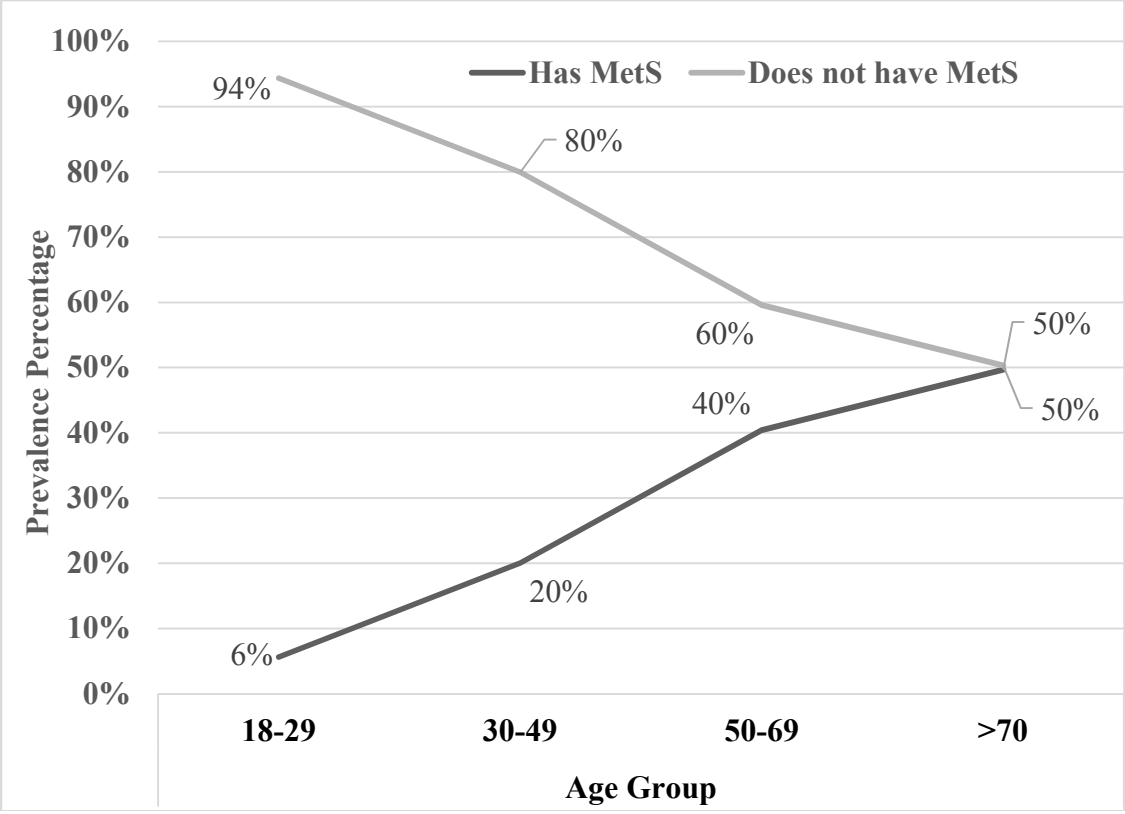
Prevalence of MetS Statuses Based on Age Groups for Men



Compared to men, women have a steeper linear increase in MetS prevalence that continually increases and does not plateau, as seen in figure 50. There is an increase of 18% from the 18 to 29 age group to the 30 to 49 age group. Then a 20% increase from the 30 to 49 age group to the 50 to 69 age group. In contrast to men, the prevalence continues to increase another 10% to where half of all the women have MetS after age 70.

Figure 50

Prevalence of MetS Statuses Based on Age Groups for Women



Summary

In this study, 27% of men and 28% of women were classified as having MetS. Age was the demographic variable that was most associated with the different prevalence of MetS status. MetS prevalence was low in both sexes and race in the youngest age group but as age increased, MetS prevalence increased. Hispanic females over the age of 70 had the highest MetS prevalence at 62%. Overall, Asians had the lowest average MetS prevalence across all age groups. There were four significant predictors of MetS stats, the TG:HDL ratio, insulin levels, testosterone levels, and vigorous physical activities. The TG:HDL ratio and insulin levels were higher in cases with MetS across age groups and race for both men and women. Testosterone had more of an effect on predicting MetS in men compared to women. Men with MetS had lower levels of testosterone across age groups and race. Participants who engaged in vigorous physical activities for at least 10 minutes a week were less likely to have MetS compared to those who did not. Chapter 5 will present a discussion of the results, limitations to the study, implications for positive social change, and recommendations for future research.

Chapter 5: Discussion, Conclusions, and Recommendations

As of 2018, the current estimated obesity prevalence for adult Americans stands at 42.5%, and an additional 31.1% are overweight (Fryar, 2021). With over 73% of all American adults being either overweight or obese, the majority of Americans are now living in an unhealthy state. Continual weight gain leads to a myriad of other chronic, noncommunicable diseases that eventually develop into MetS. MetS is a strong risk factor for heart disease, the primary cause of mortality in the US. The purpose of this study was to identify health, dietary and behavioral variables taken from the 2015-2016 NHANES to determine which ones would significantly predict MetS status. Identifying the predictors of MetS would help to target specific dietary and physical activity behaviors across race, sex, and age.

In my sample, there were a total of 2,303 participants; 28% (636 cases) were classified as having MetS while 72% (1,667 cases) were not. Men and women had similar MetS prevalence values at 27% and 28%, respectively. MetS prevalence was low for younger age groups, then consistently increased as age increased across all race categories in both sexes. Based on logistic regression, there were four variables that significantly predicted MetS status: the TG:HDL ratio, insulin levels, testosterone levels, and vigorous recreational activity. These four predictors correctly classified 39% of MetS cases and 95% of non-MetS cases for an overall success rate of 79%.

The strongest predictor for MetS status was the TG:HDL ratio, which represents the ratio between a prothrombotic state (increased triglycerides) and an antithrombotic state (increased HDL). For each age group and race, the TG:HDL ratio was always higher

in the group that had MetS than in the group that did not. Insulin levels were also consistently higher in those with MetS. Insulin is a hormone that is released from the pancreas in response to increased glucose in circulation. Chronic high levels of insulin are associated with insulin resistance and are seen in people with MetS (Chissini, 2020). Testosterone is a hormone that affects both men and women but is physiologically higher in men throughout adulthood. In this study, testosterone had a negligible effect in differentiating MetS status in women. In men, testosterone levels were significantly lower in men who had MetS compared to men without MetS across race and age group.

While the TG:HDL ratio, insulin, and testosterone levels were continuous variables, vigorous recreational activity was a categorical variable. Participants either responded with a yes or no to participating in vigorous recreational activity lasting 10 minutes or more per week. Those who responded with a *yes* to participating in vigorous recreational activities were less likely to have MetS than those who answered *no*. For Whites, Blacks, and Hispanics in both sexes, the greatest discrepancy between MetS status due to vigorous recreational activity was in the 50 to 69 age group.

This chapter will discuss the interpretation of the study's findings for each of the significant predictors found. The TG:HDL ratio, insulin, and testosterone levels were taken from the NHANES lab section. Vigorous recreational activity represented a behavioral variable that participants either engaged in or not. The reasoning behind why these variables were significant predictors of MetS will be explained through the framework of the HBM and the concept of evolutionary mismatch. Limitations to the study in regard to generalizability, validity, and reliability will then be described.

Recommendations to resolve these limitations will be made. Finally, the potential for positive social change from this study will be explained. In discussing the results, this study had a sufficient sample size to make valid conclusions for Whites, Blacks, Hispanics and Asians, but there was a low number of cases for the Other race category. The low number of cases for the Other race category did not allow for valid conclusions to be made, so there will be no discussion of the Other race category.

Interpretation of the Findings

The Triglyceride:HDL Ratio in Age Group and Race Categories for Men

As discussed previously on the topic of sugar as a cause for obesity, excess calories that are not used for energy from processed foods, sodas with HFCS, and foods with a glycemic index are converted by the liver into triglycerides. High TG:HDL ratio values would mean diets high in these types of processed foods. For all men, MetS prevalence reaches its peak at 36% in the 50 to 69 age group and remains the same for the above 70 age group.

As shown in Figure 51, White men who did not have MetS had a TG:HDL ratio below 2.0 across all age groups, while those with MetS had a TG:HDL ratio above 2.0 across all age groups. The widest discrepancy between the TG:HDL ratio value and those with MetS were in the 18 to 29 age group. This shows that the youngest age group had the poorest diet, but only 13% of this age group had MetS. Then as age increased, the TG:HDL ratio values declined, but MetS prevalence increased incrementally. This implies that the years of poor dieting in early adulthood had lasting effects into their middle ages even though their diets may have improved.

Figure 51

TG:HDL Ratios and MetS Status Across Age Groups in White Men

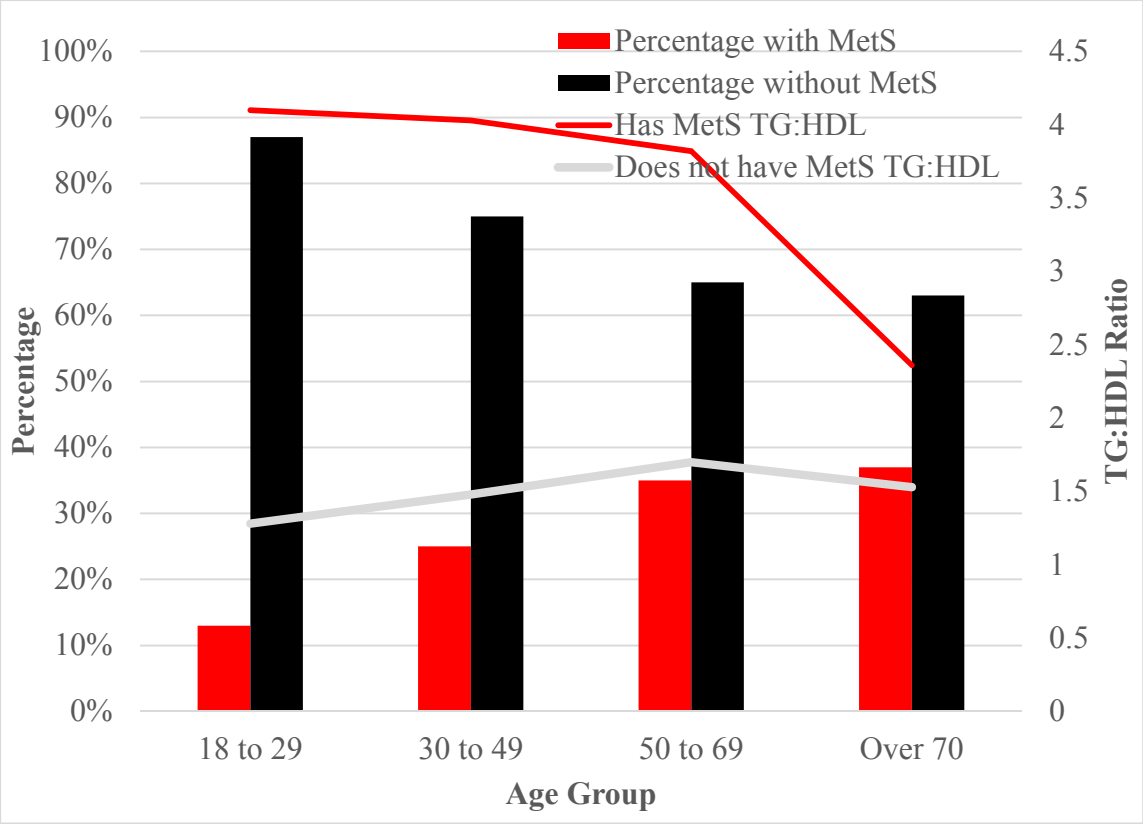


Figure 52 shows the TG:HDL ratio values and MetS prevalence in Black men across age groups. Black men without MetS had TG:HDL ratio values below 2.5 across all age groups. Black men with MetS had their highest TG:HDL ratio of 5.05 in the 30 to 49 age group which correlates to a MetS prevalence of 30%. The TG:HDL ratio value decreased in the subsequent age group, but MetS increased to 33% in the 50 to 69 age group. There was a decrease to 25% in the over 70 age group, which correlates to a TG:HDL ratio of 2.39 which is in the healthy range. This might suggest that changing to a healthy diet can reverse MetS prevalence even in the oldest age group.

Figure 52

TG:HDL Ratios and MetS Status Across Age Groups in Black Men

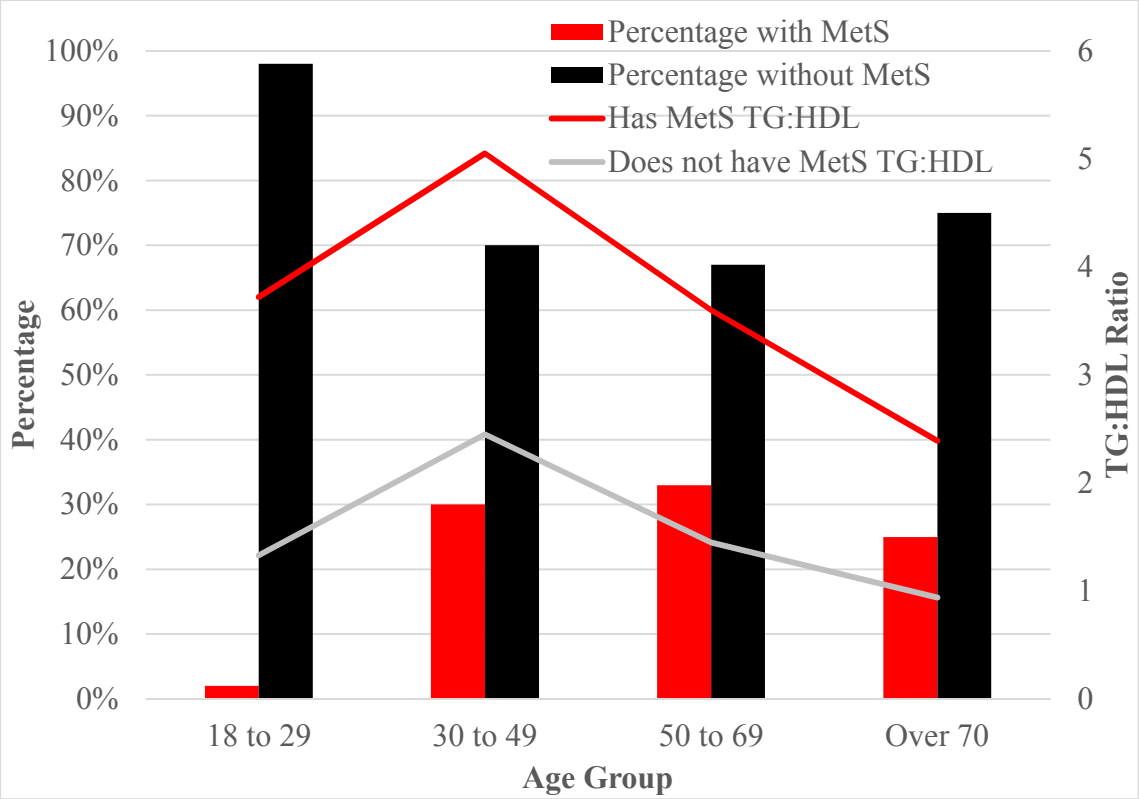


Figure 53 shows the TG:HDL ratio values and MetS prevalence in Hispanic men across age groups. Hispanic men had the highest prevalence of MetS at 35% amongst males. Hispanic men without MetS in the 30 to 49 age group still had a high TG:HDL ratio of 3.06. The ratio in the same age group in Hispanic men with MetS was 6.12 and increased to 6.98 in the 50 to 69 age group, which correlated to the highest MetS prevalence for all men at 46%. These results indicate that Hispanic men would be at the most risk for developing MetS in their middle ages and consequently heart disease.

Figure 53

TG:HDL Ratios and MetS Status Across Age Groups in Hispanic Men

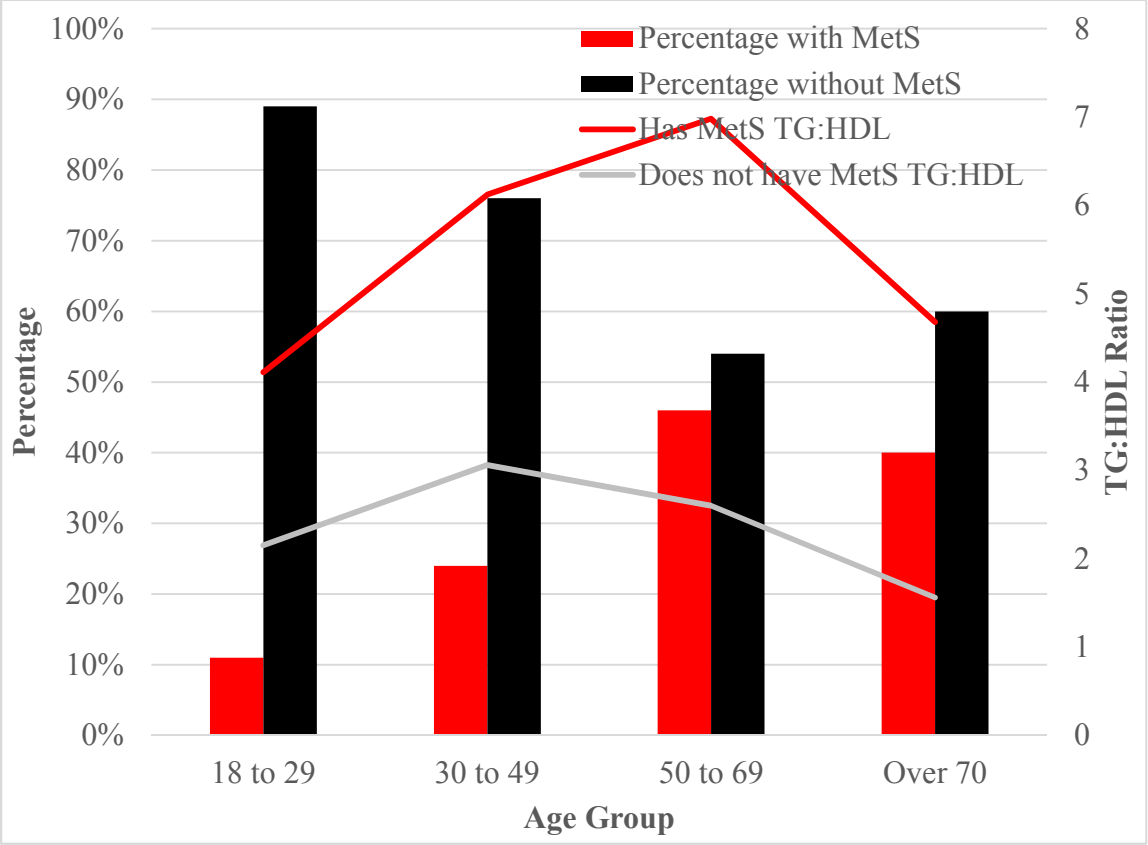
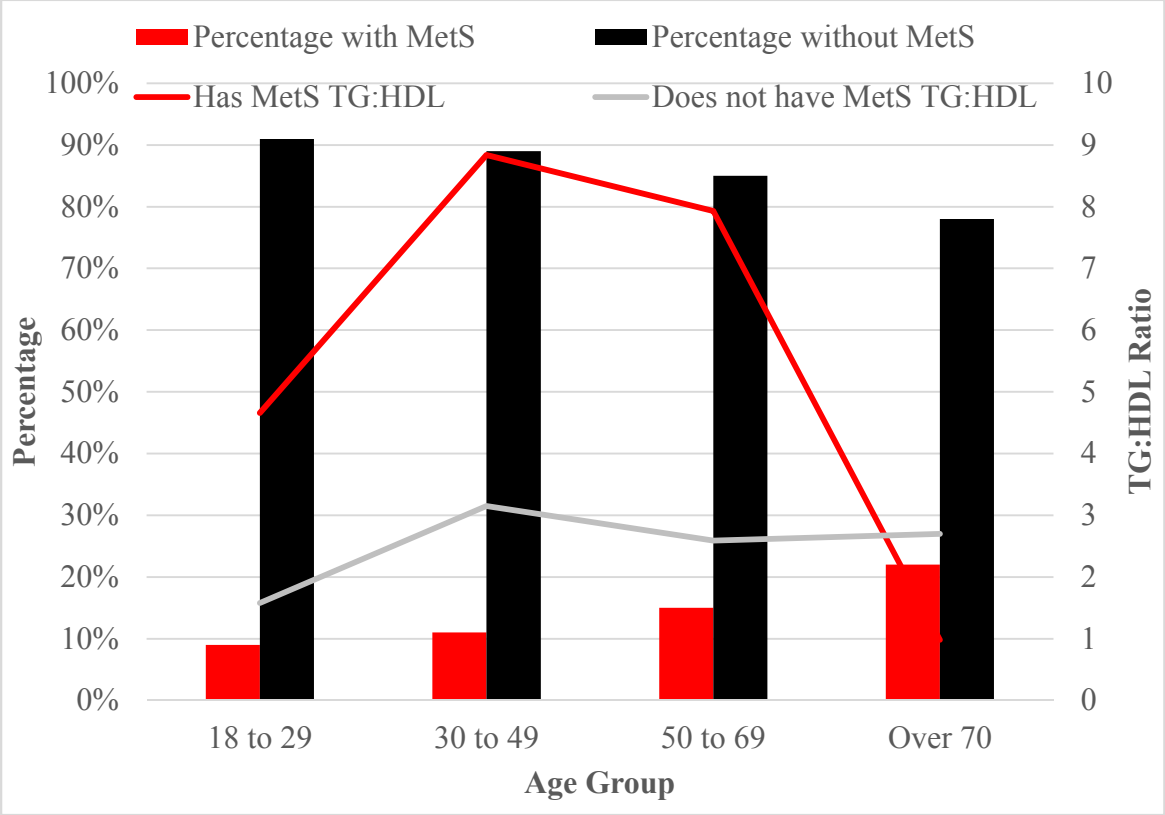


Figure 54 shows the TG:HDL ratio values and MetS prevalence in Asian men across age groups. Though Asian men had the lowest prevalence of MetS at 13%, the 30 to 49 and 50 to 69 age groups had high ratio values of 8.84 and 7.93, respectively. These ratio values were higher than those in the other races in men. Asian men without MetS in the 30 to 49, 50 to 69 and above 70 age groups had unhealthy TG:HDL ratio values above the 2.5 cutoff mark. This may be interpreted as Asian men possibly being more robust against MetS, and that it takes higher levels of triglycerides for Asian men to develop MetS compared to other races.

Figure 54

TG:HDL Ratios and MetS Status Across Age Groups in Asian Men



The Triglyceride:HDL Ratio in Age Group and Race Categories for Women

Figure 55 shows the TG:HDL ratio values across age group in White women. White women without MetS all had healthy TG:HDL ratio value below 2.0. White women with MetS had their highest TG:HDL mean ratio value of 4.1 in the youngest age group where MetS prevalence was at its lowest. Only 3% of White women had MetS, but that prevalence increased to 22% , 41%, and 38%, respectively for the three subsequent age groups. This may indicate that for those who go on to develop MetS, poor diet in their youth affects their health outcomes in the long-term.

Figure 55

TG:HDL Ratios and MetS Status Across Age Groups in White Women

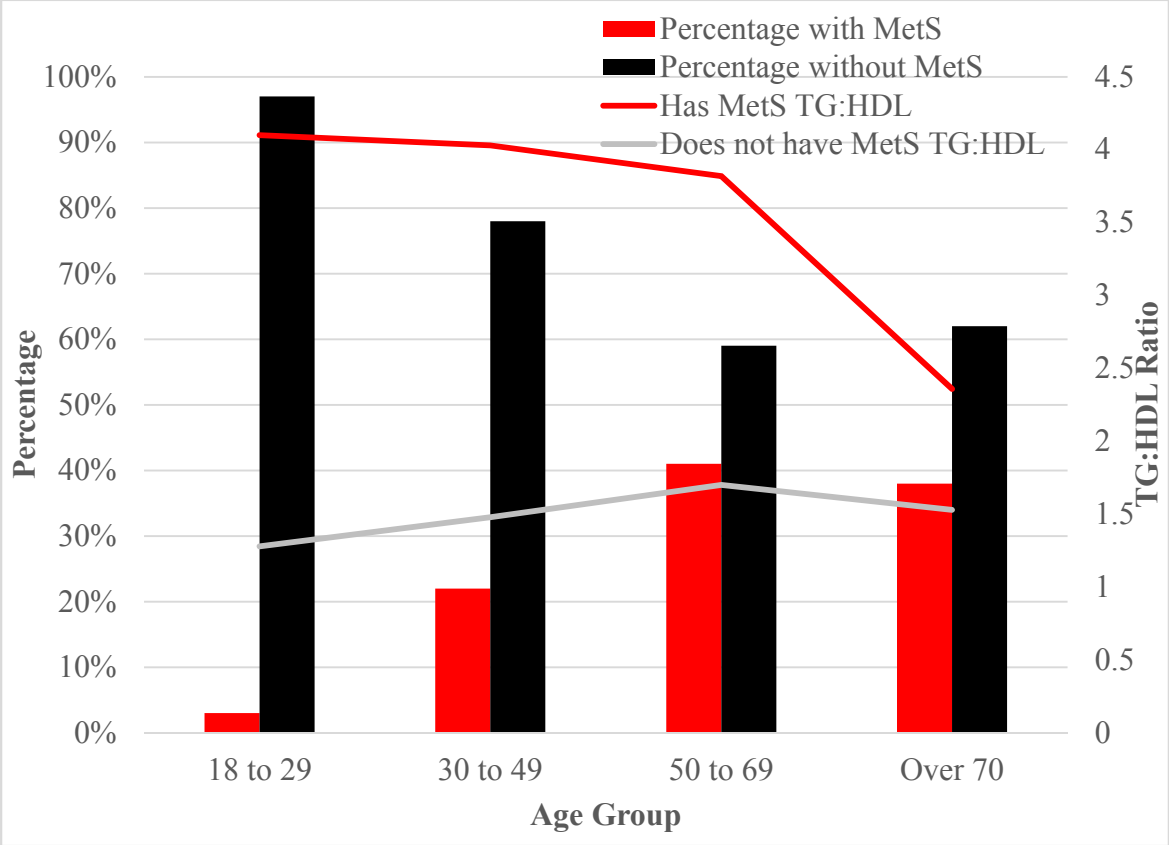


Figure 56 shows the TG:HDL ratio values across age groups in Black women. Black women with MetS had TG:HDL mean ratios within the normal range for all age groups, but Black women with MetS also had normal TG:HDL ratio values below 2.5. If Black women have normal TG:HDL ratio values and still go on to develop MetS, then this suggests that Black women of all age groups are at risk for MetS and are susceptible to the detrimental health effects of a poor diet compared to other racial groups. The prevalence of MetS in Black women begins with a low 4% in the youngest age group and

reaches a peak of 50% in the over 70 age group. So Black women should avoid poor dietary behavior while still young to avoid developing the components of MetS.

Figure 56

TG:HDL Ratios and MetS Status Across Age Groups in Black Women

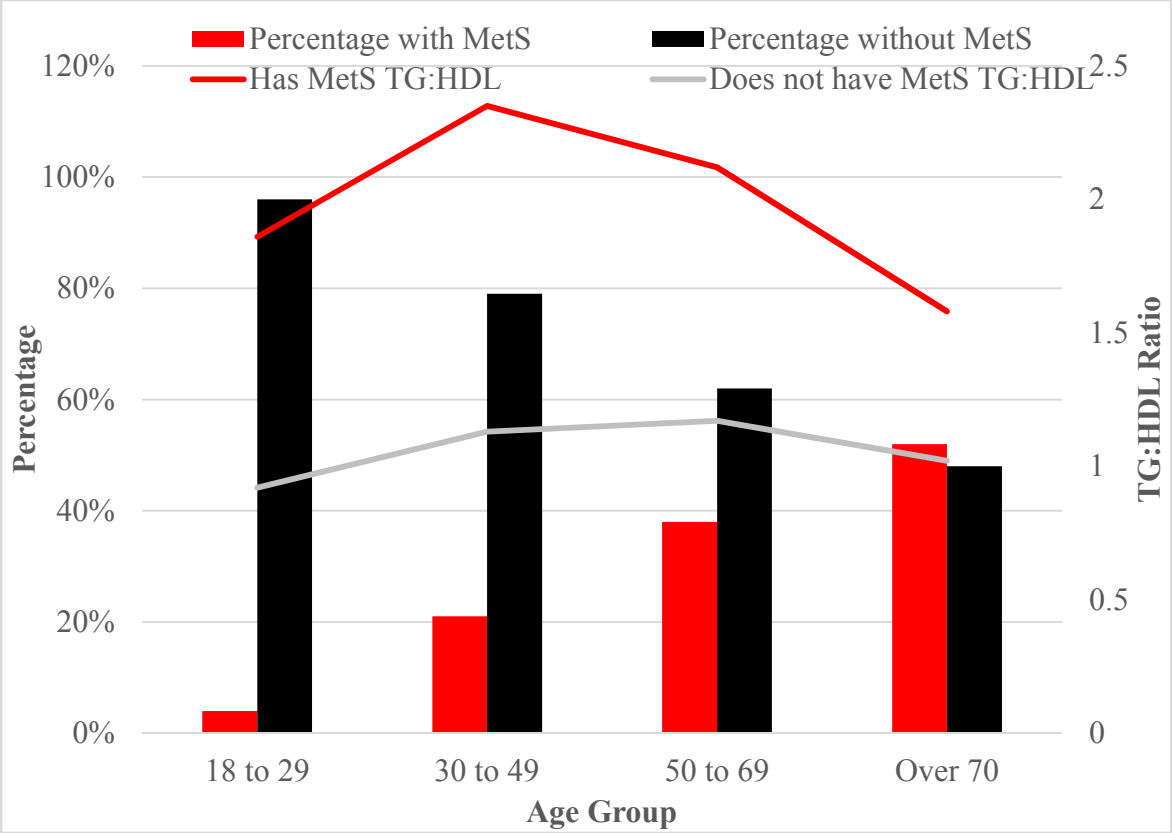


Figure 57 shows the TG:HDL ratio values across age groups in Hispanic women. Hispanic women had the highest overall MetS prevalence for women at 35% with a MetS prevalence of 65% in the over 70 age group, the highest for both men and women. Hispanic women without MetS had healthy TG:HDL ratio values below 2.0 across all age groups. Hispanic women with MetS had a narrow range of TG:HDL mean values from 3.35 to 3.87. This shows that a relatively constant TG:HDL ratio throughout life will

increase the incidence of MetS in Hispanic women until over half will develop MetS after age 70.

Figure 57

TG:HDL Ratios and MetS Status Across Age Groups in Hispanic Women

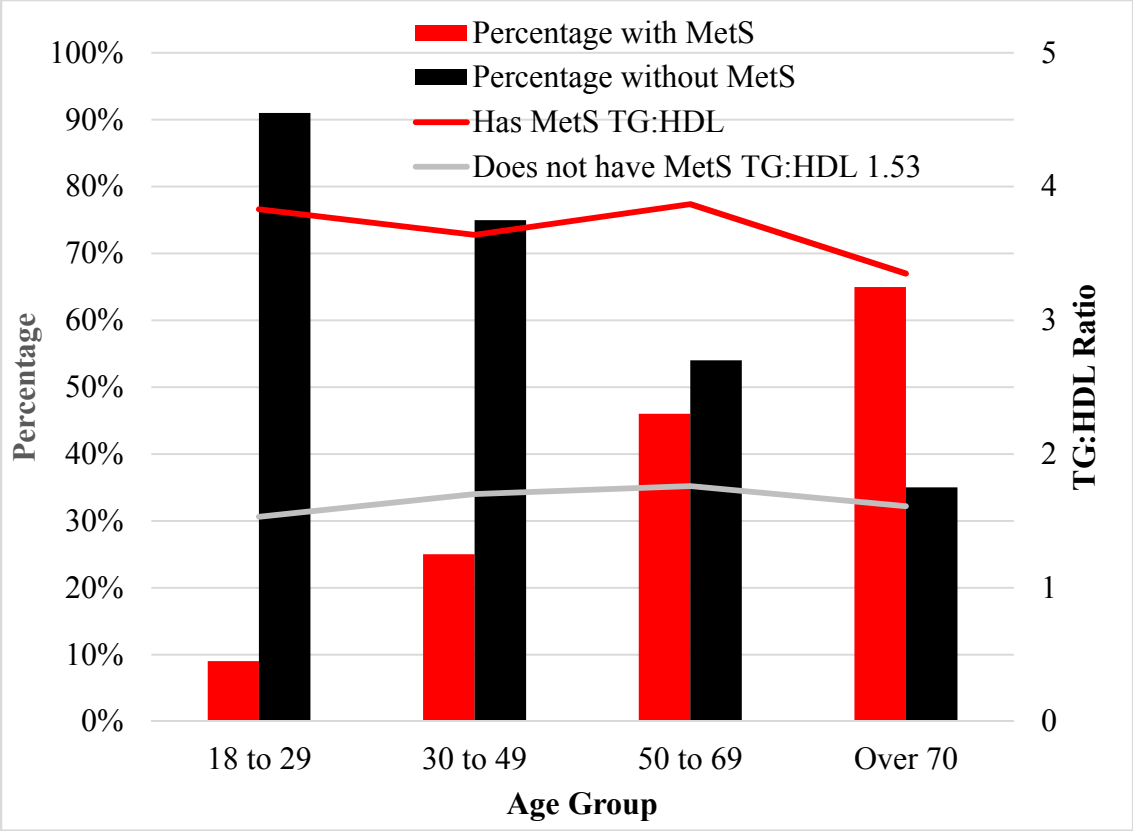
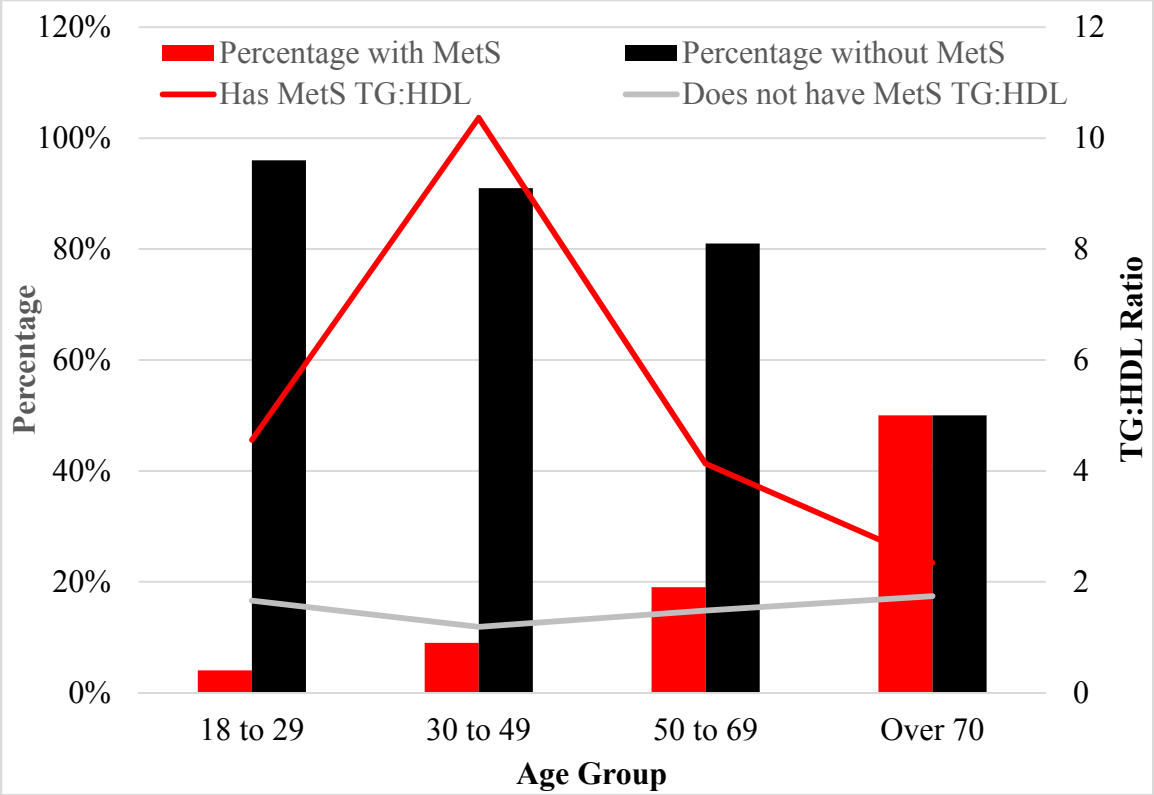


Figure 58 shows the TG:HDL ratio values across age groups in Asian women. Asian women had the lowest overall MetS prevalence among women at 14%, but the 30 to 49 age group had a very high TG:HDL mean ratio of 10.37. Only 9% of Asian women in the 30 to 49 age group had MetS. However, MetS prevalence increased to 19% and then to 50% in the 50 to 69 and over 70 age groups, respectively. This bimodal

distribution of MetS prevalence in Asian women may suggest that these women are robust against developing MetS in youth but susceptible to MetS in the middle ages.

Figure 58

TG:HDL Ratios and MetS Status Across Age Groups in Asian Women



Insulin Levels and HOMA-IR in Age Groups and Race Categories for Men

Based on the HOMA-IR calculation, the results for insulin sensitivity levels in men showed that many men across age groups and race did not have optimal insulin sensitivity and were either resistant to the effects of insulin or at risk for IR. Their IR may have possibly been due to their comorbid obesity combined with a poor diet. Most men of all races without MetS are still in the "at risk for developing IR" classification and consequently at risk for MetS. With the exception of Asian men with MetS 70 and above,

all of the HOMA-IR values for men with MetS were over the HOMA-IR cutoff value of 2.5 and were classified as having IR. There is a general pattern of increasing HOMA-IR values associated with higher MetS prevalence for all races.

Figure 59 shows the HOMA-IR values across age group in White men. White men with MetS were insulin resistant, with the youngest age group having the highest HOMA-IR value at 20.05. This is a relatively high value compared to all the other scores, and only 13% of White men in the youngest age group had MetS. The HOMA-IR values decreased for the subsequent age groups, but MetS prevalence increased to 35% for the 50 to 69 age group and to 37% for the over 70 age group. HOMA-IR values remained comparatively lower for White men without MetS for all age groups, though none of these men were insulin sensitive.

Figure 59

HOMA-IR Values and MetS Status Across Age Groups in White Men

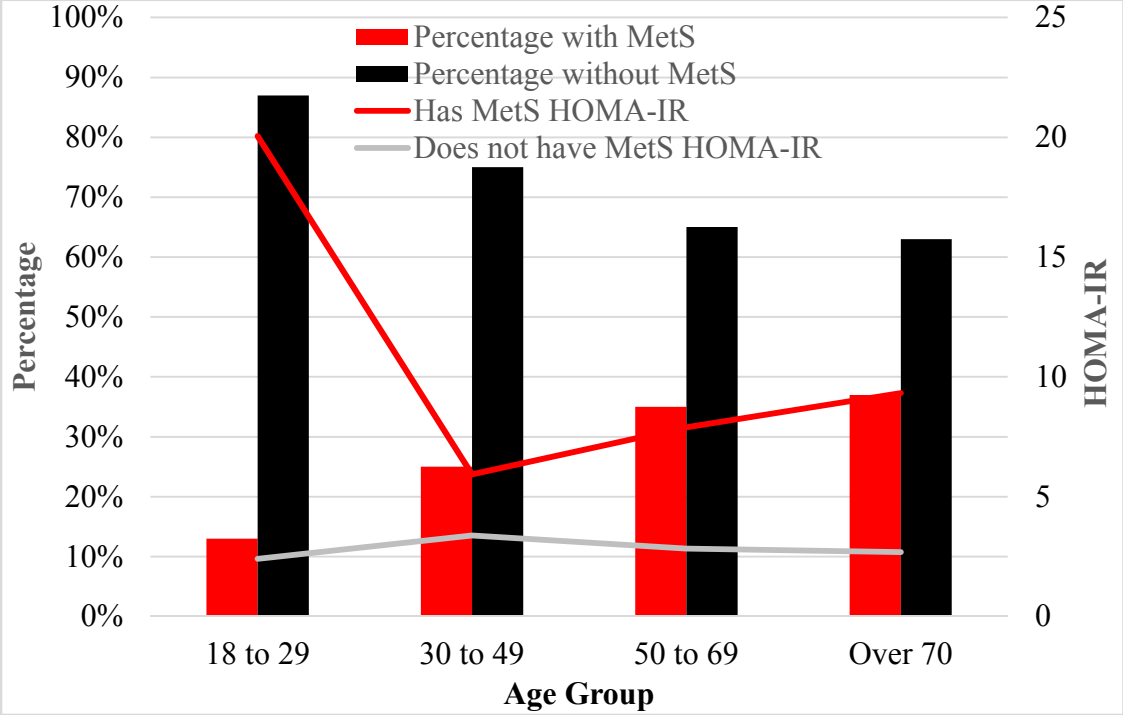


Figure 60 shows the HOMA-IR values across age groups in Hispanic men. The HOMA-IR values for Hispanic men with MetS were stable, with a range from 5.55 to 8.02. The youngest age group of Hispanic men had the highest value at 8.02, and then the values consecutively declined to 7.62, 6.65, and 5.55 for the remainder of the age groups. However, the prevalence of MetS increased from 11% to a high of 46% in the 50 to 69 age group. Hispanic men without MetS in the 18 to 29 age group already started with IR at a HOMA-IR value of 3.08, and no age group was insulin sensitive.

Figure 60

HOMA-IR Values and MetS Status Across Age Groups in Hispanic Men

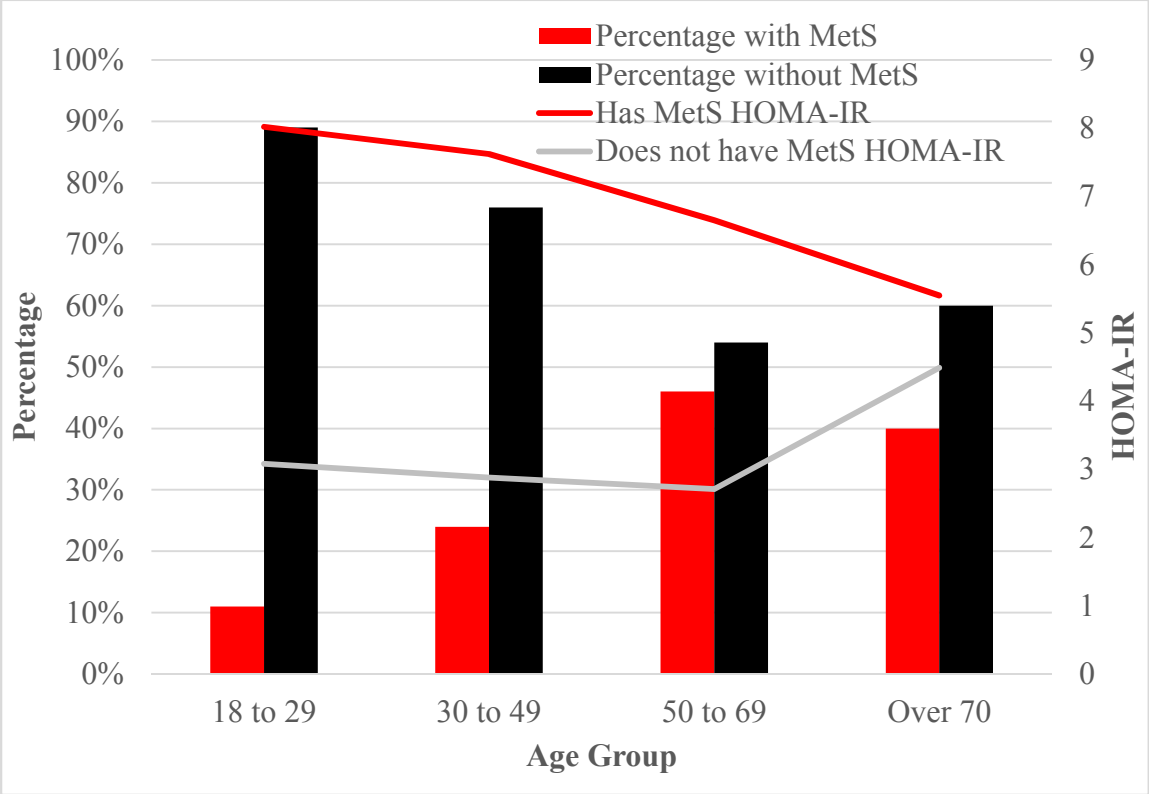


Figure 61 shows the HOMA-IR values across age groups in Black men. Black men had a wide HOMA-IR range of values from 3.13 to 13.80. The youngest age group had the lowest HOMA-IR value at 3.13, but the value increased to 12.04 and then 13.80 for the next higher age groups. This large increase could reflect Black men being more susceptible to the effects of obesity and poor dieting. Black men without MetS still had HOMA-IR values above 2.0 for age groups 18 to 29 to 50 to 69, but the over 70 group showed insulin sensitivity with a value of 1.77.

Figure 61

HOMA-IR Values and MetS Status Across Age Groups in Black Men

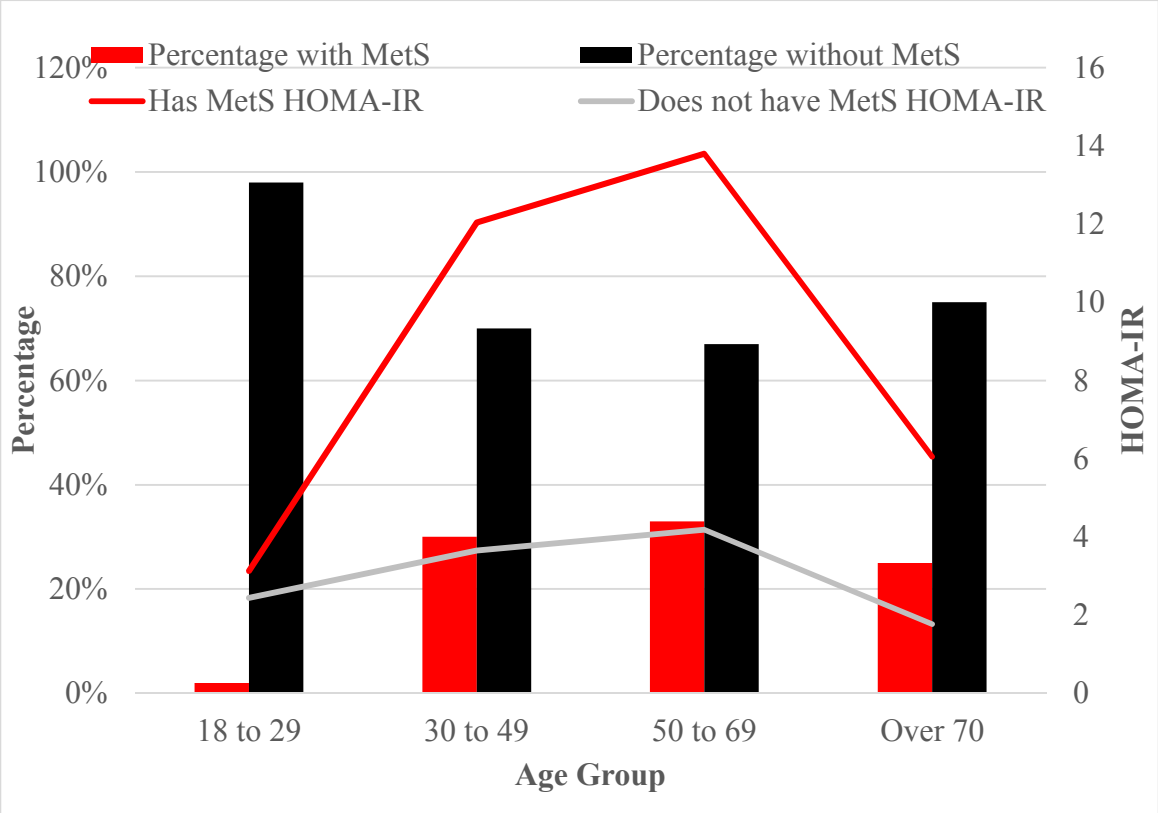
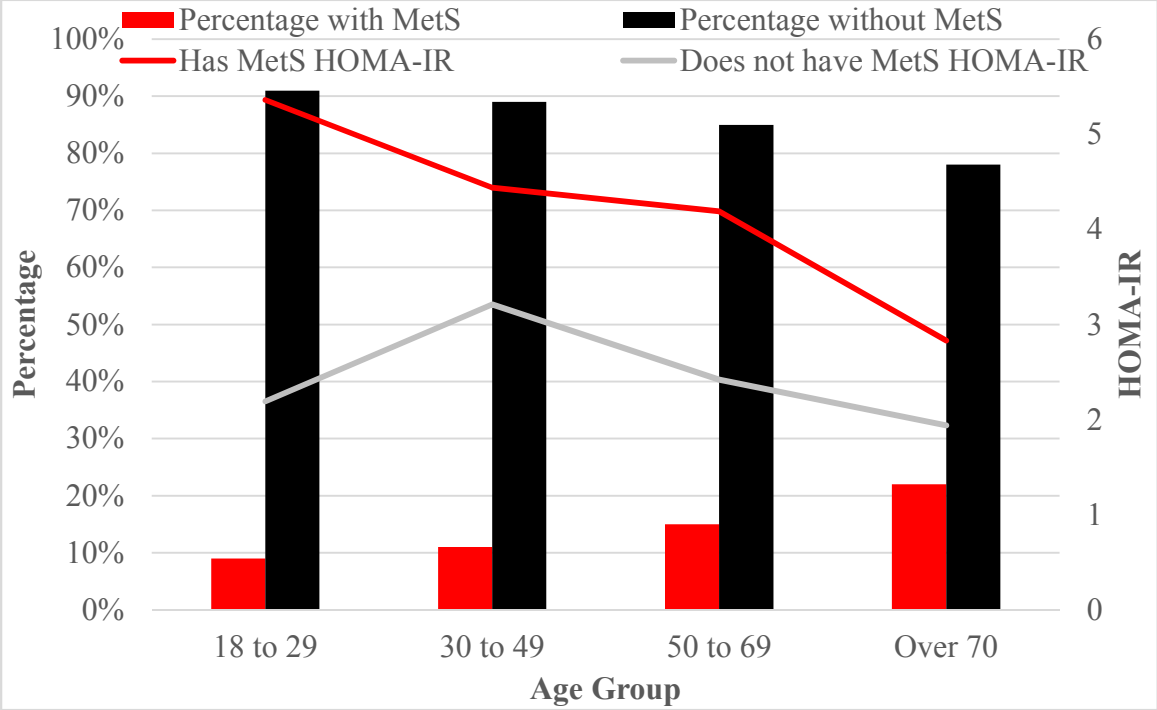


Figure 62 shows the HOMA-IR values across age groups in Asian men. Asian men with MetS had stable HOMA-IR values from 2.83 to 5.36. Asian men had the lowest overall MetS prevalence at 13%. The age group with the highest MetS prevalence for Asian men was the over 70 group at 22%, but the HOMA-IR value was a relatively low 2.83, so other factors might have influenced the development into MetS There was a gradual increase in MetS prevalence in Asian men, but that may have been independent of HOMA-IR by the time they reached the over 70 age group.

Figure 62

HOMA-IR Values and MetS Status Across Age Groups in Asian Men



Insulin Levels and HOMA-IR in Age Groups and Age Categories for Women

Similar to men, the HOMA-IR values showed that most women across age groups and races did not have optimal insulin sensitivity and were either resistant to the effects of insulin or at risk for IR. There was a general pattern of increasing HOMA-IR values associated with higher MetS prevalence in women of all races.

MetS prevalence was highest in the 50 to 69 and over 70 age groups for women. Since obesity is a factor in developing insulin resistance and takes years to develop, older women with MetS and higher than normal HOMA-IR values would suggest that they have been obese for many years. . Only White women in the 50 to 69 age group and

Asian women over 70 were classified as insulin sensitive. All women who had MetS had HOMA-IR values showing IR.

Figure 63 shows the HOMA-IR values across age groups in White women. White women had an overall MetS prevalence of 28%, and the youngest age group had only a 3% prevalence. The HOMA-IR for White women in the 18 to 29 age group with MetS was 3.16 and without MetS was 2.89, which were close in value. However, MetS prevalence increased to a high of 41% in the 50 to 69 age group, with a high HOMA-IR value of 7.60. This pattern for White women may suggest that as obesity and MetS increases, so does insulin resistance.

Figure 63

HOMA-IR Values and MetS Status Across Age Groups in White Women

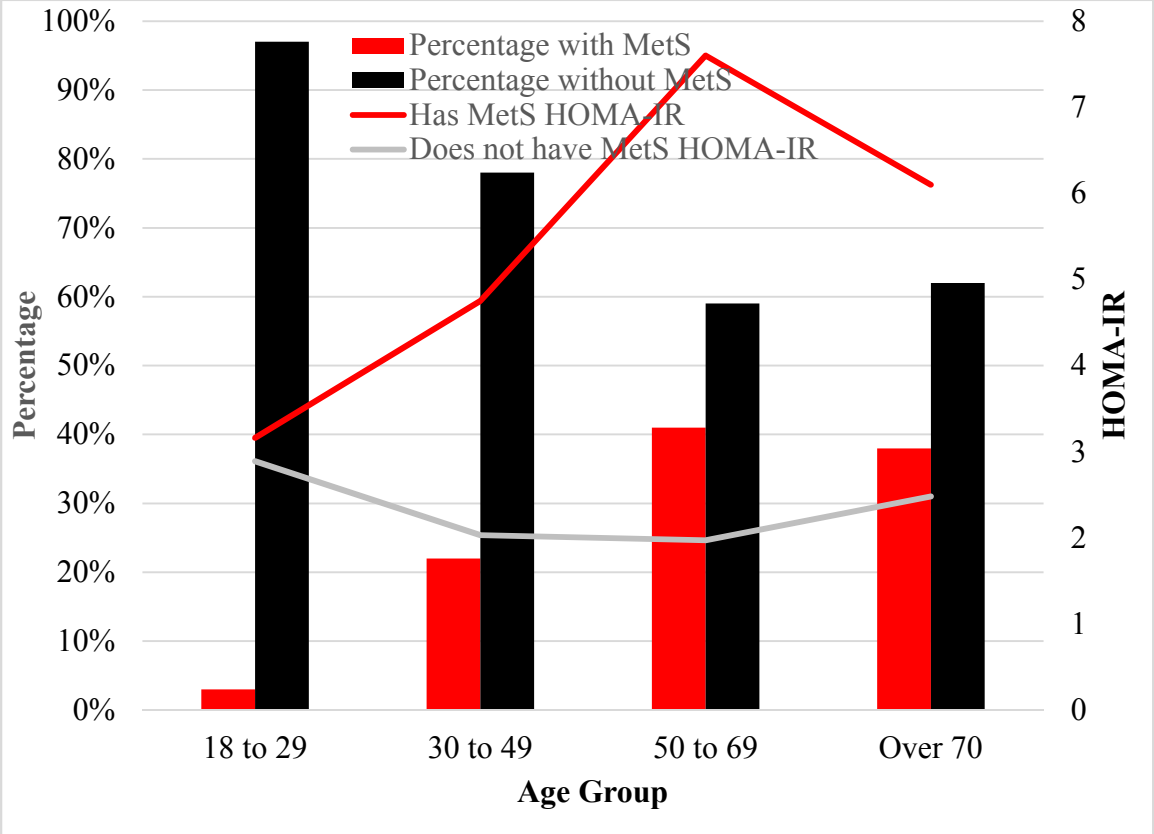


Figure 64 shows the HOMA-IR values across age groups in Hispanic women. The HOMA-IR value for Hispanic women with MetS in the youngest age group was high to begin with at 6.15, but the MetS prevalence was low at 9%. However, MetS prevalence increased to 25% for the 30 to 49 age group with a HOMA-IR value of 8.98. The MetS prevalence increase continued to 46% in the 50 to 69 age group and then reached the highest prevalence for both men and women at 65% in the over 70 age group. The over 70 age group also has a high HOMA-IR value of 10.85. The high MetS prevalence coupled with high HOMA-IR values in older Hispanic woman might be reflective of

long- term obesity that has developed into insulin resistance. Since Hispanic women had the highest MetS percentage among women and the highest HOMA-IR value, Hispanic women may have been more at risk of developing insulin resistance due to obesity and MetS compared to the other race groups.

Figure 64

HOMA-IR Values and MetS Status Across Age Groups in Hispanic Women

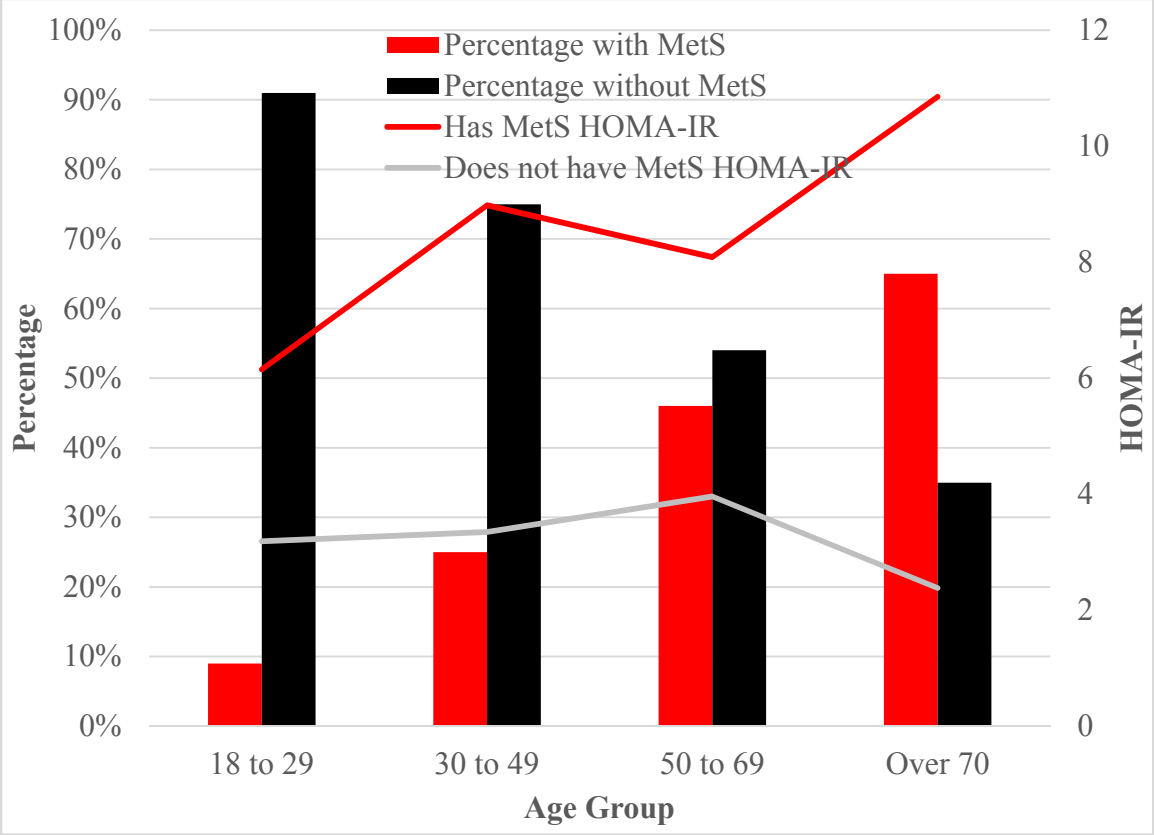


Figure 65 shows the HOMA-IR values across age groups in Black women. Similar to White and Hispanic women, Black women had a low MetS prevalence in the youngest age group at 4%, with a HOMA-IR value at 5.64, but the MetS prevalence increased to over 21% in the 30 to 49 age group, with a high HOMA-IR value of 11.63.

Black women reached their highest MetS prevalence of 52% in the over age 70 group, with a HOMA-IR value of 4.11. This follows a pattern where White, Hispanic, and Black women started off with a low MetS prevalence below 10% but then reached over 20% in the next age bracket and then reached its highest prevalence in middle-age or over 70 age group.

Figure 65

HOMA-IR Values and MetS Status Across Age Groups in Black Women

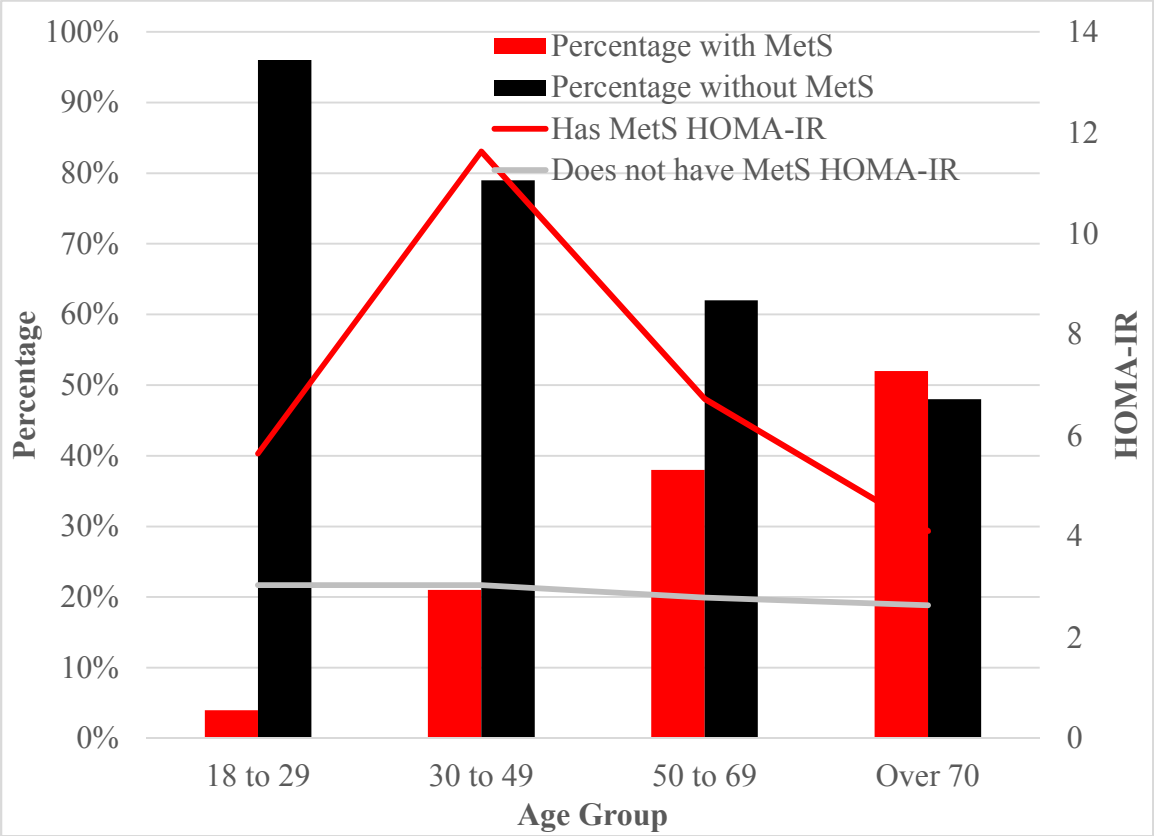
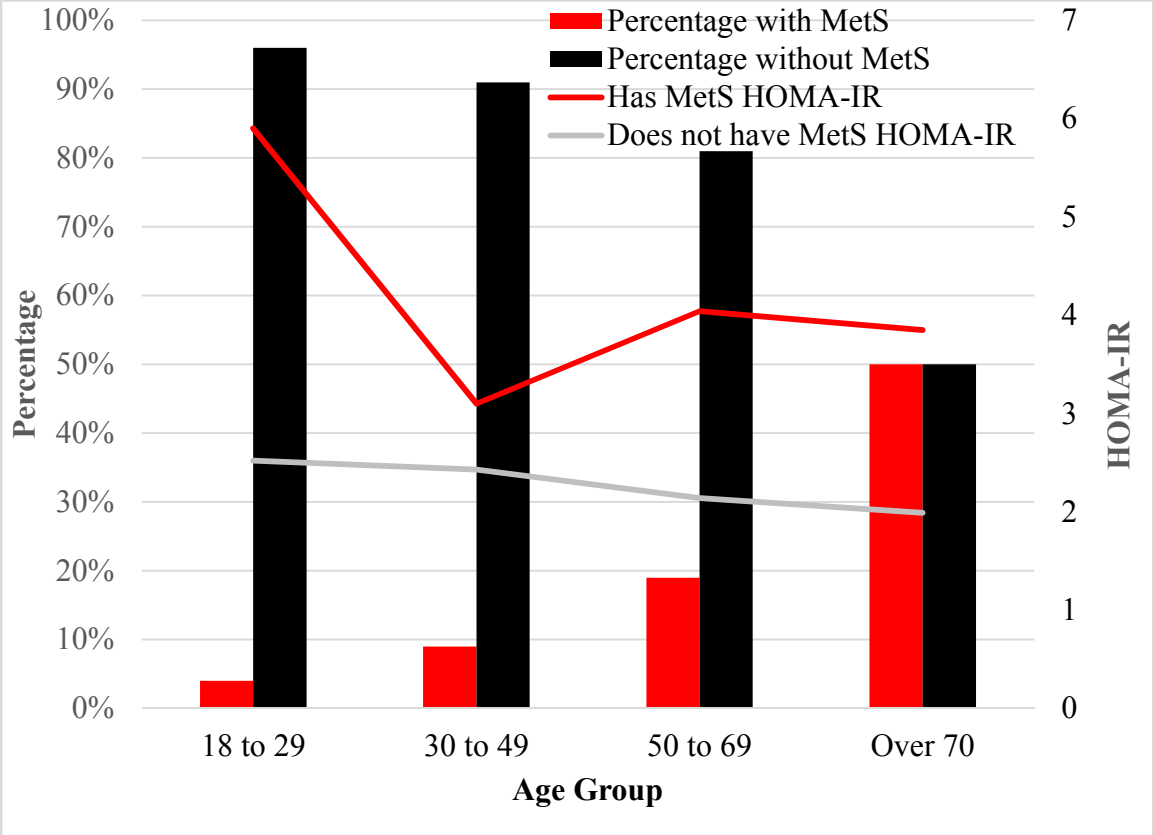


Figure 66 shows the HOMA-IR values across age groups in Asian women. Asian women had the lowest prevalence of MetS at 14%. The prevalence for Asian women with MetS stayed under 10% for the first two age groups even though HOMA-IR values were

5.90 and 3.10 for the 18 to 29 and 30 to 49 age groups, respectively. The HOMA-IR value for the 50 to 69 age group increased to 4.04 and then decreased to 3.85 for the over 70 age group. However, these last two age groups had MetS prevalence's of 19% and 50%, showing that Asian women are susceptible to MetS more in middle-age and over 70 age groups despite having similar HOMA-IR values to the younger age groups.

Figure 66

HOMA-IR Values and MetS Status Across Age Groups in Asian Women



Testosterone levels in Age Groups and Race Categories for Men

Figure 67 shows T:E2 ratios across age groups in White men. White men without MetS had high T:E2 ratios ranging from 16.68 to 22.86. For the youngest age group, White men with MetS had a T:E2 ratio value of 15.84, and the ratio values continued to decrease for the remaining age groups, which is a reflection of decreasing testosterone levels as men age. MetS prevalence increased from 13% in the youngest age group to 25% in the 30 to 49 age group with a T:E2 ratio value of 14.36 and then remained stable for the 50 to 69 and over age groups with ratio values of 13.27 and 13.65, respectively. The T:E2 ratio values were just above the normal value suggesting that middle-aged and older White men are susceptible to develop MetS with low testosterone.

Figure 67

Testosterone: Estrogen Values Across Age Groups in White Men

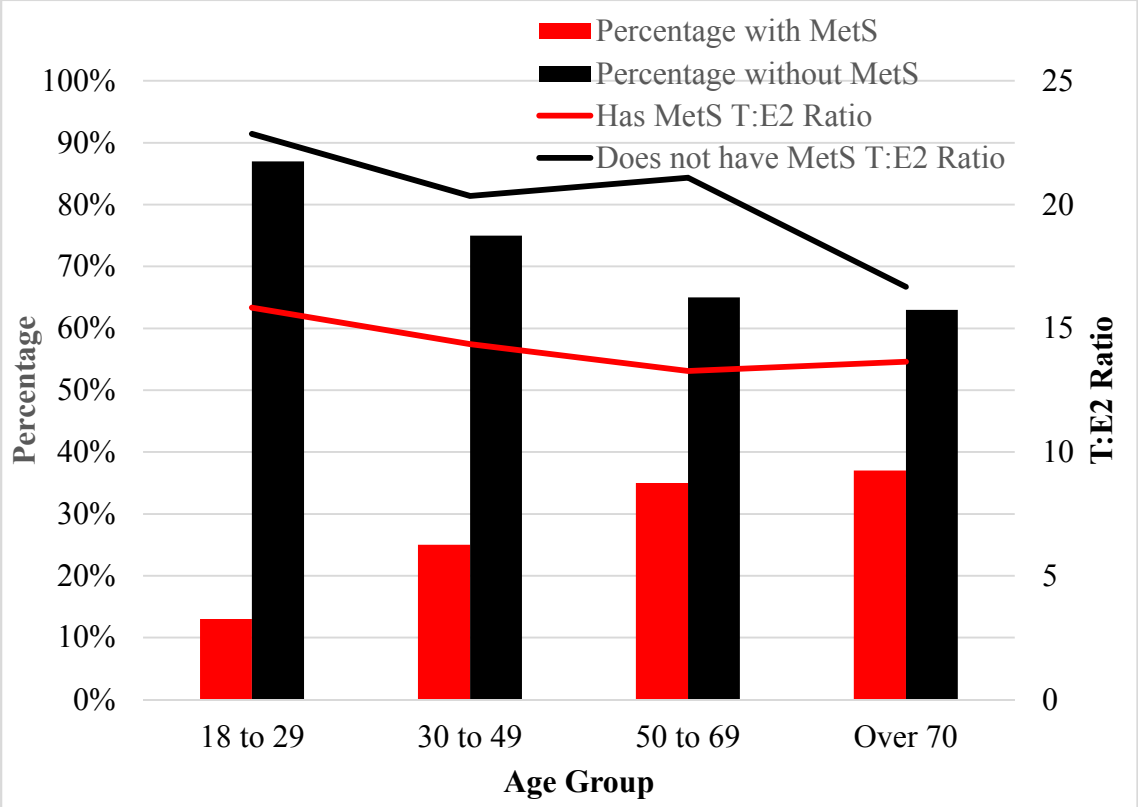


Figure 68 shows T:E2 ratios across age groups in Hispanic men. Hispanic men without MetS all had healthy T:E2 ratio values from the youngest to the oldest age group. Unlike White males with MetS, Hispanic males with MetS started off with the lowest T:E2 ratio value of all the age groups at 10.92. Then the ratio value increased to 16.06 for the 30 to 49 age group before decreasing to 14.66 and 13.48 in the 50 to 69 and 70 and above age groups, respectively. Despite having normal levels of T:E2 ratio values, Hispanic men in the 50 to 69 age group with MetS had the highest prevalence of MetS for men at 46%. This may reflect that factors other than testosterone levels are affecting their development of MetS.

Figure 68

Testosterone: Estrogen Values Across Age Groups in Hispanic Men

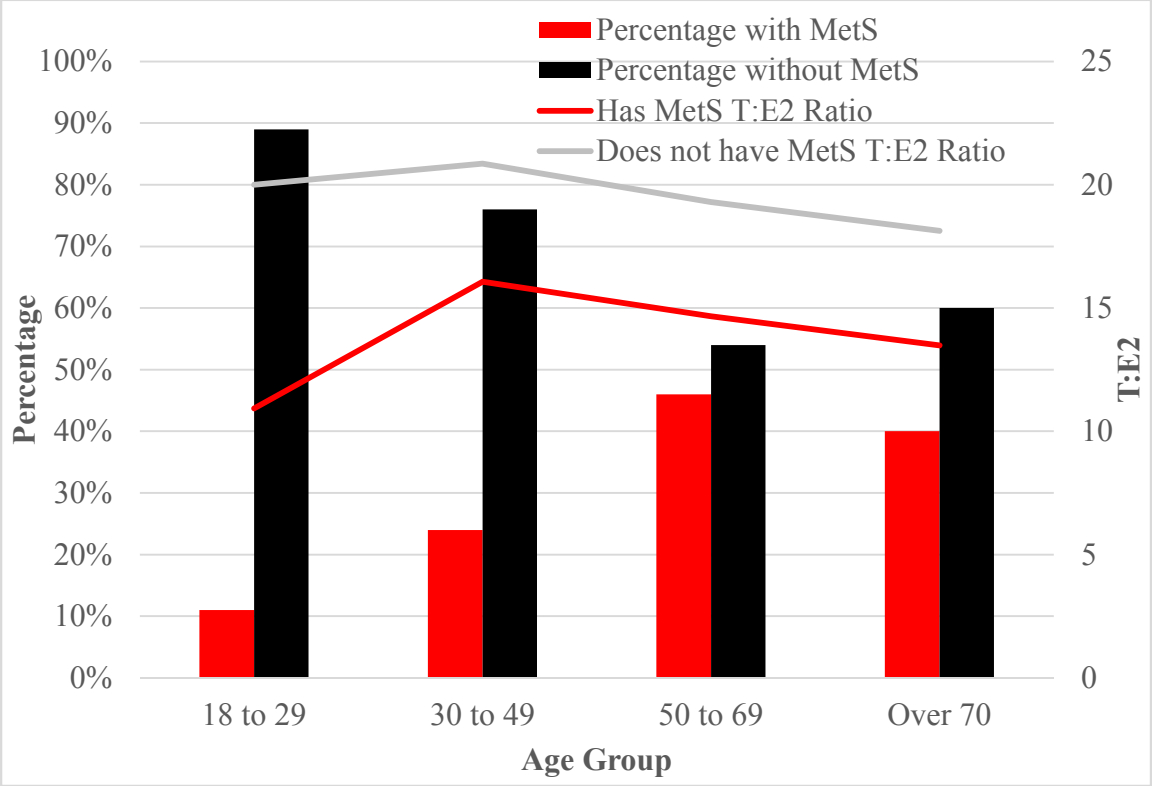


Figure 69 shows T:E2 ratios across age groups in Black men. Black men without MetS all had healthy T:E2 ratio values over 17.00 from the youngest to the oldest age group. There was only one Black male who had MetS in the 18 to 29 age group, and that participant had a lower than normal T:E2 ratio of 3.80. The T:E2 ratios for the 30 to 49 and 50 to 69 age groups were 13.14 and 13.24, respectively, before decreasing to 10.48 for the 70 and over age group. The MetS prevalence for the 30 to 49 and 50 to 69 age groups were 30% and 33%, respectively, so Black men with a T:E2 ratio of approximately 13 corresponded to a MetS prevalence of 30% to 33%.

Figure 69

Testosterone: Estrogen Values Across Age Groups in Black Men

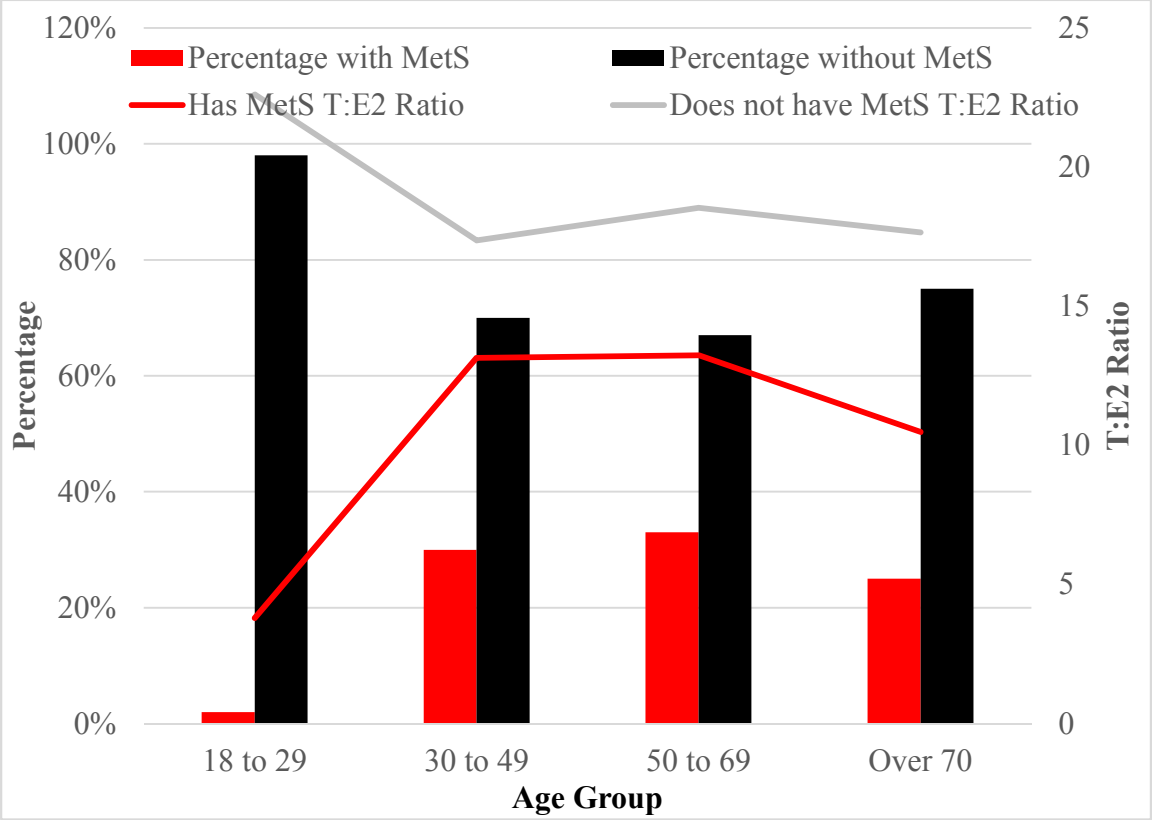
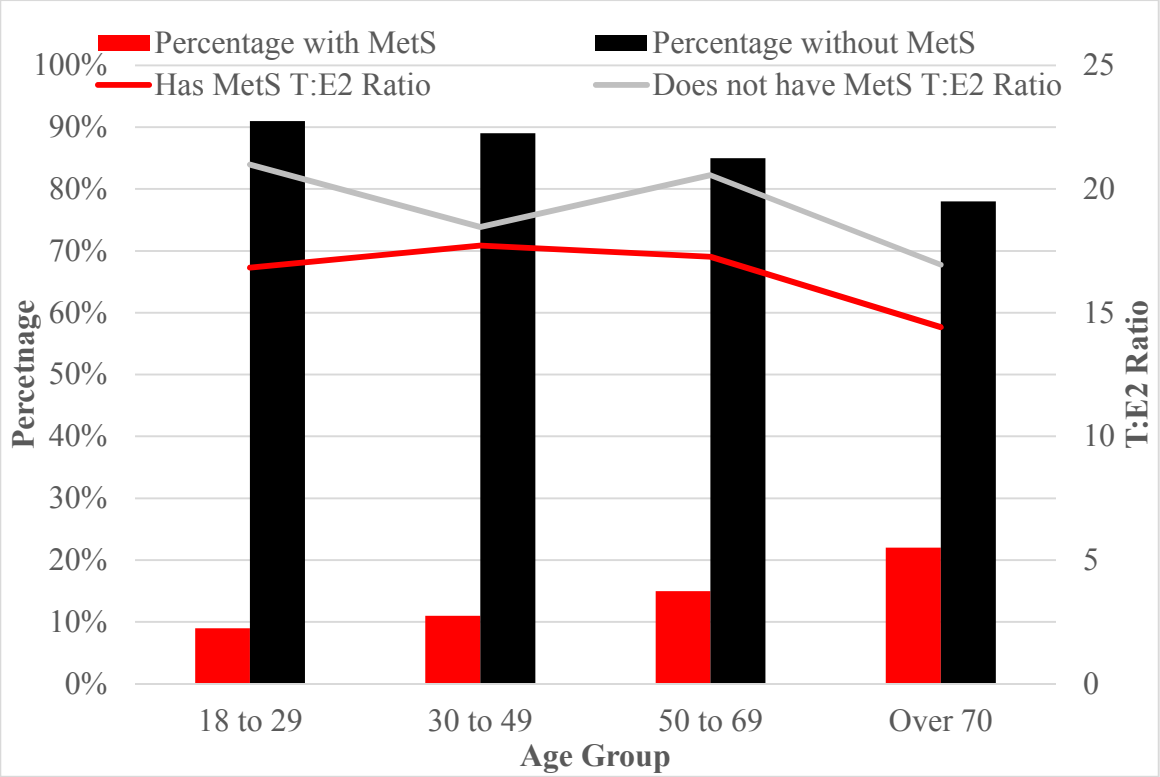


Figure 70 shows T:E2 ratios across age groups in Asian men. Asian men with MetS also had similar T:E2 ratio values that were close in value to Asian men without MetS in their respective age groups. This suggests that Asian men with MetS might be less likely to be obese, and that IR is not a significant factor in developing MetS.

Figure 70

Testosterone: Estrogen Values Across Age Groups in Asian Men



Vigorous Recreational Activity

The Vigorous Recreational Activity variable asked, "In a typical week do you do any vigorous-intensity sports, fitness, or recreational activities that cause large increases in breathing or heart rate like running or basketball for at least 10 minutes continuously?" Men who answered yes to participating in vigorous recreational activity were more than twice as likely to have MetS as those who answered with a no response. The largest discrepancy between those who did and did not have MetS was found in the 50 to 69 age groups for Whites, Blacks, and Hispanics. The 50 to 69 age group also had the highest prevalence of MetS for Blacks and Hispanics at 33% and 46%, respectively. White men

also had a high MetS prevalence of 35% in this age group which increased to 37% in the 70 and over age group.

White men benefited the most from the positive health effects of vigorous recreational activity. They were 6.8 times as likely to not have MetS if they participated in vigorous recreational activities compared to White men who did not. Black and Hispanic men also benefited from the health effects of physical activity but not as much. Black and Hispanic men were 1.8 and 1.3 times as likely to not have MetS, respectively, if they participated in vigorous recreational activities. The question did not ask specifically the duration of their activity, so it is unknown what race category did the most and least exercising. Asian men who responded to this question did not have large discrepancies in MetS status across all age groups for this predictor.

Vigorous Recreational Activity in Age Groups for Men

There are many health benefits that come from exercise, and in this study vigorous recreational activity helped the 50 to 69 year old age group the most. Examples of vigorous activities are hiking, jogging, shoveling, weight training, bicycling, and playing sports. Physical activity and weight-bearing resistance exercise are essential for bone strength and muscle development in youth, and the health benefits continue into adulthood (Gabel, 2017). In contrast, physical inactivity and poor physical fitness are major risk factors for chronic disease and increase risk of death (Lo, 2020). Physical activity in middle-aged and older adults is also associated with reducing heart disease incidence and managing the severity for those who do have heart disease by decreasing total cholesterol and elevating HDL levels (Li, 2018).

Vigorous Recreational Activity in Age Groups for Women

Women also benefited more from vigorous recreational activities compared to men. All women who participated in vigorous recreational activities were 3.3 times as likely not to have MetS compared to men who were 2.6 times as likely not to have MetS. Like men, White, Black, and Hispanic women in the 50 to 69 age group showed the largest discrepancy in MetS status. This is the same age group that had the largest MetS prevalence for women. White and Hispanic women had similar ORs and were 4.8 and 4.7 times as likely to not have MetS if they participated in vigorous recreational activity. Black women were 2.6 times as likely to not have MetS if they participated in vigorous recreational activity.

Limitations of the Study

There were several limitations to this study that made it difficult to interpret the results to make clearer conclusions. The first limitation was due to the nature of using secondary data. Data were used from the 2015-2016 NHANES and were taken from the CDC website, so the present study was not able to ask follow-up questions to the questionnaire variables. The question about engaging in vigorous recreational activity for ten minutes or more per week could only be answered with a yes or no response. Participants who answered yes could have engaged in such activity for much longer than ten minutes. Knowing the actual time participants engaged in vigorous recreational activity would have helped to explain the differences between those who had MetS and did not have MetS.

The second limitation was the unavailability of the participants' past medical history. From previous journal literature reviews, there were many NHANES variables that were significantly associated with metabolic diseases but did not significantly predict MetS status in the present study. This may be due to participants having previously been already diagnosed with diseases associated with MetS that were currently being treated with medication and diet. Data from the NHANES did not specify what medications participants were using and for what reason.

Lastly, though there were enough cases to make conclusions for Whites, Blacks, Hispanics, and Asians of both sexes and all age groups, there was a low number of cases for the Other race category, which included mixed-race cases. NHANES did not specify any race for the Other race category, so no conclusions could be reached for races outside of Whites, Blacks, Hispanics, and Asians.

Recommendations for Future Studies

This study showed how chronic disease prevalence increases with age. Currently, one in four adult Americans has two or more chronic conditions, while approximately half of older adults have three or more chronic conditions (Raghupathi, 2018). Since the stated goal of the NHANES program is to assess the health and nutritional status of adults and children in the United States, there are several recommendations to be made to make this assessment more accurate.

This study showed that over a third of all adults will have developed MetS by middle age, so NHANES should formally provide a definition of MetS status and provide cut-off values for each of the components of MetS. If a participant has MetS, then follow-

up questions should be asked to address how he/she is treating his/her symptoms. Since vigorous recreational activity was found to be a significant predictor in the present study, questions about duration and number of times per day one engages in all types of physical activities would be useful to differentiate MetS Status and also differentiate how well one demographic group responds to physical activities compared to other groups.

Another suggestion for NHANES data is to ask more questions about past medical history and the types of medications taken. Knowing what medications a person is taking for a certain condition would help to explain their lab results. A participant on diabetic medication with high glucose would be indicative of a body that is not responding well to the medication, while a normal glucose value would be indicative of the medication working.

Implications for Social Change

Chronic diseases such as those associated with MetS are among the most prevalent and costly health conditions in the US. A chronic disease is defined as a physical or mental health condition that lasts more than one year and causes functional restrictions and requires continual observation and treatment (Basu, 2016). Chronic diseases include cancer, diabetes, hypertension, stroke, heart disease, respiratory diseases, arthritis, and obesity. These non-communicable health conditions are the leading causes of death and disability in the US and lead to a combination of hospitalization, home-healthcare, long-term disability, reduced quality of life and eventual death.

The costly treatment of chronic diseases make up a significant portion of the nation's $3.8 trillion annual health care costs (CDC, 2021). If the US population were to

be aware of the threat these chronic diseases are to their health and take the actions necessary to avoid such a fate, the nation's healthcare costs would be reduced and people's quality of life would improve. The high prevalence of MetS shows that while Americans may be aware that unhealthy lifestyles will lead to a dysfunctional metabolism, they do not take the appropriate actions to prevent or protect against chronic diseases until symptoms start to appear. This study showed that MetS prevalence does not decrease as age increases. By preventing the development of MetS while in young adulthood, MetS prevalence would be lower than current levels in the middle-age and elderly age groups. Unlike infectious diseases, chronic conditions are not caused by the spread of bacteria or viruses but are mostly caused by unhealthy behavior over the course of years. Evidence that these health conditions do not have to be a part of later life comes from the health status of indigenous communities from different continents of the world. Our human ancestors and today's hunter-gatherers do not suffer from the chronic diseases seen in industrialized nations due to having a traditional diet of wild game and native plants. These indigenous tribes survive by hunting and foraging for their food, so they also get enough physical activity to keep their bodies healthy, including their cardiovascular system free from arterial plaque.

The lives of the Hadza and Tsimane demonstrate that it is possible to live out entire lives without the risk factors for heart disease and thus not die from it. While these indigenous population live close to the lifespan seen in industrialized nations, mortality is usually caused by infections due to poor sanitation and living in an environment where parasites thrive. In contrast, industrialized nations suffer from high rates of chronic

diseases but have significantly reduced the threat of infectious diseases through childhood vaccinations, antibiotics, and modern sanitation.

Public health policies and campaigns can educate the population, but to start positive social change, individuals must act upon this information and make behavioral changes that will affect their health for the rest of their lives. The predictors for MetS from this study showed that proper dieting and physical activity are important to practice while in early adulthood. Though the high prevalence of MetS occurs past age 50, MetS does not suddenly develop in middle ages. The behaviors of young adults are key to preventing the symptoms of MetS from developing. Proper dieting will prevent abdominal obesity and developing arterial plaque, while physical activity will develop the skeletal muscular system and protect against heart disease. A third of Americans develop and suffer from MetS by middle age, but that also means approximately 70% do not. Social change will occur when those Americans who would have developed MetS decide to make changes in their lifestyle to put them on a path that would not lead them to develop MetS.

Americans may not consciously be aware that overconsumption of Western diets is radically different from the diets of hunter-gatherers, and the consequences will lead to dysregulation of their metabolism. The organ systems of the human body have remained the same since our hunter-gatherer ancestors, but the dieting behavior of consuming today's Western diets are not what the human body was designed for. The Health Belief Model states that people will not act upon their health unless they perceive that there is a threat to their well-being. The difficulty with making positive social change with chronic

diseases is that there are no acute symptoms that might be perceived as threats. The values of the TG:HDL and T:E2 ratios and HOMA-IR values across age groups can be explained by the Health Belief Model. The high TG:HDL ratios seen in early adulthood are reflective of poor dietary behavior when most do not have MetS. With no action taken to prevent MetS from developing, MetS incidence and prevalence continue to increase. The high HOMA-IR ratio and low T:E2 ratios seen in the older age-groups with MetS are reflective of the consequences of years of poor dieting from early adulthood. What is needed then for positive social change for the high prevalence of MetS is for Americans to realize that being asymptomatic in the setting of overconsumption and lack of physical activity is also dangerous to their well-being and future quality of life. Since MetS begins with being overweight, abdominal obesity should be the first sign for people to realize that there is something wrong with their health, even though they do not have any acute symptoms. Young adult Americans have to do more than just acknowledge the long-term dangers from unhealthy lifestyles and consciously make long-term lifestyle changes for the better, because it is difficult to reverse chronic conditions once they develop.

Summary and Conclusions

A health syndrome is a group of medical concurrent symptoms that collectively characterize a disease. This study explored the health and dietary predictors for developing MetS, a cluster of at least three out of five health conditions: abdominal obesity, hyperglycemia, hypertension, high blood triglycerides, and low HDL levels. A diagnosis of MetS is associated with a high risk of developing heart disease, the leading cause of death for Americans. In addition to the financial burdens for treating and

managing MetS, there is also reduced quality of life from not being able to perform daily activities as easily as someone without MetS. Out of the many potential variables from the NHANES data, there were only four that were found to be significant predictors in this study. They were the TG:HDL ratio, insulin levels, testosterone levels in men but not women, and vigorous recreational activity. These four predictors share a relationship in the metabolism of humans.

A high TG:HDL ratio means that there is a higher than normal level of triglycerides in blood circulation and is a reflection of poor nutrition, such as a diet consisting of refined sugars and processed carbohydrates commonly seen in fast food items. High triglyceride levels lead to triglycerides being stored in the adipocytes as fat, primarily in the abdominal region leading to abdominal obesity. Abdominal obesity leads to insulin resistance, and circulating glucose is not able to efficiently enter cells that need glucose for energy to function, leading to hyperglycemia. High insulin levels also cause triglyceride and glucose to be stored as fat inside the adipocytes.

Abdominal obesity is associated with the release of the hormone aromatase, which converts testosterone to estrogen and also lowers levels of testosterone produced in the testes due to negative feedback from the pituitary. Higher than normal levels of estrogen would affect the health of men more than women and is the reason why high testosterone levels is a significant predictor of MetS for men but not for women. Finally, engaging in vigorous recreational activity is a behavior that protects against the effects of metabolic disorders, so is a significant preventive measure against MetS.

Among the demographic variables, age group was the variable that significantly differentiated MetS prevalence. The younger age groups had lower MetS prevalence, and prevalence increased as age increased. The TG:HDL ratio values and HOMA-IR values for men and women across race categories suggested that the 18 to 29 and 30 to 49 age groups are the ages in which poor dietary habits are occurring, the components of MetS are developing and MetS incidence is increasing but has not yet reached its prevalence peak. Then in the 50 to 69 and 70 and over age groups is when MetS prevalence reaches its highest levels. This means that the unhealthy behaviors that occur during young adulthood affect their health in the long term for the worse. The HBM provides an explanation for these behaviors in that there are no overt symptoms felt other than becoming overweight. Living through adulthood upon reaching retirement should be a time when Americans can remain free from preventable chronic diseases. However, for 36% of men and 40% of women in the 50 to 69 age group, MetS can significantly decrease their quality of life by decreasing their physical capability to enjoy life. The financial costs to treat and manage MetS are an extra burden.

The Hadza of Africa and Tsimane of South America practice fasting, eat no processed foods, and walk many miles a day to hunt for their food. This active lifestyle results in excellent cardiovascular health. Young Americans do not have to live like hunter-gatherers to have good heart health but have to be aware that their dietary habits will have a lasting effect on their metabolism. With a healthy diet eaten in the right amounts, there is a normal TG:HDL ratio and no abdominal obesity. Consequently, there is no insulin resistance and no decrease in testosterone.

This study concludes that gaining weight for any race and age group is the first metabolic step in the development of MetS, and the way to prevent and protect against further metabolic insults is to lower caloric intake for those who are overweight and engage in weekly physical exercises to strengthen and build muscle and to protect against heart disease. Then Americans can benefit from good cardiovascular and musculoskeletal health and be able to physically and mentally function for most of their lifespan.

References

Abbasi J. (2018). Interest in the ketogenic diet grows for weight loss and type 2 diabetes. *JAMA, 319*(3), 215–217. https://doi.org/10.1001/jama.2017.20639

Abouroab, A., Aly Marzok, H., & Ismail, S. (2021). Free serum testosterone versus total testosterone/estradiol ratio in low sexual desire in old men. *Egyptian Journal of Hospital Medicine*, *83*, 1062–1067. https://doi.org/10.21608/ejhm.2021.160618

Agnera, V., Garciab, M., Taffarela, A., Mourãoa, C., Paulo da Silvad, I., Pereira da Silvaa, S., Peccinc, M., & Lombardi, I. (2018). Effects of concurrent training on muscle strength in older adults with metabolic syndrome: A randomized controlled clinical trial. Archives of *Gerontology and Geriatrics, 75*, 158-164. https://doi.org/10.1016/j.archger.2017.12.011

Andersson, E., Frank, P., Ponten, M., Ekblom, B., Ekblom, M., Moberg, M., & Sahlin, K. (2017). Improving strength, power, muscle aerobic capacity, and glucose tolerance through short-term progressive strength training among elderly people. *Journal of Visualized Experiments*, *125*, 1-25. https://doi.org/10.3791/55518

Armelagos, G., Brown, P., & Turner, B. (2005). Evolutionary, historical and political economic perspectives on health and disease. *Social Science & Medicine, 61*(4), 755–765. https://doi.org/10.1016/j.socscimed.2004.08.066

American Heart Association (2019). Symptoms and Diagnosis of Metabolic Syndrome. https://www.heart.org/en/health-topics/metabolic-syndrome/symptoms-and-diagnosis-of-metabolic-syndrome

Agner, V., Garcia, M., Taffarel, A., Mourão, C., da Silva, I., da Silva, S., Lombardi, J. (2018). Effects of concurrent training on muscle strength in older adults with metabolic syndrome: A randomized controlled clinical trial. *Archives of Gerontology and Geriatrics*, *75*, 158–164. https://doi.org/10.1016/j.archger.2017.12.011

Aschengrau, A. & Seage, G. (2018). *Essentials of Epidemiology in Public Health* (4th ed.). Jones and Bartlett Publishers.

Baar, K. (2017). Minimizing injury and maximizing return to play: Lessons from engineered ligaments. *Sports Medicine*, *47*, 5-11. https://doi.org/10.1007/s40279-017-0719-x

Basu, J., Avila, R., & Ricciardi, R. (2016). Hospital readmission rates in U.S. States: Are readmissions higher where more patients with multiple chronic conditions cluster? *Health Services Research*, *51*, 1135-1151. https://doi.org/10.1111/1475-6773.12401

Bhagavan, N. & Ha, C. (2015). *Essential of Medical Biochemistry* (2nd ed.). Academic Press.

Belchior, T., Paschoal, V., Magdalon, J., Chimin, P., Farias, T., Chaves-Filho, A., Gorjão, R., St-Pierre, P., Miyamoto, S., Kang, J., Deshaies, Y., Marette, A., & Festuccia, W. (2015). Omega-3 fatty acids protect from diet-induced obesity, glucose intolerance, and adipose tissue inflammation through PPARγ-dependent and PPARγ-independent actions. *Molecular Nutrition & Food Research, 59*(5), 957-967. https://doi.org/10.1002/mnfr.201400914

Benjamin, E. (2017). Heart disease and stroke statistics 2017 Update: A report from the American Heart Association. *Circulation, 135*(10), 146-603. https://doi.org/10.1161/cir.0000000000000491

Bettis, T., Kim, B., & Hamrick, M. (2018). Impact of muscle atrophy on bone metabolism and bone strength: Implications for muscle-bone crosstalk with aging and disuse. *Osteoporosis International, 29*(8), 1713-1720. https://doi.org/10.1007/s00198-018-4570-1

Bray, G., Nielson, S., Popkin, B. (2004). Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. *American Journal of Clinical Nutrition*, *79*, 537-543. https://doi.org/10.1093/ajcn/79.4.537

Bianchi, V. (2018). The anti-inflammatory effects of testosterone. *Journal of the Endocrine Society, 3*(1), 91-107. https://doi.org/10.1210/js.2018-00186

Blaak, E., Canfora, E, Theis, S., Frost, G., Groen, A., Mithieux, G., Nauta, A., Scott, K., Stahl, B., van Harsselaar, J., van Tol, R., Vaughan, E., Verbeke, K. (2020). Short chain fatty acids in human gut and metabolic health. *Beneficial Microbes, 11*(5), 411-455. https://doi.org/10.3920/bm2020.0057

Blackwell, A., Trumble, B., Maldonado Suarez, I., Stieglitz, J., Beheim, B. A., Snodgrass, J. J., Kaplan, H., & Gurven, M. (2016). Immune function in Amazonian horticulturalists. *Annals of Human Biology*, 43, 382-396. https://doi.org/10.1080/03014460.2016.1189963

Bou, M., Berge, G., Baeverfjord, G., Sigholt, T., Ostbye, T., Romarheim, O. & Ruyter, B. (2017). Requirements of n-3 very long-chain PUFA in Atlantic salmon: Effects of different dietary levels of EPA and DHA on fish performance and tissue composition and integrity. *British Journal of Nutrition, 117*(1), 30-47. https://doi.org/10.1017/s0007114516004396

Center for Disease Control (2020a). *Defining adult overweight and obesity.* https://www.cdc.gov/obesity/adult/defining.html

Center for Disease Control (2020b). *About high blood pressure*. https://www.cdc.gov/bloodpressure/about.htm

Center for Disease Control (2020c). National Health and Nutrition Examination Survey, 2015–2016 overview. https://wwwn.cdc.gov/nchs/data/nhanes/2015-2016/documents/2015-16_NHANES_Overview.pdf

Center for Disease Control (2019). Deaths: Final data for 2017. *National Vital Statistics Reports, 68*(9), 1-77.

Chavanelle, V., Boisseau, N., Otero, Y. F., et al. (2017). Effects of high-intensity interval training and moderate-intensity continuous training on glycaemic control and skeletal muscle mitochondrial function in db/db mice. *Scientific Reports, 7*(1), 204-213. https://doi.org/10.1038/s41598-017-00276-8

Chen, Y., Michalak, M., & Agellon, L. (2018). Importance of Nutrients and Nutrient Metabolism on Human Health. The *Yale Journal of Biology and Medicine, 91*(2), 95-103.

Chissini, R., Kuschnir, M., de Oliveira, C., Giannini, D., & Santos, B. (2020). Cutoff values for HOMA-IR associated with metabolic syndrome in the study of cardiovascular risk in adolescents (ERICA Study). *Nutrition*, 71, 1-6. https://doi.org/10.1016/j.nut.2019.110608

Cioffi, F., Senese, R., Lasala, P., Ziello, A., Mazzoli, A., Crescenzo, R., & Iossa, S. (2017). Fructose-Rich Diet Affects Mitochondrial DNA Damage and Repair in Rats. *Nutrients*, *9*(4), 323-337. https://doi.org/10.3390/nu9040323

Cooper, G. (2019). *The Cell*. (8th ed.). Oxford University Press.

Dalen, J. & Devries, S. (2014). Diets to prevent coronary heart disease 1957-2013: what have we learned? *The American Journal of Medicine, 127*(5), 364-369. https://doi.org/10.1016/j.amjmed.2013.12.014

Duran, I., Schulze, J., Martakis, K., Stark, C., & Schoenau, E. (2018). Diagnostic performance of body mass index to identify excess body fat in children with cerebral palsy. *Developmental Medicine and Child Neurology, 60*(7), 680–686. https://doi.org/10.1111/dmcn.13714

de Lorgeril M., Salen P., Martin, J., Monjaud, I., Delaye, J. & Mamelle, N. (1999). Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation, 99*(6), 779-785. https://doi.org/10.1161/01.cir.99.6.779

Dreon, D., Fernstrom, H., Campos, H., Blanche, P., Williams, P. &Krauss, R. (1998). Change in dietary saturated fat intake is correlated with change in mass of large low-density-lipoprotein particles in men. *The American Journal of Clinical Nutrition, 67*(5), 828-836. https://doi.org/10.1093/ajcn/67.5.828

Dobzhansky, T. (1973), Nothing in Biology Makes Sense Except in the Light of Evolution. *American Biology Teacher, 35* (3), 125–129. https://doi.org/10.2307/4444260

Duwaerts, C. & Maher, J. (2019). Macronutrients and the Adipose-Liver Axis in Obesity and Fatty Liver. *Cellular and Molecular Gastroenterology and Hepatology, 7*(4), 749-761. https://doi.org/10.1016/j.jcmgh.2019.02.001

Eaton, S. & Konner, M. (1985). Paleolithic nutrition: A consideration of its nature and current implications. New *England Journal of Medicine*, 312, 283-289. https://doi.org/10.1056/nejm198501313120505

Ebbert, J., & Jensen. M. (2013). Fat depots, free fatty acids, and dyslipidemia. *Nutrients, 5*(2), 498-508. https://doi.org/10.3390/nu5020498

Ferrier, D. (2017). *Lippincott Illustrated Reviews: Biochemistry* (7th ed.). Wolters Kluwer.

Fishman, S. L., Sonmez, H., Basman, C., Singh, V., & Poretsky, L. (2018). The role of advanced glycation end-products in the development of coronary artery disease in patients with and without diabetes mellitus: A review. *Molecular Medicine*, 24(59), 1-12. https://doi.org/10.1186/s10020-018-0060-3

Forrester, S., Kikuchi, D., Hernandes, M., Xu, Q., & Griendling, K. (2018). Reactive oxygen species in metabolic and inflammatory signaling. *Circulation Research*, 122, 877-902. https://doi.org/10.1161/circresaha.117.311401

Fournet, M., Bonté, F., & Desmoulière, A. (2018). Glycation damage: A possible hub for major pathophysiological disorders and aging. *Aging and disease, 9*(5), 880–900. https://doi.org/10.14336/ad.2017.1121

Fowles, E. (2006). What's a Pregnant Woman to Eat? A review of current USDA Dietary guidelines and My Pyramid. *The Journal of Perinatal Education*, 15, 28-33. https://doi.org/10.1624/105812406x151394

Friedman, J. (2016). The long road to leptin. *The Journal of Clinical Investigation, 126*(12), 4727-4734. https://doi.org/10.1172/jci91578

Fryar, C., Carroll, M., & Afful, J. (2021). Prevalence of overweight, obesity, and severe obesity among adults aged 20 and over: United States, 1960–1962 through 2017–2018. *National Center for Health Statistics, Health E-Stats December 2020*, 1-7.

Fui, M. N., Dupuis, P., & Grossmann, M. (2014). Lowered testosterone in male obesity: mechanisms, morbidity and management. *Asian Journal of Andrology, 16*(2), 223–231. https://doi.org/10.4103/1008-682x.122365

Gabel, L., Macdonald, H., Nettlefold, L., & McKay, H. (2017). Physical activity, sedentary time, and bone strength from childhood to early adulthood: A mixed longitudinal HR-pQCT study. *Journal of Bone and Mineral Research, 32*(7), 1525–1536. https://doi.org/10.1002/jbmr.3115

Gail, A. (2018). Gut Microbiome. In L. Corrigan, K. Roberts, & E. Steiger (Eds.), Short Bowel Syndrome: Nutritional, Medical, and Surgical Management (45-54). Academic Press.

Gamboa, J., Garcia-Cazarin, M., & Andrade, F. (2011). Chronic hypoxia increases insulin-stimulated glucose uptake in mouse soleus muscle. American journal of physiology. *Regulatory, integrative and comparative physiology, 300*(1), 85-91. https://doi.org/10.1152/ajpregu.00078.2010

Gibson R., Makrides M., Smithers L., Voevodin M., & Sinclair A. (2009) The effect of dairy foods on CHD: a systematic review of prospective cohort studies. *British Journal of Nutrition,* 102, 1267–1275. https://doi.org/10.1017/s0007114509371664

Gibson, R., Muhlhausler, B., Makrides, M. (2011). Conversion of linoleic acid and alpha-linolenic acid to long-chain polyunsaturated fatty acids (LCPUFAs), with a focus on pregnancy, lactation and the first 2 years of life. *Maternal and Child Nutrition, 7*(2), 17-26. https://doi.org/10.1111/j.1740-8709.2011.00299.x

Giordano A, Smorlesi A, Frontini A, Barbatelli G, Cinti S. (2014). White, brown and pink adipocytes: the extraordinary plasticity of the adipose organ. *European Journal of Endocrinology*, 170, 159-171. https://doi.org/10.1530/endoabs.35.s27.1

Go, A. (2014). Heart disease and stroke statistics 2014 update. *Circulation, 129*(3), 101-106.

Goloubinoff, P., Sassi, A., Fauvet, B., Barducci, A., & De Los Rios, P. (2018). Chaperones convert the energy from ATP into the nonequilibrium stabilization of native proteins. *Nature Chemical Biology, 14*(4), 388–395. https://doi.org/10.1038/s41589-018-0013-8

Green, S. & Salkind, N. (2013). Correlation, regression, and discriminant analysis procedures. *In Using SPSS for Windows and Macintosh* (7th ed.) (pp.231-270). Upper Saddle River.

Grinko, V. (2022). *Human Atherosclerosis*. 123RF. https://www.123rf.com/photo_12186049_vienna-human-atherosclerosisthe-structure-of-a-veins-the-veins-in-the-manifestation-of-the-disease.html?downloaded=1.

Grinko, V. (2022). *Plaque formation in artery*. 123RF. https://www.123rf.com/photo_11943433_plaque-formation-in-artery.html?downloaded=1.

Gulick, S., Bralower, T., Ormo, J., Hall, B., Grice, K., Schaefer, B., & Wittmann, A. (2019). The first day of the Cenozoic. *Proceedings of the National Academy of Sciences of the United States*, 39, 19342-19351. https://doi.org/10.1073/pnas.1909479116

Gurven, M., Stieglitz, J., Trumble, B., Blackwell, A. D., Beheim, B., Davis, H., & Kaplan, H. (2017). The Tsimane Health and Life History Project: Integrating anthropology and biomedicine. *Evolutionary Anthropology, 26*(2), 54–73. https://doi.org/10.1002/evan.21515

Gurven M, Kaplan H. (2007). Longevity among hunter-gatherers: a cross-cultural examination. *Population and Development Review*, 33, 321–365. https://doi.org/10.1111/j.1728-4457.2007.00171.x

Hadza Stock Photos and Images (2022). 123RF. https://www.123rf.com/stock-photo/Hadza.html?sti=o50d3jfa9ndeyzyyb3|&oriSearch=Hadza.

Hardy, O., Czech, M., & Corvera, S. (2014). What causes the insulin resistance underlying obesity? *Current opinion in endocrinology, diabetes, and obesity, 19*(2), 81–87. https://doi.org/10.1097/med.0b013e3283514e13

Heydenreich, J., Kayser, B., Schutz, Y., & Melzer, K. (2017). Total energy expenditure, energy intake, and body composition in endurance athletes across the training season: A systematic review. *Sports medicine, 3*(1), 1-24. https://doi.org/10.1186/s40798-017-0076-1

Horakova, D., Stepanek, L., Janout, V., Janoutová, J., Pastucha, D., Kollarova, H., Petrakova, A., Stepanek, L., Husar, R., & Martinik, K. (2019). Optimal homeostasis model assessment of insulin resistance (HOMA-IR) cut-offs: a cross-sectional study in the Czech population. *Medicina, 55*(5), 150-158. https://doi.org/10.3390/medicina55050158

Idris, C., Sundram, K., & Razis, A. (2018). Effect of Consumption Heated Oils with or without Dietary Cholesterol on the Development of Atherosclerosis. *Nutrients, 10*(10), 1-11. https://doi.org/10.3390/nu10101527

Indumathy, J., Pal, G., Pal, P., Ananthanarayanan, P., Parija, S., Balachander, J., & Dutta, T. (2018). Contribution of insulin resistance to decreased baroreceptor sensitivity & cardiometabolic risks in pre-obesity & obesity. *The Indian Journal of Medical Research, 148*(2), 151–158. https://doi.org/10.4103/ijmr.ijmr_1751_16

Johnson, G. & Fritsche, K. (2012). Effect of dietary linoleic acid on markers of inflammation in healthy persons: A systematic review of randomized controlled trials. *Journal of the Academy of Nutrition and Dietetics, 112*(7), 1029-1041. https://doi.org/10.1016/j.jand.2012.03.029

Jornayvaz, F. R., & Shulman, G. I. (2010). Regulation of mitochondrial biogenesis. *Essays in biochemistry*, 47, 69-84. https://doi.org/10.1042/bse0470069

Kaplan, H., Thompson, R., Trumble, B., Wann, L., Allam, A., Beheim, B., & Thomas, G. (2017). Coronary atherosclerosis in indigenous South American Tsimane: a cross-sectional cohort study. *The Lancet, 389*(10080), 1730–1739. https://doi.org/10.1016/s0140-6736(17)30752-3

Katoh, S., Beyene, Y., Itaya, T., Hyodo, H., Hyodo, M., Yagi, K., & Suwa, G. (2016). New geological and paleontological age constraint for the gorilla-human lineage split. *Nature, 530*(7589), 215–218. https://doi.org/10.1038/nature16510

Kearns, C., Schmidt, L. & Glanz, S. (2016). Sugar Industry and Coronary Heart Disease Research: A Historical Analysis of Internal Industry Documents. *JAMA Internal Medicine, 176*(11), 1680-1685. https://doi.org/10.1001/jamainternmed.2016.5394

Keys, A. (1971). Sucrose in the diet and coronary heart disease. *Atherosclerosis, 14*(2), 193-202. https://doi.org/10.1016/0021-9150(71)90049-9

Kaplan, H., Thompson, R., Trumble, B. C., Wann, L., Allam, A. H., Beheim, B., & Thomas, G. (2017). Coronary atherosclerosis in indigenous South American Tsimane: a cross-sectional cohort study. *The Lancet, 389*(10080), 1730–1739. https://doi.org/10.1016/s0140-6736(17)30752-3

Kiddie, J. (2018). *Evidence that Refined Carbs with Vegetable Oils Cause Weight Gain*. The Low Carb Healthy Fat Dietian. Retreived from https://www.lchf-rd.com/2018/06/26/evidence-that-refined-carbohydrate-with-vegetable-oils-cause-weight-gain/.

Kokubo, Y., Higashiyama, A., Watanabe, M., & Miyamoto, Y. (2019). A comprehensive policy for reducing sugar beverages for healthy life extension. *Environmental Health and Preventive Medicine, 24*(1), 1-4. https://doi.org/10.1186/s12199-019-0767-y

Kumar, V., Abbas, A., Fausto, N., & Aster, J. (2017). *Pathological basis of disease* (10th ed.). Saunders Elsevier.

La Berge, A. (2008). How the Ideology of Low Fat Conquered America. *Journal of the History of Medicine and Allied Science, 63*(2), 139-177. https://doi.org/10.1093/jhmas/jrn001

Laughlin, M. (2014). Normal Roles for Dietary Fructose in Carbohydrate Metabolism. *Nutrients*, 8, 3117-3129. https://doi.org/10.3390/nu6083117

Li, William (2019). *Eat to Beat Disease*. Grand Central Publishing.

Li, Q., Youn, J. Y., & Cai, H. (2015). Mechanisms and consequences of endothelial nitric oxide synthase dysfunction in hypertension. *Journal of Hypertension, 33*(6), 1128–1136. https://doi.org/10.1097/hjh.0000000000000587

Lo, Y., Chiang, S., Lin, C., Liu, H., & Chiang, L. (2020). Effects of individualized aerobic exercise training on physical activity and health-related physical fitness among middle-aged and older adults with multimorbidity: A randomized controlled trial. *International Journal of Environmental Research and Public Health, 18*(1), 1-16. https://doi.org/10.3390/ijerph18010101

Lovegrove, A., Edwards, C., De Noni, I., Patel, H., El, S., Grassby, T., & Shewry, P. (2017). Role of polysaccharides in food, digestion, and health. *Critical Reviews in Food Science and Nutrition, 57*(2), 237–253. https://doi.org/10.1080/10408398.2014.939263

Lu, C., Wang, D., Feng, Y., Feng, L., & Li, Z. (2021). miR-720 regulates insulin secretion by targeting rab35. *BioMed Research International*, 1–9. https://doi.org/10.1155/2021/6662612

Lustig, R. (2012). *Fat Chance*. Avery.

Lyon, P. (2022, March 25). *Macronutrients and the Ketogenic Diet.* Ruled Me. https://www.ruled.me/macronutrients-and-ketogenic-diet.

MacLean, P., Higgins, J., Giles, E., Sherk, V., & Jackman, M. (2015). The role for adipose tissue in weight regain after weight loss. *Obesity Reviews*, 16, 45–54. https://doi.org/10.1111/obr.12255

Martin, M., Lassek, W., & Gaulin S. (2012). Fatty acid composition in the mature milk of Bolivian forager-horticulturalists: controlled comparisons with a US sample. *Maternal & Child Nutrition, 8*(3), 404-418. https://doi.org/10.1111/j.1740-8709.2012.00412.x

Martini, F. (2018). *Fundamentals of Anatomy and Physiology* (11th ed.). Pearson.

Matthews, D., Hosker, J., Rudenski, A., Naylor,B., Treacher, D. & Turner, R. (1985). Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia, 28*(7), 412-419. https://doi.org/10.1007/bf00280883

McGandy, R., Hegsted, D., Stare, F. (1967). Dietary fats, carbohydrates and atherosclerotic vascular disease. *New England Journal of Medicine, 277*(4), 186-192. https://doi.org/10.1056/nejm196707272770405

Moore, J., Chaudhary, N., & Akinyemiju, T. (2017). Metabolic syndrome prevalence by race/ethnicity and sex in the United States, National Health and Nutrition Examination Survey, 1988–2012. *Preventing Chronic Disease, 14*(24), 1-16. https://doi.org/10.5888/pcd14.160287

Murphy, S., Xu, J., Kochane, K., Curtin, S., & Arias E. (2017). Deaths: Final data for 2015. *National Vital Statistics Reports, 66*(6), 1-75. https://doi.org/10.15620/cdc:106058

Nair, P. (2013). Brown and Goldstein: The Cholesterol Chronicles. *Proceedings of the National Academy of Sciences of the United States of America, 10*(37), 14829–14832. https://doi.org/10.1073/pnas.1315180110

National Center for Health Statistics (2018). Prevalence of Obesity Among Adults and Youth: United States, 2015–2016. *NCHS Data Brief*, 288, 1-8.

Nur Zati Iwani, A., Jalaludin, M., Wan Mohd Zin, R., Fuziah, M., Hong, J., Abqariyah, Y., Mokhtar, A., & Wan Mohamud, W. (2019). TG : HDL-C Ratio Is a Good Marker to Identify Children Affected by Obesity with Increased Cardiometabolic Risk and Insulin Resistance. *International Journal of Endocrinology*, 2019, 1-9. https://doi.org/10.1155/2019/8586167

DiNicolantonio, J., & O'Keefe, J. (2018). Omega-6 vegetable oils as a driver of coronary heart disease: the oxidized linoleic acid hypothesis. *Open Heart, 5*(2), 1-6. https://doi.org/10.1136/openhrt-2018-000898

Ogundipe, E., Tusor, N., Wang, Y., Johnson, M. R., Edwards, A., & Crawford, M. (2018). Randomized controlled trial of brain specific fatty acid supplementation in pregnant women increases brain volumes on MRI scans of their newborn infants. *Prostaglandins, Leukotrienes, And Essential Fatty Acids*, 138, 6-13. https://doi.org/10.1016/j.plefa.2018.09.001

Oppenheimer, G. M., & Benrubi, I. D. (2014). McGovern's Senate Select Committee on Nutrition and Human Needs versus the meat industry on the diet-heart question (1976-1977). *American Journal of Public Health, 104*(1), 59-69. https://doi.org/10.2105/ajph.2013.301464

Page, I. (1961). Dietary Fat and Its Relation to Heart Attacks and Strokes. *Circulation* 23, 133-136. https://doi.org/10.1161/01.cir.23.1.133

Pal, M., Khan, J., Kumar, R., Surolia, A., & Gupta, S. (2019). Testosterone supplementation improves insulin responsiveness in HFD fed male T2DM mice and potentiates insulin signaling in the skeletal muscle and C2C12 myocyte cell line. PloS one, 14(11), 1-17. https://doi.org/10.1371/journal.pone.0224162

Patton, D. (2011). *Essentials of Anatomy and Physiology*. Mosby.

Popkin, B. & Hawkes, Corinna. (2016). Sweetening of the global diet, particularly beverages: patterns, trends, and policy responses. *The Lancet Diabetes & Endocrinology, 4*(2), 174-186. https://doi.org/10.1016/s2213-8587(15)00419-2

Pontzer, H. (2021). *Burn*. Avery: New York, New York.

Pontzer, H., Durazo-Arvizu, R., Dugas, L., Plange-Rhule, J., Bovet, P., Forrester, T., & Luke, A. (2016). Constrained Total Energy Expenditure and Metabolic Adaptation to Physical Activity in Adult Humans. *Current Biology, 26*(3), 410–417. https://doi.org/10.1016/j.cub.2015.12.046

Pontzer, H., Wood, B., & Raichlen, D. (2018). Hunter-gatherers as models in public health. *Obesity Reviews, 19*(1), 24-35. https://doi.org/10.1111/obr.12785

Puchalska, P., & Crawford, P. (2017). Multi-dimensional Roles of Ketone Bodies in Fuel Metabolism, Signaling, and Therapeutics. *Cell Metabolism, 25*(2), 262–284. https://doi.org/10.1016/j.cmet.2016.12.022

Quispe, R., Manalac, R., Faridi, K., Blaha, M., Toth, P., Kulkarni, K., Nasir, K., Virani, S., Banach, M., Blumenthal, R. S., Martin, S., & Jones, S. (2015). Relationship of the triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) ratio to the remainder of the lipid profile: The Very Large Database of Lipids-4 (VLDL-4) study. *Atherosclerosis, 242*(1), 243–250. https://doi.org/10.1016/j.atherosclerosis.2015.06.057

Raghupathi, W. & Raghupathi, V. (2018). An empirical study of chronic diseases in the United States: A visual analytics approach to public health. *International Journal of Environmental Research and Public Health, 15*(3), 431-455. https://doi.org/10.3390/ijerph15030431

Ramji, D. (2018). Polyunsaturated Fatty Acids and Atherosclerosis: Insights from Pre Clinical Studies. *European of Lipid Science and Technology, 121*(1), 1-7. https://doi.org/10.1002/ejlt.201800029

Ren, X., Ren, L., Wei, Q., Shao, H., Chen, L., & Liu, N. (2017). Advanced glycation end-products decreases expression of endothelial nitric oxide synthase through oxidative stress in human coronary artery endothelial cells. *Cardiovascular Diabetology*, 16(1), 1-12. https://doi.org/10.1186/s12933-017-0531-9

Reiss, A., Casertano, S., Yuan, W., Lucas, M., & Scolnic, D. (2019). Large Magellanic Cloud Cepheid Standards Provide a 1% Foundation for the Determination of the Hubble Constant and Stronger Evidence for Physics Beyond ΛCDM. *The Astrophysical Journal, 1*(876), 1-25. https://doi.org/10.3847/1538-4357/ab1422

Rito, T., Vieira, D., Silva, M., Conde-Sousa, E., Pereira, L., Mellars, P., & Soares, P. (2019). A dispersal of Homo sapiens from southern to eastern Africa immediately preceded the out-of-Africa migration. *Scientific Reports, 9*(1), 1-10. https://doi.org/10.1038/s41598-019-41176-3

Russell, F. & Bürgin-Maunder, C. (2012). Distinguishing health benefits of eicosapentaenoic and docosahexaenoic acids. *Marine drugs, 10*(11), 2535–2559. https://doi.org/10.3390/md10112535

Sanchez-Garcia, A., Rodríguez-Gutierrez, R., Mancillas-Adame, L., Gonzalez-Nava, V., Diaz Gonzalez-Colmenero, A., Solis, R., Alvarez-Villalobos, N., & Gonzalez-Gonzalez, J. (2020). Diagnostic accuracy of the triglyceride and glucose index for insulin Resistance: a systematic review. *International Journal of Endocrinology*, 2020, 1–7. https://doi.org/10.1155/2020/4678526

Scheen, A. & Paquot, N. (2013). Metformin revisited: A critical review of the benefit-risk balance in at-risk patients with type 2 diabetes. *Diabetes & Metabolism, 39*(3), 179-190. https://doi.org/10.1016/j.diabet.2013.02.006

Schraer, C., Risica, P., Ebbesson, S., Go, O., Howard, B., & Mayer, A. (1999). Low fasting insulin levels in Eskimos compared to American Indians: are Eskimos less insulin resistant? *International Journal of Circumpolar Health*, 58, 272–280.

Shah, N., Lloyd-Jones, D., O'Flaherty, M. (2019). Trends in cardiometabolic mortality in the United States, 1999-2017. *JAMA, 322*(8), 780-782. https://doi.org/10.1001/jama.2019.9161

Shai, I., Schwarzfuchs, D., Henkin, Y., Shahar, D. R., Witkow, S., Greenberg, I., Stampfer, M. J. (2008). Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *The New England Journal of Medicine, 359*(3), 229–241. https://doi.org/10.1056/nejmoa0708681

Shanahan, C. & Shanahan, L. (2016). *Deep Nutrition*. Flatiron Books.

Simopoulos, A. (2016). An increase in the omega-6/omega-3 fatty acid ratio increases the risk for obesity. *Nutrients, 8*(3), 128-145. https://doi.org/10.3390/nu8030128

Simopoulos, A. (2013). Dietary Omega-3 Fatty Acid Deficiency and High Fructose Intake in the Development of Metabolic Syndrome, Brain Metabolic Abnormalities, and Non-Alcoholic Fatty Liver Disease. *Nutrients*, 5, 2901-2923. https://doi.org/10.3390/nu5082901

Simopoulos, A. (2002). The importance of the ratio of omega-6/omega-3 essential fatty acids. *Biomedicine Pharmacotherapy, 56*(8), 365-79. https://doi.org/10.1016/s0753-3322(02)00253-6

Singh, A., Singh, S., Singh, N., Agrawal, N., & Gopal, K. (2011). Obesity and dyslipidemia. International *Journal of Biological & Medical Research 2*(3), 824-828.

Stanhope, M. & Lancaster, J. (1996). *Community Health Nursing. Promoting Health of Aggregates, Families and Individuals* (4th ed.). Mosby.

Sultani, R., Tong, D., Peverell, M., Lee, Y., Baradi, A. & Wilson, A. (2020). Elevated triglycerides to high-density lipoprotein cholesterol (TH:HDL-C) ratio predicts long-term mortality in high-risk patients. *Heart, Lung, and Circulation, 29*(3), 414-421. https://doi.org/10.1016/j.hlc.2019.03.019

Tabas, I., Garcia-Cardena, G., & Owens, G. (2015). Recent insights into the cellular biology of atherosclerosis. *Journal of Cell Biology*, *209*(1), 13–22. https://doi.org/10.1083/jcb.201412052

Tampakakis, E., Tabit, C. E., Holbrook,M., Linder, E. A., Berk, B. D., Frame, A. (2016). Intravenous lipid infusion induces endoplasmic reticulum stress in endothelial cells and blood mononuclear cells of healthy adults. *Journal of the American Heart Association*, *55*(1), 1-9. https://doi.org/10.1161/jaha.115.002574

Taubes, G. (2001). The soft science of dietary fat. *Science*, 291, 2536-2545.

Timothy, N. & Johann, W. (2017). Evidence that supports the prescription of low-carbohydrate high-fat diets: a narrative review. *British Journal of Sports Medicine*, *51*(2), 133. https://doi.org/10.1136/bjsports-2016-096491

Travison, T., Vesper, H., Orwoll, E., Wu, F., Kaufman, J., Wang, Y., Lapauw, B., Fiers, T., Matsumoto, A., & Bhasin, S. (2017). Harmonized Reference Ranges for Circulating Testosterone Levels in Men of Four Cohort Studies in the United States and Europe. *Journal of Clinical Endocrinology & Metabolism, 102*(4), 1161–1173. https://doi.org/10.1210/jc.2016-2935

Tyson, N., & Frank, M. (2018). Childhood and adolescent obesity definitions as related to BMI, evaluation and management options. *Best Practice & Research Clinical Obstetrics & Gynaecology,* 48, 158–164. https://doi.org/10.1016/j.bpobgyn.2017.06.003

United States Department of Agriculture (2019). Dietary Guidelines for Americans. https://www.fns.usda.gov/cnpp/dietary-guidelines-americans.

United States Department of Agriculture (2019). Food availability (per capita) data system. Loss-adjusted food availability sugar and sweeteners. https://www.ers.usda.gov/data-products/food-availability-per-capita-data-system/

United States Department of Agriculture (2019). Food availability (per capita) data system. Loss-adjusted food availability fats and oils. https://www.ers.usda.gov/data-products/food-availability-per-capita-data-system/

van den Heuvel, J., Eggels, L., van Rozen, A., Luijendijk, M., Fliers, E., Kalsbeek, & Fleur, S. (2014). Neuropeptide Y and leptin sensitivity is dependent on diet composition. *Journal of Neuroendocrinology, 26*(6), 377–385. https://doi.org/10.1111/jne.12155

Wells, J., Nesse, R., Sear, R., Johnstone, R., & Stearns, S. (2017). Evolutionary public health: introducing the concept. *The Lancet, 390*(10093), 500-509. https://doi.org/10.1016/s0140-6736(17)30572-x

Vilaca, K., Alves, N., Carneiro, J., Ferriolli, E., Lima, N., & Moriguti, J. (2013). Body composition, muscle strength and quality of active elderly women according to the distance covered in the 6-minute walk test. *Nihon Rinsho, 17*(3), 289-296 https://doi.org/10.1590/s1413-35552012005000093

Vinet, A., Obert, P., Dutheil, F., Diagne, L., Chapier, R., Lesourd, B. (2015). Impact of a lifestyle program on vascular insulin resistance in metabolic syndrome subjects: The RESOLVE study. *Journal of Clinical Endocrinology and Metabolism, 100*(2), 442-450. https://doi.org/10.1210/jc.2014-2704

Wu, L. & Parhofer, K. (2014). Diabetic dyslipidemia, *Metabolism, 63*(12), 1469-1479. https://doi.org/10.1016/j.metabol.2014.08.010

Yang, X. (2014). Glucose homeostasis and the pathogenesis of diabetes mellitus. *Progress in Molecular Biology and Translational Science*, 121, 133-163. https://doi.org/10.1016/c2013-0-13234-5

Yenipinar, A. (2019). Determining sample size in logistic regression with G-Power. *Black Sea Journal of Engineering and Science, 2*(1), 16-22.

Youssef, S., Nelder, M., & Sun, G. (2021). The Association of Upper Body Obesity with Insulin Resistance in the Newfoundland Population. *International Journal of Environmental Research and Public Health, 18*(11), 5858-5873. https://doi.org/10.3390/ijerph18115858

Yudkin, J., Szanto, S., Kakkar, V., Yudkin, J., & Szanto, S. (1969). Sugar intake, serum insulin and platelet adhesiveness in men with and without peripheral vascular disease. *Postgraduate Medical Journal, 45*(527), 608-611. https://doi.org/10.1136/pgmj.45.527.608

Yudkin, J. (1972). *Pure, white, and deadly*. Penguin.

Zhang, X. & Lerman, L. (2016). The metabolic syndrome and chronic kidney disease. *Translational Research*, 183, 14-25. https://doi.org/10.1016/j.trsl.2016.12.004

Zimdars, M. (2016). Fat acceptance TV?: Rethinking reality television with TLC's big sexy and the carnivalesque. *Popular Communication, 13*(3), 232-246. https://doi.org/10.1080/15405702.2015.1048344