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A Trend Analysis of Prevalence and Association Between Cardiovascular Disease Risk and Key Anthropometrics: 2007-2016 NHANES Data

Ato Tetteh

ABSTRACT

A Trend Analysis of Prevalence and Association Between Cardiovascular Disease Risk and Key Anthropometrics: 2007-2016 NHANES Data

by

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Introduction:

There is the need for consistent research on cardiovascular diseases and the associated risks to provide more information towards prevention, control, and management.

Aim:

This study estimated linear trends of cardiovascular disease risks and its association with selected anthropometric measurements.

Methods:

Five bi-annual data from 2007 to 2016 was obtained from the National Health and Nutrition Examination survey. Analysis was performed on all participants aged between 20 and 80 years (n = 29,201). The outcome variable was cardiovascular disease risk (CVDRisk), estimated as the ratio of total cholesterol (TCHOL) to high-density lipoprotein (HDL). Analyses of linear trends were performed for all lipid profiles and selected anthropometric variables. The multiple linear regression analysis procedure was used to estimate anthropometric variables that best predict CVDRisk.

Results:

The mean CVDRisk for the studied population was 4.0 (95% CI: 3.8-4.2). There was a decrease of 0.05 in mean CVDRisk bi-annually from 4.1 in 2007-2008 to 3.9 in 2015-2016 (t = -3.27, p =

0.0467). The percentage with desirable CVDRisk decreased by 0.07 bi-annually from 0.42% in 2007-2008 to 0.1% in 2015-2016 ($p = 0.0689$). Borderline risk increased by 0.8 bi-annually from 90.7% in 2007-2008 to 93.8% in 2015-2016 ($p = 0.1176$). High CVDRisk decreased by 0.7 from 8.9% in 2007-2008 to 6.2% in 2015-2016 ($t = -1.95$, $p = 0.1464$). CVDRisk was consistently higher in males than females for all the cohorts ($p < 0.0001$). The risk was high among the 30-69 years age group but declined after age 70. Overall, waist circumference (WC), weight (WT), and the WC*WT interaction term, adjusted for age, gender and race/ethnicity significantly helped to predict CVDRisk ($p < 0.0001$).

Discussion:

Majority of the studied population had either borderline or high risk for cardiovascular diseases based on the TCHOL/HDL ratio. Thus suggesting, the need to intensify existing primary prevention efforts to minimize risk and avert cardiovascular disease progression.

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by

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APPROVAL PAGE

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CHAPTER I

1.0 INTRODUCTION

Cardiovascular disease (CVD) refers to a complex of abnormalities of the heart and circulatory system. These include coronary heart/artery disease, stroke, hypertension, heart failure, and acute coronary syndrome, which may occur alone, or in varying combinations (Harris, 2019). Together, these conditions contribute to 17.9 million deaths, representing 31% of global deaths annually (WHO, 2017). The underlying cause is the long-term development of plaques in vessels, atherosclerosis (Francula-Zaninovic and Nola, 2018). Recent estimates suggest that CVD causes approximately 18 million deaths globally, with 35.6 million surviving with diverse forms of disability (Kyu *et al*., 2018). Increasing evidence in the United States shows that the total number of individuals with at least one CVD is more than 85 million (Members *et al*., 2016). With this, CVDs together account for the highest number of deaths, over 900,000 deaths annually, in the United States (Mokdad *et al*., 2019; Johnson *et al*., 2014).

Although morbidity due to CVDs persist, advancement in diagnosis and management has led to a steady decline in mortality in the 20th century in the United States (Benjamin *et al*., 2017; Ford *et al*., 2007; Wang *et al*., 2013). Several methods exist for predicting the chance of an individual developing any of the CVDs. Age and sex disparities occur in the United States, with males developing CVDs 10 years earlier than females, while the risk increases with age (Mozaffarian *et al*., 2015). Life-time risk declines after age 70 because lifestyle risk factors either decrease or remain unchanged than younger individuals (Lloyd-Jones *et al*., 2006). CVD risk varies by race/ethnicity, with prevalence being more than twice as high in American Indian/Alaskan Native adults (9.3%) than Asian adults (3.7%). Prevalence is, however, not

significantly different among Hispanic (5.1%), African American (5.4%), and white adults (5.6%) (CDC, 2015).

Cardiovascular disease risk is directly related to an individual's modifiable risk factor profiles: smoking, physical inactivity, poor diet, high blood pressure, diabetes dyslipidemia, obesity, and non-modifiable risk factors, sex, age, and race/ethnicity (Reiner et al., 2011). Specifically, it represents the probability of an individual experiencing a CVD event, representing a combined effect of all existing risks. The magnitude of the risk is dependent on the combined effect of co-existing factors. The single most common and important risk factor is dyslipidemia (elevated cholesterol indexes), directly associated with diet and physical activity.

These measurements, total cholesterol (TCHOL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TRIG), are independent predictors of CVD risk. Consistent monitoring of lipid levels is a vital measure, which can help influence the treatment and control of CVDs. Established from both past and recent studies on cardiovascular disease risk is the contribution of the ratio of total cholesterol to high-density lipoprotein (CVDRisk = TCHOL/HDL). This ratio is the most useful and consistently applied determination of cardiovascular disease risk (Linn *et al*., 1991), especially because associated pathology develops from diet and throughout life. Estimated CVDRisks for individuals in a population are deemed central in making medical and interventional decisions. These may include at least one of the following; when to prescribe medications, dietary adjustments, or a physical activity intervention to implement (WHO, 2002). The CVDRisk is categorized (low, moderate, high, very high) to help physicians approximate severity and determine when a CVD could manifest (Piepoli *et al*., 2016). Trends in these categories provide a useful gauge for diagnosis and monitoring of individuals who may have increased risk for developing CVDs. This estimate is useful in projecting burden and

mortality to identify where prevention and management progress has stalled. Thus, there is the need to establish a long-term retrospective analysis of available data. This study evaluated a ten-year National Health and Nutrition Examination Survey (NHANES) trend of CVDRisk (estimated as TCHOL/HDL) and its association with selected anthropometric measurements.

CHAPTER II

2.0 LITERATURE REVIEW

2.1 Cardiovascular disease in the US

Cardiovascular diseases (CVD) are conditions that occur due to narrowed or blocked blood vessels. Generally, fats deposit on the arterial inner walls, forming the thrombus (clot), which blocks the vessels, preventing blood from reaching the heart or brain (Freeman *et al*., 2016). CVD may occur as heart disease, stroke, hypertension, congestive heart failure, hardening of the arteries, other circulatory system diseases, or various combinations. Global mortality will increase from 17.3 million annually to 23.6 million in both genders by 2030 (Mozaffarian *et al*., 2015). Pathologies associated with CVDs are known to affect approximately 84 million adults and account for over 40% of mortality in the United States (Go *et al*., 2014). It is known that about 50% of people with CVD in the US are less than 60 years old and that the risk is higher in males across all age groups (Lloyd-Jones *et al*., 2006; Wilkins *et al*., 2012). According to the American Heart Association report of 2014, CVD causes the death of at least one affected individual every 36 seconds in the US. Health expenditures (direct cost) and lost productivity (indirect cost) exceed US$320.1 billion (Virani *et al*., 2012; Mozaffarian *et al*., 2015). Prevention depends on four health behavior modifications (no smoking, healthy diet, regular physical activity, healthy body mass index) and three health factors (desirable total cholesterol, blood pressure, and fasting blood glucose) (AHA, 2016).

2.2 Risk factors associated with CVDs

Risk factors for CVDs, often categorized into lifestyles (Tobacco use, poor diet, physical inactivity), cardio-metabolic (dyslipidemia, high blood pressure, elevated blood glucose, elevated C-reactive protein), environmental/psychosocial/physical, genetic, and several other non-specific contributing factors (Harris, 2019). These factors may have a direct association (causation) or may act as an indirect predictor or intermediate for only one or multiple diseases (Stampfer *et al*., 2004). Lifestyle and metabolic risk factors are modifiable, compared to unmodifiable factors such as age, sex, family history of CVDs, and genetic factors (Mendis *et al*., 2011).

Lifestyle-related factors such as insufficient exercise, alcohol abuse, poor nutrition (especially with inadequate fruits and vegetables), and smoking play established key roles in increasing the risk of CVDs (Lopez *et al*., 2006; O'donnell *et al*., 2010). Regarding exercise, both moderate and high intensity are protective against CVDs (Esteghamati *et al*., 2012). Although alcohol abuse is detrimental to CVDs, light-to-moderate consumption is known to be linearly associated with a reduced risk of acute myocardial infarction (Gémes *et al*., 2016). Poor nutrition, specifically high-fat and high sodium chloride, less/no roughages, and smoking contribute immensely to the risk and outcomes of CVDs (Yusuf *et al*., 2014).

Factors such as obesity, diabetes, high cholesterol, and high blood pressure constitute the major risk factors (Stoner *et al*., 2012; Yusuf *et al*., 2004). The leading risk factor among these is hypertension. Obesity is known to elevate the risk of CVDs and their risks such as hypertension and elevated cholesterol (Lavie *et al*., 2009). Type II diabetes also elevates CVDs, and about 50% of deaths in people with diabetes occur because of heart disease (Harris, 2019). Elevated low-density lipoprotein is associated with CVDs (Wong *et al*., 1991).

In addition to lifestyle and metabolic factors, there are environmental, psychosocial, and physical factors that negatively impact CVDs. The worsening air pollution in various regions of the world potentially aggravates CVDs and could increase mortality which results from ischemic heart disease and stroke (Cosselman *et al*., 2015). One reason for the lack of exercise is space unavailability (Humpel *et al*., 2004) for walking, running, and cycling. Of concern is the lack of standard dietary regulations on high sodium chloride foods, which contributes to a large extent to plaque formation in blood vessels (Glanz *et al*., 2005). Although data from low-income countries are scanty and remain inconclusive, populations in low socio-economic settings tend to suffer most from CVD complications than those at the higher level (de Mestral and Stringhini, 2017). It presupposes that some CVDs are associated with economic conditions and not by individual choices. Other factors referred to as psychosocial risk factors include unsuitable work environment, neuroticism, that, is an individual's tendency toward anxiety, depression, self-doubt, and other negative feelings, and depression could potentially aggravate the risk and severity of CVDs (Theorell and Karasek, 1996; Jokela *et al*., 2014; Lichtman *et al*., 2014).

Non-modifiable risk factors, that is, age, sex, family history, and genetic differences present a great challenge in the management of CVDs. Generally, CVD events worsen with age in both genders, even though the risk reduces after age 70. Until recently, females experienced fewer CVD events later in life compared to males. However, recent evidence shows an increased prevalence of myocardial infarction and inflammatory heart disease among females in midlife compared to males of similar age (Vaidya *et al*., 2011). Being a first-generation offspring and having a sibling with a history of coronary heart disease increases the risk and the incidence and progression of subclinical atherosclerosis (Nasir *et al*., 2007; Pandey *et al*., 2014).

2.3 Hypertension – high blood pressure

According to the American Heart Association, systolic pressure of < 120 mmHg and diastolic of < 80 mmHg are considered normal (Mozaffarian *et al*., 2015). Raised values are regarded as vital risk factors for CVD events, including coronary heart disease, mortality, and disability. The world health organization estimates that 13% of deaths globally and 3.7% of DALYs result from high blood pressure (WHO, 2009). About 31% of the world's population who were more than 25 years old (approximately 1.4 million adults) are diagnosed with hypertension (Forouzanfar *et al*., 2017), This global prevalence is similar to that in the US population, which is 31.9% (Muntner *et al*., 2018). A continental level case-control study, the INTERHEART Study, showed that hypertensives and those with a history of hypertension have an increased risk of heart attack events juxtaposed with those without it (Yusuf *et al*., 2004). Elevated systolic and diastolic readings are known to trigger the incidence of CVDs, including stroke, coronary death, angina, heart failure, and peripheral arterial disease (Rapsomaniki *et al*., 2014). Cardiovascular disease risk at age 30 has been estimated at 63.3% for individuals with hypertension, compared to 46.1% in non-hypertensive individuals (Rapsomaniki *et al*., 2014). To minimize CVD risk among individuals with high blood pressure, they must resort to lifestyle modification, early and aggressive blood pressure lowering treatments by choosing the appropriate drugs and promoting patient adherence to the therapy (Antonakoudis *et al*., 2007).

2.4 Type 2 diabetes - Adult-onset

Another important independent CVD risk factor is Type 2 diabetes (Grundy *et al*., 1999). Globally, there were approximately 451 million people between the ages of 18 and 99 known to

be living with diabetes in 2017. These figures will reach a projected value of 693 million people living with diabetes by 2045 (Cho *et al*., 2018). The 2018 crude estimates for the United States indicate that 34.2 million people of all ages had diabetes, with prevalence increasing with age (CDC, 2020). Like other CVD risks, factors that contribute to developing diabetes include obesity, unhealthy diet, sedentary lifestyle, family history of diabetes, race/ethnicity, advancement in age, and socio-economic factors. People with both diagnosed and undiagnosed diabetes are known to have a higher propensity for developing CVD episodes such as heart attack, stroke, peripheral artery disease, angina, and heart failure (Aguiree *et al*., 2013). The risk of suffering a heart attack and stroke-related deaths in people with diabetes is higher than those without diabetes (Yusuf *et al*., 2004). Evidence from clinical trials points out that reducing or maintaining blood glucose at desirable levels contributes significantly to minimizing CVD events such as myocardial infarction, stroke, or death from CVDs (Mannucci *et al*., 2013).

2.5 Dyslipidemia

An increase or decrease in the individual components of the blood lipid profile, namely, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides, is known to directly impact CVD events (Fruchart *et al*., 2004; Casterlli, 1996). The influence of hyperlipidemia as a risk factor for CVD is well known, and its measurement is essential for prevention and management. The disproportion of cholesterol levels, especially LDL and HDL, can elevate CVD events such as myocardial infarction and stroke. High triglycerides also contribute to hyperlipidemia. Triglycerides, together with cholesterol, can catalyze the build of plaques in the vessels to initiate CVDs (Cooney *et al*., 2009). Hypercholesterolemia is prevalent in high-income countries compared to low-income countries (Farzadfar *et al*., 2011). Past studies

in the United States have established that approximately 53% of adults have high LDL cholesterol levels (CDC, 2011), while 31 million have high total cholesterol levels (Virani *et al*., 2020). Management includes reducing saturated trans fats, increasing physical activity, avoiding smoking, and reducing body mass index. Secondary measures include correcting biliary obstructions, kidney complications, type 2 diabetes, hypertension, hypothyroidism, and early identification of genetic risks (Virani *et al*., 2020). There is an inconclusive association between hyperlipidemia, race, and gender. However, African Americans are known to have increased incidence (Ogden *et al*., 2014). Detection in young and older adults is important for early risk assessment and management.

2.6 Lipid profile and CVD risk assessment

Achieving primary prevention of CVDs requires the estimation of the risk everyone in a population has. Although the process of plaque formation in vessels is multifactorial, detecting abnormalities in the complete lipid profile test remains the most important measure to assess the potential of developing CVDs. These abnormalities represent roughly 50% of the population-attributable risk of developing a CVD (Yusuf *et al*., 2004). Literature in the past has considered all measurements in the lipid profile, especially LDL, as independent predictors of CVDs. However, this is considered sub-optimal (Superko and King, 2008) for intermediate-risk individuals (Arad *et al*., 2005). This is because many patients often experience CVDs even with sufficiently controlled LDL values since there are other risks that require management (Superko and King, 2008).

Atherogenic or Castelli index, total cholesterol/HDL, and LDL/HDL ratio is known to increase the lipid profile test's analytical capacity. Although these ratios are less often used, they

offer more useful evidence of CVD risk, which is otherwise difficult to assess by routine analysis. Elevated total cholesterol, which is a result of increased LDL, is a known atherogenic lipid marker. Reduced HDL concentration correlates with many risk factors, such as the components of metabolic syndrome. Populations with high ratios have higher CVD risk due to the imbalance between cholesterol-carrying atherogenic and protective proteins, HDL apolipoprotein (apo A-1). Apolipoprotein A-1, which is the main component of HDL is involved in the reverse transport of cholesterol through the macrophage ATP-binding cassette transporter ABCA1 (Nevab *et al*., 2011) This imbalance results from the rise in the HDL's atherogenic component, which reduces the anti-atherosclerotic trait of HDL (oxidation of apo A-1), or both. (Nevab *et al*., 2011; Criqui and Golomb, 1998). Three large observational studies, the Framingham Study (Castelli *et al*., 1986), the Lipid Research Clinics Prevalence Cohort (LRCP) (Grover *et al*., 1994), and the Prospective Cardiovascular Münster (PROCAM) (Assmann *et al*., 1988), emphasizes that the atherogenic index, total cholesterol/HDL, is a strong predictor of coronary risk than when lipid profile measures are used independently. Additionally, in the Quebec Cardiovascular Study, the researchers found the LDL/HDL ratio calculation to underrate ischemic heart disease when equated with the quality of estimation realized using the total cholesterol/HDL ratio (Lemieux *et al*., 2001).

2.7 Anthropometric measurements and CVD

Recently established data shows that over two billion adults globally are either overweight or obese (Hawkes and Fanzo, 2017), and these have unhealthy consequences in humans. Existing literature indicates a rapid rise in the prevalence of obesity in developing economies due to rapid urbanization and the adoption of westernized diets (Harris, 2019; Ford *et al*., 2017). In the United

States, obesity is considered an epidemic, where about a third of the entire population is obese. It is expected that this may increase to about 50% of the population by the year 2030 (Ogden *et al*., 2015; Finkelstein *et al*., 2012). Obesity is an utmost risk factor for the development of CVD risk factors such as hypertension, type 2 diabetes, and dyslipidemia (Lavie *et al*., 2009). Body mass index (BMI) > 30 kg/m2, waist circumference (WC), waist-to-hip ratio (WHR) > 1.0 for men and >0.85 in women are routinely used and are suggestive of an unhealthy abdominal fat buildup, which has been strongly associated with cardiometabolic diseases (Ashwell and Gibson, 2016; Taylor *et al*., 2010). Though widely used, body mass index has inherent limitations; it does not predict central (abdominal) obesity and has different demographical standards (Gupta *et al*., 2019). Waist circumference varies based on height, sex, and race differences, while WHR does not respond to WC changes (Guan *et al*., 2016; Vikram *et al*., 2016). Another safe, less costly, and non-invasive method for assessing central obesity is the bioelectrical impedance analysis (BIA). The BIA is limited by ethnicity, environment, phase of the menstrual cycle, dehydration, and underlying medical conditions. Therefore, most studies continue to rely on BMI, WC, and WHR for analysis. Currently, the waist circumference-to-height ratio (WHtR) is deemed the most accurate and is used widely for CVD assessment. It provides much more precise information about obesity (Gupta *et al*., 2019; Correa *et al*., 2016; Ashwel and Gibson, 2016). A commonly recognized limit of WHtR < 0.5 is protective for CVD and type 2 diabetes events (Browning *et al*., 2010).

CHAPTER III

3.0 METHODS

3.1 Design and Data Source

This study is based on a cross-sectional data collected by the US National Center for Health Statistics – the 2007-2016 National Health and Nutrition Examination Survey (NHANES). The NHANES assesses the health and nutritional status of the United States population. In NHANES, questionnaire responses and biological samples of a nationally representative samples are collected every year and reported every two years. This study's data are based on five two-year cycles: 2006-2008 (cohort 0), 2009-2010 (cohort 1), 2011-2012 (cohort 2), 2013-2014 (cohort 3), and 2015-2016 (cohort 4).

3.2 Consent and Ethical Clearance

The NHANES data are pre-approved for public use and do not require Georgia State University Institutional Review Board (IRB) approval.

3.3 Study Variables

3.3.1 Demographics

In NHANES, participants reported their age at the time of the survey. In this study age was categorized as 20-29, 30-39, 40-49, 50-59, 60-69, and ≥ 70 years. Both the male and female gender in the age category of interest were included in the study. Five racial/ethnicity groups created in the NHANES survey were adopted and used for this study. These included Mexican American, Other Hispanic, Non-Hispanic White, Non-Hispanic Black, and other race, including Multi-Racial. In NHANES marital status were categorized as either married, widowed, divorced,

separated, never married, or living with a partner. These categories were maintained for this study. Educational categories as defined in NHANES data were used in this study and included "less than 9^{th} grade" "$9\text{-}11^{th}$ grade" "high school graduate/GED or equivalent" "some college or AA degree, or college graduate or above".

3.3.2 Lipid Profile

Four lipid variables, including total cholesterol (TCHOL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides were employed in this study. These were extracted from the NHANES laboratory data files. Reference ranges established by the American Heart Association (Benjamin *et al.*, 2017) were used throughout this study. Data on total cholesterol measured in milligrams per deciliter (mg/dL). Total cholesterol < 200 mg/dL was categorized as desirable, 200-230 mg/dL borderline risk, and > 230 mg/dL high risk. High density lipoprotein was categorized as low - <40 mg/dL, healthy levels – 40-59 mg/dL, and desirable - ≥ 60 mg/dL. With regards to LDL, serum concentrations < 130 mg/dL was categorized as desirable, 131-159 mg/dL – borderline risk, and > 159 mg/dL – high risk. Triglycerides were categorized into desirable - < 150 mg/dL, borderline high – 150-199 mg/dL, high – 200-499 mg/dL, and very high - ≥ 500 mg/dL. Cardiovascular risk was calculated as TCHOL divided by HDL. A CVDRisk of < 4.5 was categorized as desirable, 4.5-6.4 borderline high, while ≥ 6.5 was high risk.

3.3.3 Anthropometrics

Three body measurements, weight (kg), waist circumference (cm), and height (cm), were measured by trained health technicians and recorders during the NHANES survey. Following this, body mass index (BMI) in kg/m^2 was calculated as weight in kilograms (kg) divided by the square of the height (m^2) and made available in the data set. Body mass index was later categorized in to underweight - <18.5 kg/m^2, normal weight – 18.5-24.9 kg/m^2, overweight – 25-29.9 kg/m^2, class I obesity – 30-34.9 kg/m^2, class II obesity – 35-39.9 kg/m^2, and class III obesity - ≥40 kg/m^2 according to the classification by the Centers of Disease Control and Prevention (CDC, 2020). Waist circumference to height ratio (WHtR) was calculated by dividing waist circumference with height. The WHtR was classified as no risk - < 0.5, increased risk - 0.5-0.6, and very high risk - > 0.6.

3.4 Statistical Procedures

Data files (XPT files) were downloaded and read in SAS® version 9.4 (SAS Institute Inc., Cary, NC, USA) for statistical analysis. Cardiovascular risk (CVDRisk) was calculated as the ratio of TCHOL to HDL and used to estimate both weighted and unweighted risk prevalence using the surveyfreq procedure. Linear trends for risks were plotted for all lipid profile measurements, body mass index (BMI), and waist circumference (WC) to height ratio (WHtR) using the GraphPad Prism® Version 6.01. SAS surveyreg procedure was used to determine the regression coefficient estimates for the relationship between CVDRisk (dependent variable) and age, gender, race/ethnicity (independent variables). The multiple linear regression analysis procedure was done to estimate whether BMI, WC, weight (WT), or the interaction term WC*WT best predict cardiovascular disease risk. The interaction term was tested using the postprocessing linear modeling (proc PLM) to generate SLICEFIT plots.

CHAPTER IV

4.0 RESULTS

4.1 Demographic Characteristics

A total of 29,201 participants aged between 20-80 years available in the 2007-2016 NHANES study were analyzed in this study. Out of this total, 48.5% (14,161/29,201) were males while 51.5% (15,040/29,201) were females (Table 1). As well, 16.7% (4863/29,201) were within the 20-29 years old category, 13.6% (3982/29,201) within 30-39 years, 16.9% (4932/29,201) within 40-49 years, 15.9% (4652/20,201) within 50-59 years, 16.3% (4757/29,201) within 60-69 years, while 17.1% (5003/29,201) were within the ≥ 70 years age group. Mexican Americans and other Hispanics constituted 15.3% (4475/29,201) and 10.8% (3152/29,201) respectively. Non-Hispanic Whites were 41.5% (12,113/29,201), Non-Hispanic Blacks 21.2% (6179/29,201), while the remaining including multi-racial were 11.3% (3282/29,201). With regards to educational attainment, 26.0% (7579/29,201) have had up to 11^{th} grade, 22.6% (6596/29,201) have had high school/GED or equivalent, 28.6% (8366/29,201) have had some college degree or AA degree, and 22.7% (6621/29,201) are college graduates or above. Among the total, 50.8% (14,836/29,201) were married, 8.4% (2446/29,201) widowed, 10.9% (3180/29,201) divorced, 3.4% (983/29,201) separated, 18.6% (5439/29,201) never married, and 7.9% (2296/29,201) were living with partner. The weighted mean age was estimated as 46.8 years (std error = 0.432889, 95%CL: 45.9-47.7) (Table 1).

Table 1: Demographic characteristics of participants – 2007-2016

Demographic characteristics	Unweighted		Weighted	
Gender	**N = 29,201**	**Percentage**	**N = 1,121,740,245**	**Percentage**
Male	14161	48.5	539502781	48.1
Female	15040	51.5	582237464	51.9
Age range (years)*				
20-29	4863	16.7	211424572	18.8
30-39	4994	17.1	199534145	17.8
40-49	4932	16.9	213245995	19.0
50-59	4652	15.9	207734291	18.5
60-69	4757	16.3	151889320	13.5
≥ 70	5003	17.1	137911923	12.3
Race/Ethnicity				
Mexican American	4475	15.3	95853731	8.5
Other Hispanic	3152	10.8	63976692	5.7
Non-Hispanic White	12113	41.5	747413846	66.6
Non-Hispanic Black	6179	21.2	127799427	11.4
Other – Including Multi-racial	3282	11.2	86696549	7.7
Educational Level				
< 9^{th} grade	3275	11.2	66222661	5.9
9-11^{th}	4304	14.7	126198089	11.3
High School/GED or Equivalent	6596	22.6	248202687	22.1
Some College Degree or AA Degree	8366	28.6	351446876	31.3
College graduate or above	6621	22.7	328872703	29.3
Refused	11	0.0	315772	0.0
Don’t know	28	0.1	481457	0.0
Marital Status				
Married	14836	50.8	617436723	55.0
Widowed	2446	8.4	66175507	5.9
Divorced	3180	10.9	115028012	10.3
Separated	983	3.4	26905430	2.4
Never married	5439	18.6	207309640	18.5
Living with partner	2296	7.9	88466086	7.9
Refused	17	0.1	369882	0.0
Missing	4	0.0	2	0.0

*(Weighted mean age = 46.8 years, Standard error of mean = 0.432889, 95% CL for mean: 45.9-47.7

4.2 Weighted averages for key variables

The study estimated means BMI, Total Cholesterol (TCHOL), High-Density Lipoprotein (HDL), Low-Density Lipoprotein (LDL), Cardiovascular Disease Risk (CVDRisk), Waist Circumference to Height Ratio (WHtR), and Waist Circumference (WC). These Weighted mean estimates for the selected variables are as shown in Table 2. Mean BMI was 28.5 kg/m^2 for the 2007-2008 cohort (Cohort 0), 28.7% for both 2009-2010 (Cohort 1) and 2011-2012 (Cohort 2), and 29.2% for both 2013-2014 (Cohort 3) and 2015-2016 (Cohort 4) ($p < 0.0001$). The means for TCHOL in all cohorts were statistically different ($p < 0.01$), likewise LDL, TRIG, HDL, and CVDRisk.

Table 2: Weighted averages of variables

	BMI	TCHOL	LDL	TRIG	HDL	WHtR	WC	CVDRisk
2007-2008 (Cohort 0)								
Unweighted frequency	5607	5332	2549	2613	5332	5373	5378	5332
Weighted Mean	28.5	197.2	115.7	137.1	52.0	0.580	97.8	4.1
Std Error of Mean	0.164	0.826	0.826	2.686	0.533	0.003	0.455	0.034
95%CL for Mean	28.2-28.9	195.5-199.0	113.0-117.5	131.4-142.8	50.8-53.1	0.575-0.586	96.9-98.8	4.05-4.2
2009-2010 (Cohort 1)								
Unweighted frequency	5994	5696	2714	2762	5696	5698	5706	5696
Weighted Mean	28.7	196.3	116.1	127.5	53.1	0.583	98.2	4.0
Std Error of Mean	0.129	0.929	0.947	2.360	0.415	0.003	0.435	0.021
95%CL for Mean	28.5-29.0	194.3-198.3	114.1-118.1	122.5-132.5	52.3-54.0	0.577-0.589	97.3-99.1	4.0-4.1
2011-2012 (Cohort 2)								
Unweighted frequency	5237	4913	2393	2439	4913	4969	4978	4913
Weighted Mean	28.7	195.6	115.5	132.7	53.0	0.586	98.7	3.9
Std Error of Mean	0.210	0.989	0.969	4.876	0.493	0.004	0.564	0.039
95%CL for Mean	28.3-29.2	193.5-197.7	113.4-117.5	122.5-143.1	51.9-54.0	0.578-0.594	97.6-99.9	3.85-4.02
2013-2014 (Cohort 3)								
Unweighted frequency	5520	5342	2513	2553	5342	5261	5270	5342
Weighted Mean	29.2	189.5	111.3	120.9	53.2	0.592	99.6	3.9
Std Error of Mean	0.174	0.861	0.914	3.059	0.288	0.003	0.331	0.022
95%CL for Mean	28.8-29.5	187.6-191.3	109.3-113.2	114.4-127.4	52.6-53.8	0.586-0.597	98.9-100.3	3.81-3.90
2015-2016 (Cohort 4)								
Unweighted frequency	5520	5342	2513	2553	5342	5261	5270	5342
Weighted Mean	29.2	189.5	111.3	120.9	53.2	0.592	99.6	3.9
Std Error of Mean	0.174	0.861	0.914	3.059	0.288	0.003	0.331	0.022
95%CL for Mean	28.8-29.5	187.6-191.3	109.3-113.2	114.4-127.4	52.6-53.8	0.586-0.597	98.9-100.3	3.81-3.90

Units of measurement: BMI - kg/m^2; TCHOL, LDL, HDL, TRIG – mg/dL; WC – cm.

4.3 Linear trend analysis for means

Linear trends for BMI, waist circumference to height ratio (WHtR), waist circumference (WC), total cholesterol (TCHOL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TRIG), and cardiovascular risk (CVDRisk = TCHOL/HDL) for the five cohorts are as shown in figures 1-8. For the purposes of analysis, cohorts were coded as follows: 2007-2008 (Cohort 0), 2009-2010 (Cohort 1), 2011-2012 (Cohort 2), 2013-2014 (Cohort 3), and 2015-2016 (Cohort 4), shown in figures 1-8. From figure 1, the BMI trend in the US population increased significantly by 0.190 from a mean of 28.3 kg/m^2 to 29.3 kg/m^2 over the four bi-annual cohorts (t = 4.61, p = 0.0192). The WHtR increased significantly by 0.003 from 0.580 to 0.592 at the end of the 4th cohort (Figure 2). Waist circumference increased significantly from 97.8 cm from cohort 0 to 99.6 cm at cohort 4 (Figure 3).

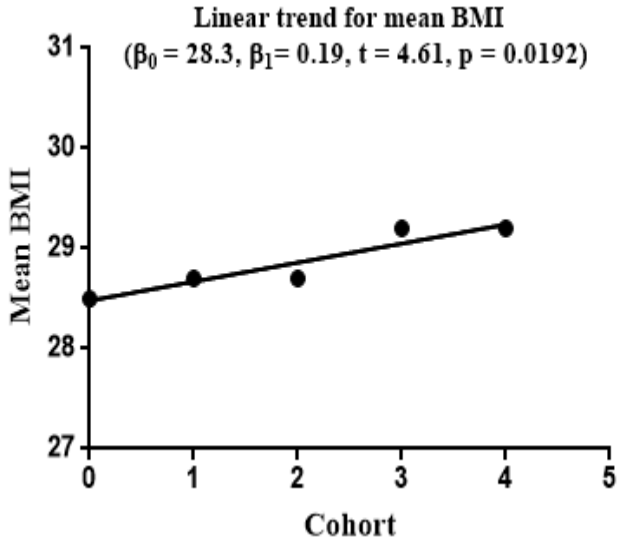

Figure 1: The linear trend for mean BMI

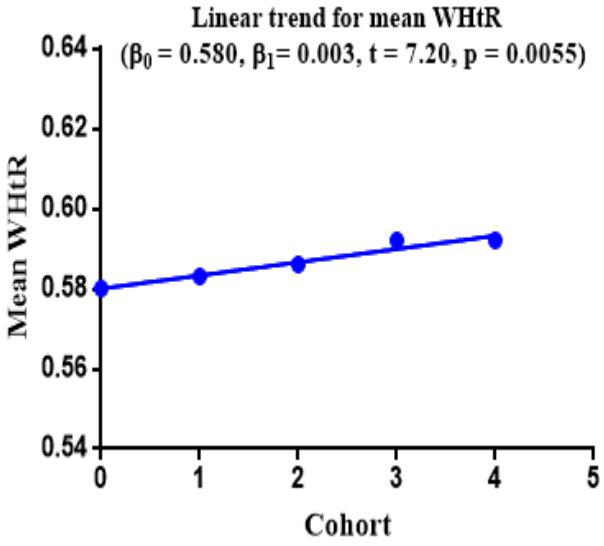

Figure 2: The linear trend for mean WHtR

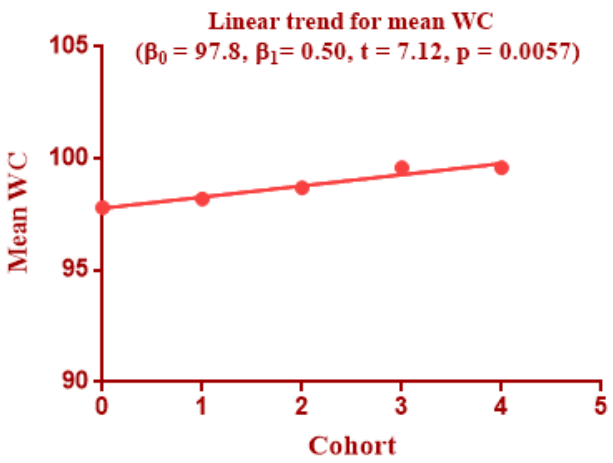

Figure 3: The linear trend for mean WC

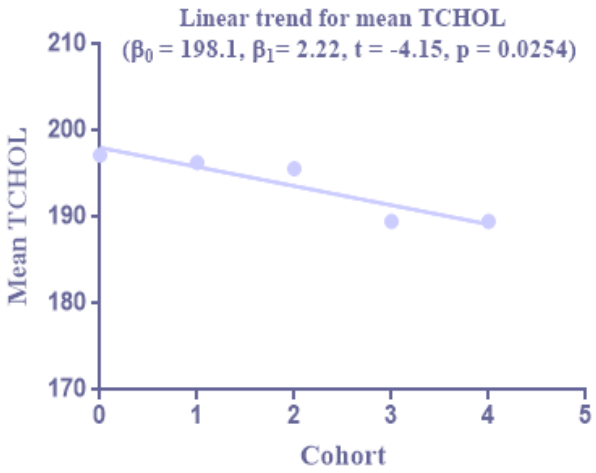

Figure 4: The linear trend for mean TCHOL

Mean TCHOL (Figure 4) decreased significantly by 2.22 bi-annually from 198.1 mg/dL in cohort 0 to 189.5 mg/dL in cohort 4 (t = -4.15, p = 0.0254). Both LDL and TRIG decreased non-significantly from cohort 0 through cohort 4 (p > 0.05) (Figure 5-6). The mean HDL increased at a statistically non-significant rate of 0.23 annually from a mean of 52.5 mg/dL at cohort 0 to 53.2 mg/dL at cohort 4 (t = -2.16, p = 0.1192) (Figure 7). Cardiovascular risk (CVDRisk) declined significantly by 0.05 annually through the cohorts (t = -3.27, p = 0.0467) (Figure 8).

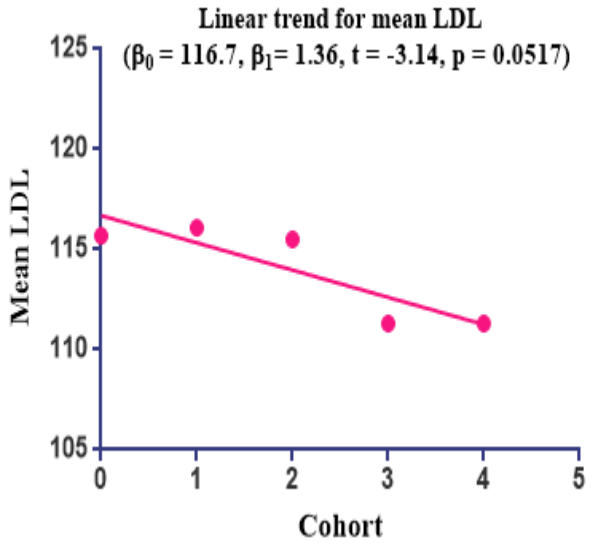

Figure 5: The linear trend for mean LDL

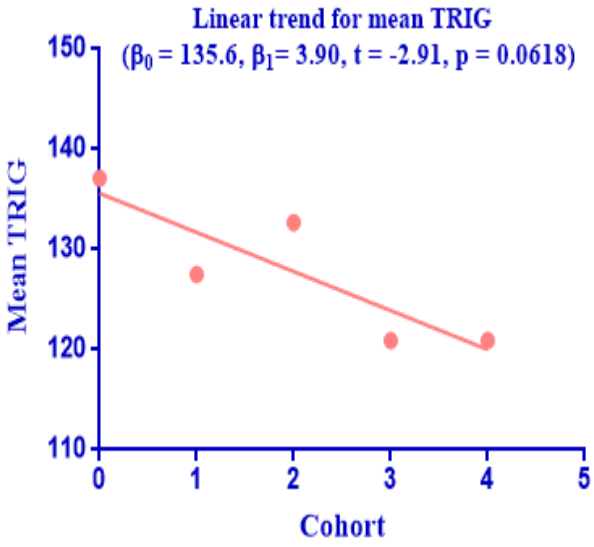

Figure 6: The linear trend for mean TRIG

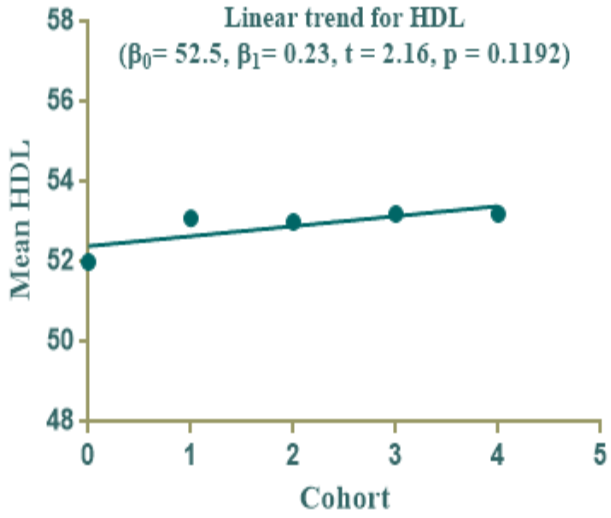

Figure 7: The linear trend for mean HDL

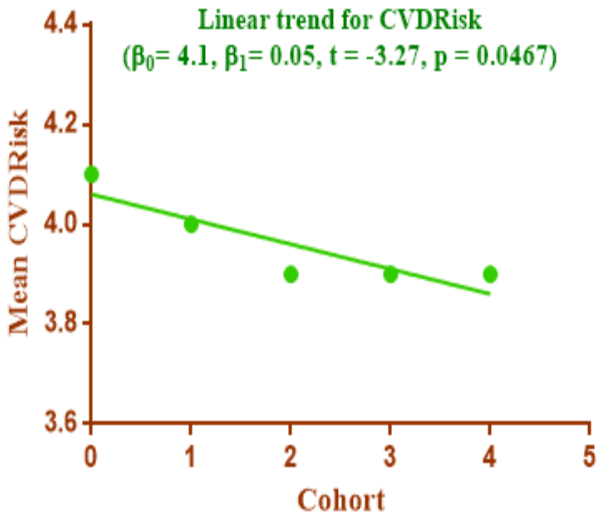

Figure 8: The linear trend for mean CVDRisk

4.4 Population percentages for CVDRisk categorization

Table 3 shows population percentages for all cohorts in all the variables considered. Body Mass Index was categorized into underweight, normal weight, overweight and obese categories I, II, III. The weighted average percentage of the underweight population was estimated to be 2.7%, normal weight 28.8%, overweight 32.3%, class I obesity 20.4%, class II obesity 9.0%, and class III obesity 6.7%. For waist Circumference to Height Ratio (WHtR), all participants were at risk, with 37.5% having increased risk, while 62.5% were in the very high-risk group.

Lipid profile, that is, TCHOL, LDL, HDL, TRIG, was categorized as well. Of the total, 63.2% were in the desirable TCHOL category, 23.9% were in the borderline risk, while 9.8% were in the high-risk category. An estimated 70.9% were in the desirable LDL category, 19.2% were borderline risk, 11.2% were high risk, while 0.8% were in the very high-risk category. High-density lipoprotein was categorized as low (23.8% of the population), healthy levels (47.6% of the population), and desirable (28.6% of the population).

Cardiovascular disease risk was estimated at the ratio of TCHOL to HDL and categorized as desirable (0.3% of the population), borderline risk (93.1% of the population), and high-risk category (6.6% of the population). The difference in population estimates was statistically significant for all the variables considered ($p < 0.01$).

Table 3: Population stratified percentages for cohorts

	Cohort (N = 1,121,740,245)				
	2007-2008	**2009-2010**	**2011-2012**	**2013-2014**	**2015-2016**
	%	%	%	%	%
BMI(kg/m^2) Pr> χ^2 < 0.0001					
Underweight (< 18.5)	3.0	2.7	2.8	2.4	2.6
Normal weight (18.5-24.9)	30.1	28.9	29.7	28.3	27.1
Overweight (25-29.9)	33.5	32.6	32.7	31.8	31.0
Class I Obesity (30-34.9)	19.4	20.3	20.3	20.6	21.6
Class II Obesity (35-39.9)	8.4	9.1	8.1	9.3	10.2
Class III Obesity (≥ 40)	5.6	6.3	6.3	7.6	7.5
Missing	n = 29	n = 28	-	-	-
WHtR Pr> χ^2 < 0.0001					
No risk (< 0.5)	-	-	-	-	-
Increased risk (0.5 - 0.6)	41.3	39.8	38.1	35.2	33.1
Very high risk (> 0.6)	58.7	60.2	61.9	64.8	66.9
Missing	n = 2103	n = 2229	n = 1982	n = 2053	n = 1888
TCHOL (mg/dL) Pr> χ^2 < 0.0001					
Desirable (< 200)	61.2	61.5	62.1	66.6	64.6
Borderline risk (200-230)	24.4	25.0	24.9	22.3	23.0
High risk (> 230)	14.4	13.5	13.0	11.2	12.4
Missing	n = 267	n = 272	n = 231	n = 201	n = 196
LDL (mg/dL)) Pr> χ^2 < 0.0001					
Desirable (< 130)	70.5	70.2	69.3	73.0	71.6
Borderline risk (131-159)	19.4	18.9	20.9	18.3	18.6
High risk (> 159)	10.1	10.9	9.7	8.7	9.8
Missing	n = 33	n = 25	n = 22	n = 26	n = 18
TRIG (mg/dL)) Pr> χ^2 < 0.0001					
Desirable (< 150)	70.3	75.3	74.5	77.0	78.4
Borderline high (150-199)	15.8	13.1	13.6	10.8	11.0
High (200-499)	12.6	10.9	10.8	11.4	10.4
Very high (≥ 500)	1.2	0.7	1.1	0.7	0.2
HDL (mg/dL) Pr> χ^2 < 0.0001					
Low (< 40)	26.6	25.4	22.1	22.5	22.2
Healthy levels (40-59)	47.5	46.0	51.7	49.0	43.9
Desirable (≥ 60)	25.9	28.5	26.3	28.5	33.9
CVDRisk Pr> χ^2 < 0.0001					
Desirable (< 4.5)	0.4	0.4	0.2	0.3	0.1
Borderline (4.5-6.4)	90.7	92.3	94.7	94.1	93.8
High (≥ 6.5)	8.9	7.2	5.2	5.6	6.2
Missing	n = 1314	n = 1425	n = 1118	n = 1146	n = 1077

BMI – Body Mass Index, WHtR – Waist Circumference to Height Ratio, LDL – Low-Density Lipoprotein, TRIG – Triglycerides, TCHOL – Total Cholesterol, HDL – High-Density Lipoprotein, CVDRisk – Cardiovascular Disease Risk

4.5 Trend analysis for the risk categories of selected variables

Prevalence trends for the risk categories of Body Mass Index (BMI), Waist to Height Ratio (WHtR), Total Cholesterol (TCHOL), Low-Density Lipoprotein (LDL, TRIG, HDL, and Cardiovascular Disease Risk (CVDRisk) are as shown in Figures 9-15.

Figure 9 shows a decline in prevalence (3.0% - 2.6%) of underweight by 0.11 bi-annually ($t = 2.144$, $p = 0.1214$), normal BMI by 0.66 bi-annually from 30.1% to 27.1% ($t = 3.180$, $p = 0.0501$) and overweight by 0.58 bi-annually from 33.5% to 31.0% ($t = 6.190$, $p = 0.0085$) from 2007-2008 (Cohort 0) to 2015-2016 (Cohort 4). All three classes of obesity show a steady increase through from Cohort 0 to Cohort 4. Class I obesity increased significantly by 0.47 bi-annually in prevalence from 19.5% in 2007-2008 to 21.6% in 2015-2016 ($t = 4.839$, $p = 0.0168$). The increase in prevalence in class II obesity (8.4% - 10.2%) was not significant ($t = 1.851$, $p = 0.1612$). Class III obesity prevalence increased significantly by 0.51 bi-annually from 5.6% to 7.5% ($t = 4.586$, $p = 0.0195$).

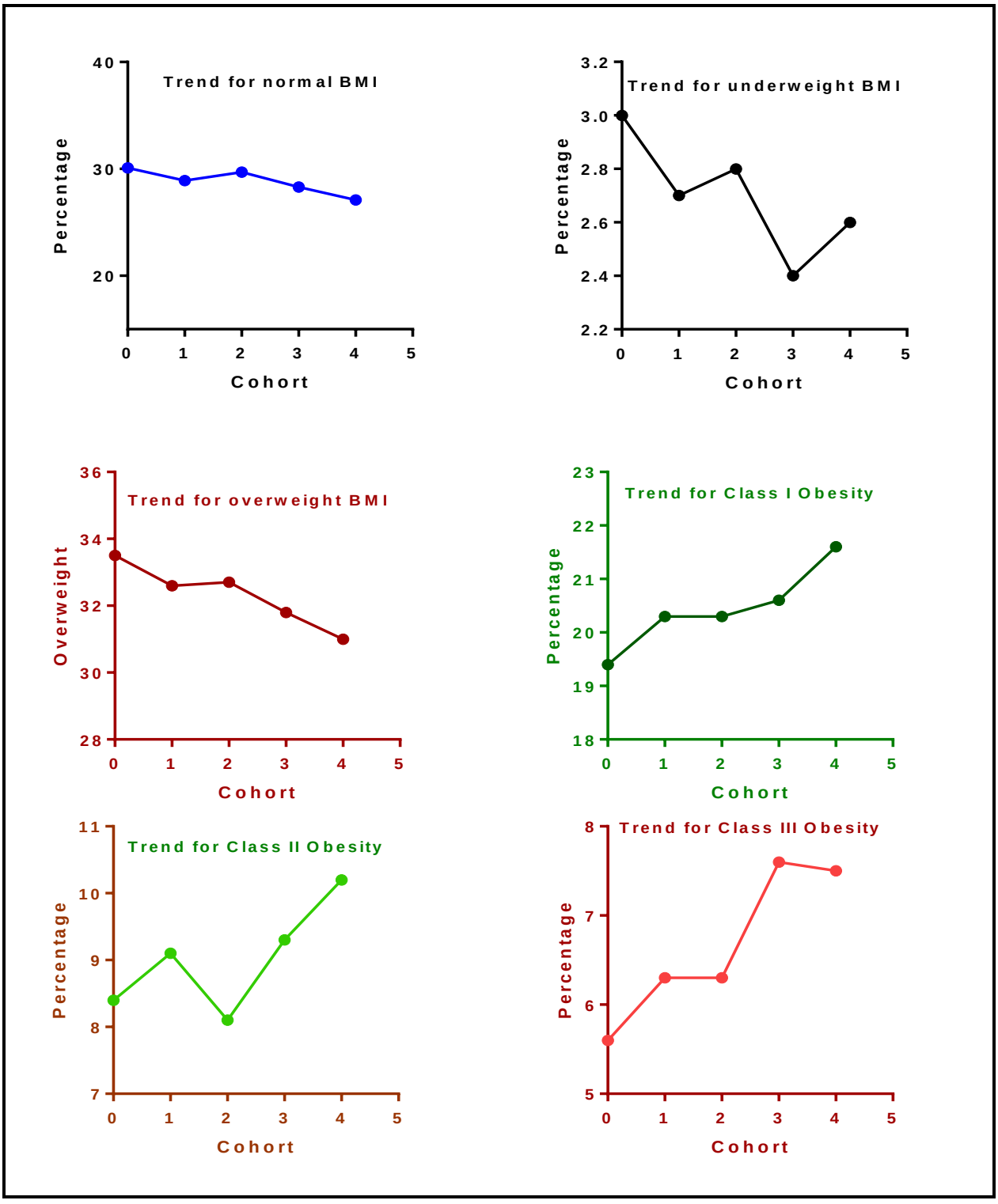

Figure 9: Trend in BMI, 2007-2016

All participants in the five cohorts were at risk of CVDs with regards to the WHtR classification. The percentage of individuals with increased risk shows a significant decline of 2.1 bi-annually in prevalence from 41.7% - 33.1% through 2007-2016 (t = 14.38, p = 0.0007). There was a significant increase in prevalence of individual with very high risk WHtR by 2.1 bi-annually from 58.3% to 66.9% (t = 14.38, p = 0.0007) (Figure 10).

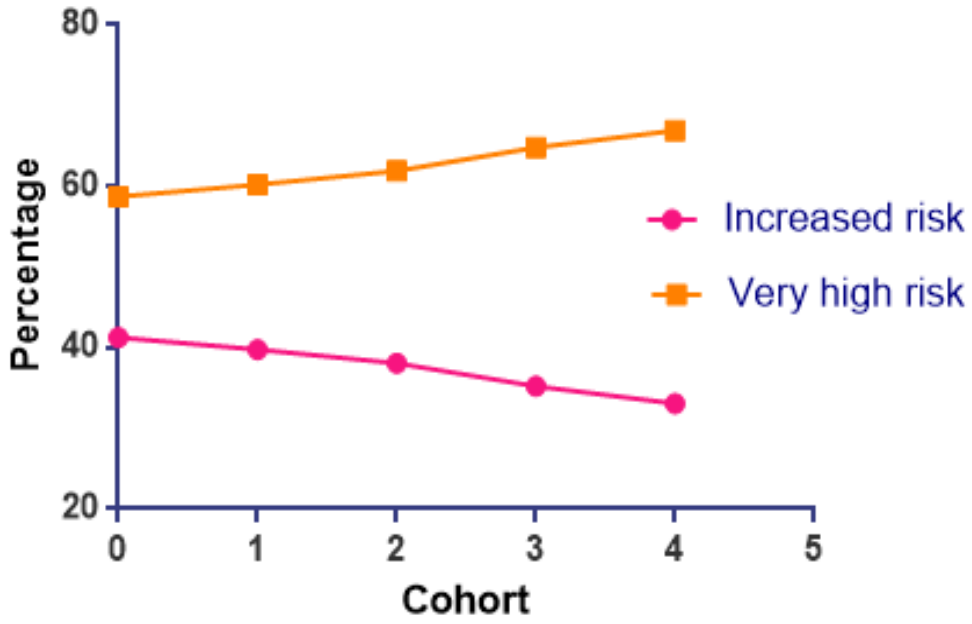

Figure 10: Trend in WHtR, 2007-2016

Most of the study participants (about 70%) had the desirable TCHOL, LDL, and TRIG. From Figures 11, 12, 13, all categories showed a non-significant change (p > 0.05). A greater proportion of participants were in the healthy level HDL category (Figure 14). There was an overall significant percentage decline in the low HDL category by 1.17 from 2007-2008 (26.6%) to 2015-2016 (22.2%) (t = 3.27, p = 0.0468). The percentage of participants with desirable HDL increased non-significantly (25.9% - 33.9%) from the 2007-2008 cohort to 2015-2016 (t = 2.26, p = 0.1093).

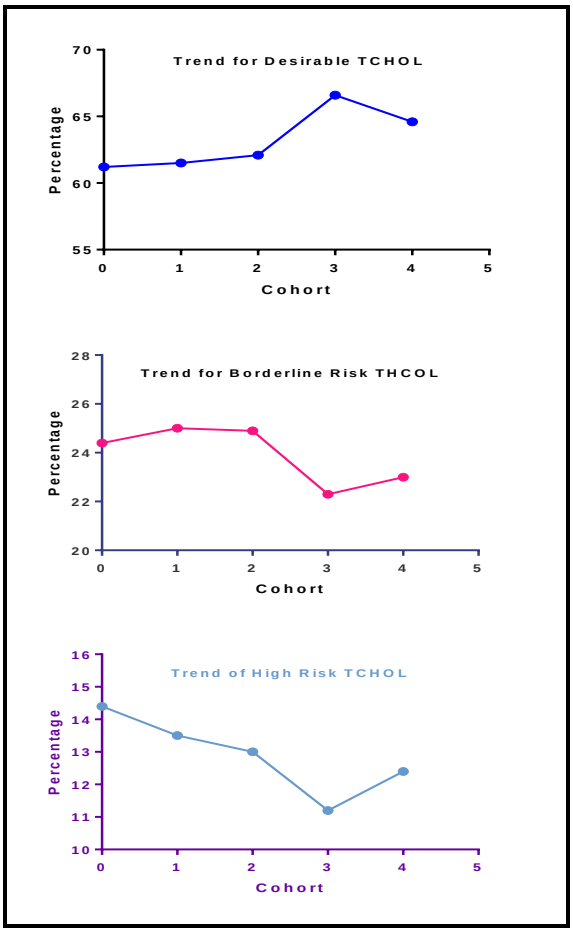

Figure 11: Trend in TCHOL, 2007-2016

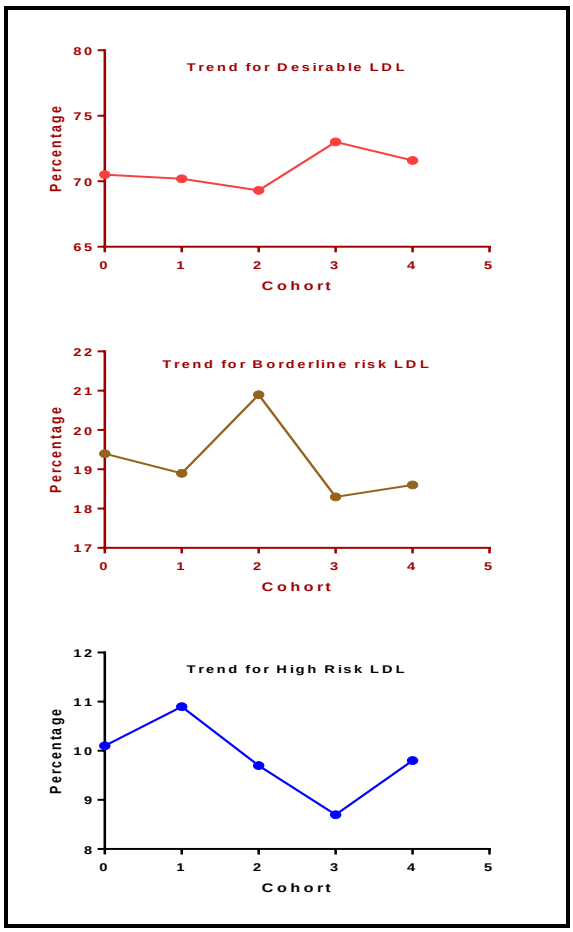

Figure 12: Trend in LDL, 2007-2016

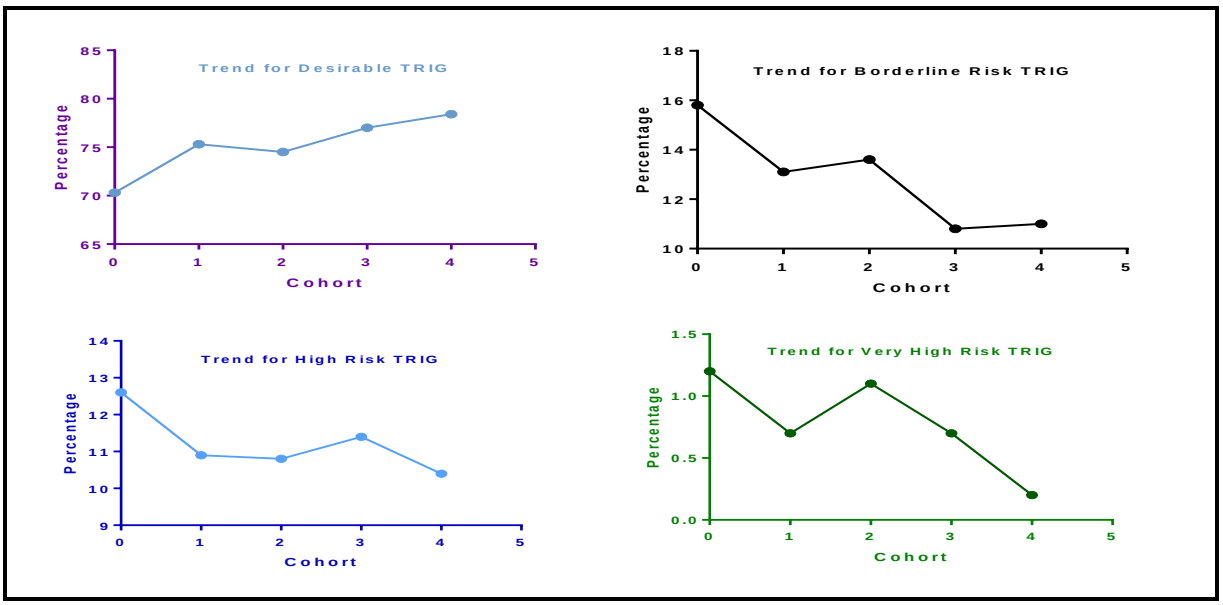

Figure 13: Trend in Triglycerides, 2007-2016

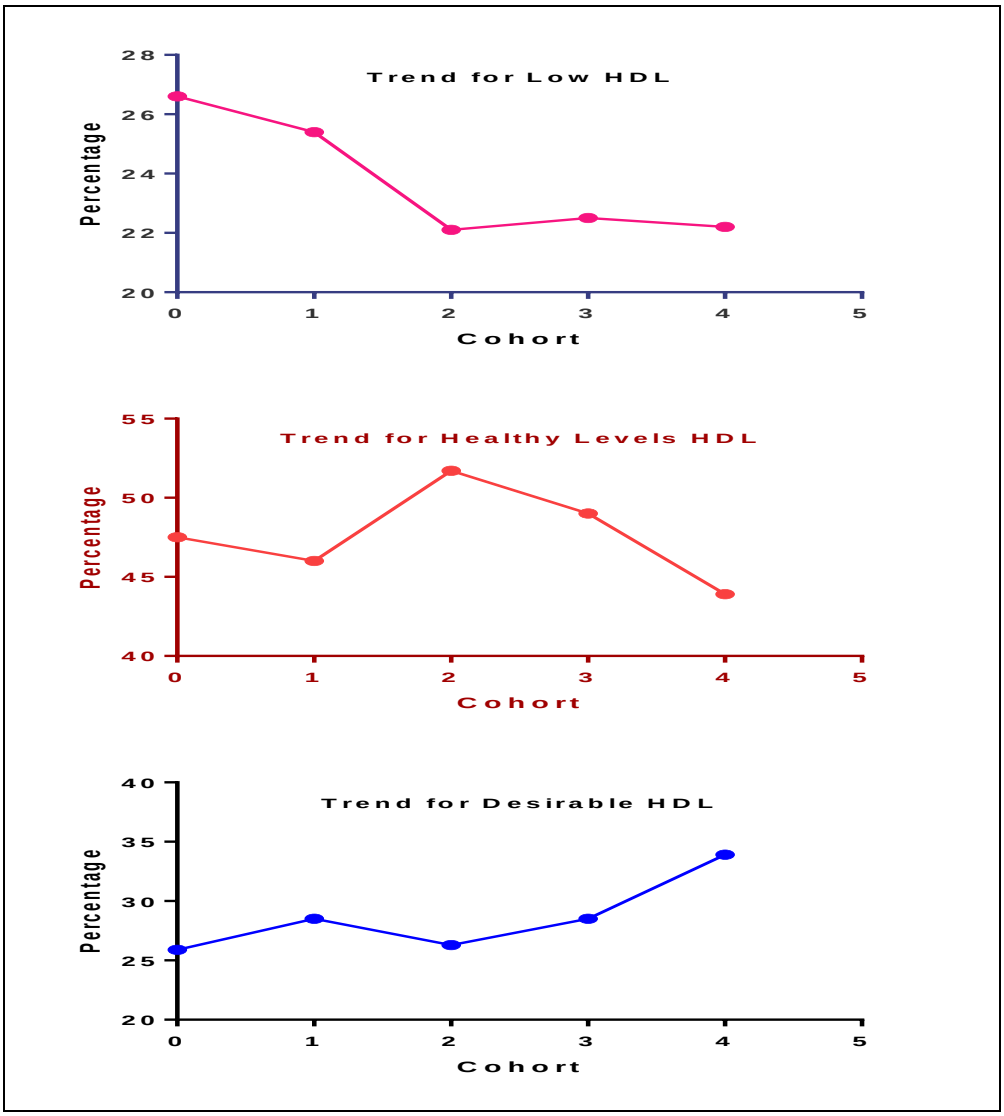

Figure 14: Trend in HDL, 2007-2016

Over 90% of the participants were in the borderline risk of the CVDRisk category for all the cohorts. The prevalence of desirable CVDRisk declined from 0.42% to 0.1% through 2015-2016 cohort ($t = 2.78$, $p = 0.0689$). There was a non-significant increase of 0.8 in the borderline risk percentage from 90.7% to 93.8% ($t = 2.18$, $p = 0.1176$). The high CVDRisk category decreased steadily from 8.9% among the 2007-2008 cohort to 6.2% among the 2015-2016 cohort but was not significant ($t = 1.95$, $p = 0.1464$) (Figure 15).

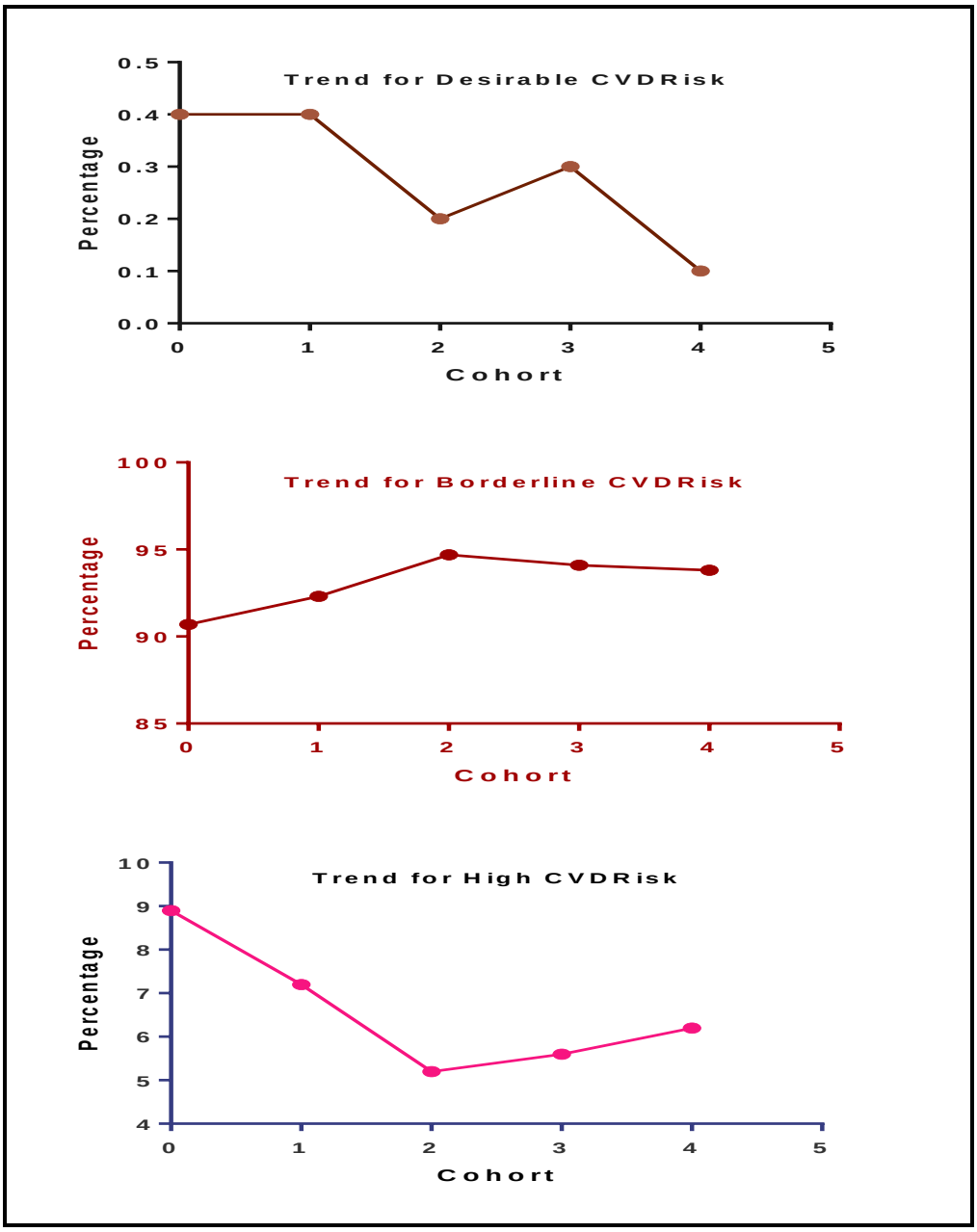

Figure 15: Trend in CVDRisk, 2007-2016

The study performed correlation analysis to estimate the association between CVDRisk and the key anthropometrics (Table 4). The strength of the relationship between CVDRisk was most robust with waist circumference, followed by weight, waist circumference to height ratio, and BMI. This trend was consistent with all the cohorts.

Table 4: Correlation between CVDRisk and anthropometrics

	2007-2008	2009-2010	2011-2012	2013-2014	2015-2016
	r	**r**	**r**	**r**	**r**
CVDRisk*WC	0.3378	0.3282	0.3528	0.3336	0.2974
CVDRisk*Weight	0.3081	0.3006	0.3251	0.3107	0.2928
CVDRisk*WHtR	0.2907	0.2755	0.2989	0.2796	0.2347
CVDRisk*BMI	0.2708	0.2604	0.2820	0.2669	0.2340

p-value < 0.0001 for all relationships
Strength of relationship with CVDRisk: WC > Weight > WHtR > BMI

CVDRisk – Cardiovascular Disease Risk, WC – Waist Circumference, BMI – Body Mass Index, WHtR – Waist Circumference to Height Ratio.

4.6 Regression Coefficients for CVDRisk with selected demographics

The study modeled Cardiovascular disease risk estimates stratified by gender, age, and race/ethnicity (Table 5). Among the 2007-2008 cohort, males had a 0.77 increase in CVDRisk, on average, compared to females, controlling for age and race/ethnicity. There were increases of 0.75, 0.59, 0.65, and 0.82 in CVDRisk of males in 2009-2010, 2011-2012, 2013-2014, and 2015-2016 respectively, compared to females, controlling for age and race/ethnicity. All age groups for this study had a significant increase in CVDRisk than the 20-29 years referent group ($p < 0.0001$). The only exception was the ≥ 70 years age group, which had a non-significant reduction in CVDRisk across all the cohorts ($p > 0.05$). The 60-69 years age group had a non-significant increase in CVDRisk among the 2013-2014 cohort ($p = 0.1164$) compared to the referent group. Mexican Americans and other Hispanics had significant increases in CVDRisk compared to the referent Non-Hispanic whites ($p < 0.0001$). Non-Hispanic blacks had a significant reduction in CVDRisk than Non-Hispanic Whites ($p < 0.0001$) for all the cohorts.

Table 5: Estimated Regression coefficient for the relationship between CVDRisk (Dependent variable) and Age, Gender, Race/Ethnicity (independent variables)

	2007-2008	2009-2010	2011-2012	2013-2014	2015-2016
Parameter	**Estimate (Pr > |t|)**	**Estimate (Pr > |t|)**	**Estimate (Pr > |t|)**	**Estimate (Pr > |t|)**	**Estimate (Pr > |t|)**
Gender					
Female	Referent	Referent	Referent	Referent	Referent
Male	0.77 (p<0.0001)	0.75 (p<0.0001)	0.59 (p<0.0001)	0.65 (p<0.0001)	0.82 (p<0.0001)
Age					
20-29	Referent	Referent	Referent	Referent	Referent
30-39	0.40 (p<0.0001)	0.50 (p<0.0001)	0.31 (p<0.0001)	0.47 (p<0.0001)	0.58 (p<0.0001)
40-49	0.43 (p = 0.0001)	0.50 (p<0.0001)	0.62 (p<0.0001)	0.52 (p<0.0001)	0.74 (p<0.0001)
50-59	0.50 (p = 0.0002)	0.44 (p = 0.0001)	0.54 (p<0.0001)	0.35 (p = 0.0084)	0.66 (p<0.0001)
60-69	0.12 (p = 0.2400)	0.40 (p<0.0001)	0.19 (p = 0.0288)	0.16 (p = 0.1164)	0.29 (p =0.0108)
≥ 70	- 0.01 (p = 0.9422)	- 0.03 (p = 0.7335)	-0.03 (p = 0.7255)	- 0. 01 (p = 0.9309)	- 0.02 (p = 0.8259)
Race/Ethnicity					
Non-Hispanic White	Referent	Referent	Referent	Referent	Referent
Mexican American	0.26 (p = 0.0053)	0.30 (p = 0.0073)	0.25 (p = 0.0228)	0.27 (p = 0.0014)	0.48 (p<0.0001)
Other Hispanic	0.11 (p = 0.2177)	0.17 (p = 0.0106)	0.22 (p = 0.0670)	0.23 (p = 0.0048)	0.32 (p = 0.0004)
Non-Hispanic Black	-0.50 (p < 0.0001)	- 0.27 (p<0.0001)	- 0.26 (p<0.0001)	- 0.30 (p<0.0001)	- 0.31 (p<0.0001)
Other Race	0.06 (p = 0.6464)	-0.001 (p = 0.9900)	- 0.07 (p = 0.2250)	- 0.02 (p = 0.7228)	0.17 (p = 0.0408)

4.7 Model fitting for CVDRisk and anthropometrics

All five models in Table 6 were tested using the regression analysis procedure. Model 1 had waist circumference (WC) only, Model 2 weight (WT) only, Model 3 WC and WT, Model 4 WC and WC*WT, Model 5 WC WT WC*WT. For the five cohorts Model 5 had the highest coefficient of determinations, $R^2 = 0.1302$, $R^2 = 0.1272$, $R^2 = 0.1277$, $R^2 = 0.1381$, $R^2 = 0.1206$ for 2007-2008, 2009-2010, 2011-2012, 2013-2014, and 2015-2016 respectively.

Afterward, in the selected models, interactions were tested using the postprocessing linear modeling (PLM) to generate SLICEFIT plots, as shown in Figures 16-20. By default, the slicing variable, weight, was fixed at five values: minimum value, first quartile value, median value, third quartile value, and maximum value. The slopes of the relationship between CVDRisk and waist circumference depend on the weight from all the figures shown. Therefore, the graphs show sufficient evidence that the interaction term belong in the model.

Table 6: Predicted model for CVDRisk and selected anthropometric measures

Year	No. of Independent variables	Models	β_0	β_1	β_2	β_3	Pr > |t|	R^2	Pr > F
2007-2008									
Model 1	1	**CVDRisk = WC**	**0.98**	**0.03**			**< 0.0001**	**0.1141**	**< 0.0001**
Model 2	1	**CVDRisk = WT**	**2.25**	**0.02**			**< 0.0001**	**0.0949**	**< 0.0001**
Model 3	2	**CVDRisk = WC, WT**	**0.95**	**0.03**	**0.02**		**0.3458**	**0.1143**	**< 0.0001**
Model 4	2	**CVDRisk = WC, WC*WT**	**0.16**	**0.05**	**-0.0001**		**0.0008**	**0.1160**	**< 0.0001**
Model 5	3	**CVDRisk = WC WT WC*WT**	**-2.24**	**0.06**	**0.05**	**-0.0004**	**< 0.0001**	**0.1302**	**< 0.0001**
2009-2010									
Model 1	1	**CVDRisk = WC**	**1.01**	**0.03**			**< 0.0001**	**0.1077**	**< 0.0001**
Model 2	1	**CVDRisk = WT**	**2.28**	**0.02**			**< 0.0001**	**0.0904**	**< 0.0001**
Model 3	2	**CVDRisk = WC, WT**	**1.21**	**0.02**	**0.01**		**0.0059**	**0.1080**	**< 0.0001**
Model 4	2	**CVDRisk = WC, WC*WT**	**0.58**	**0.04**	**-0.00004**		**0.0352**	**0.1079**	**< 0.0001**
Model 5	3	**CVDRisk = WC WT WC*WT**	**-2.43**	**0.06**	**0.05**	**-0.0004**	**< 0.0001**	**0.1272**	**< 0.0001**
2011-2012									
Model 1	1	**CVDRisk = WC**	**1.01**	**0.03**			**< 0.0001**	**0.1077**	**< 0.0001**
Model 2	1	**CVDRisk = WT**	**2.28**	**0.02**			**< 0.0001**	**0.0904**	**< 0.0001**
Model 3	2	**CVDRisk = WC, WT**	**1.21**	**0.02**	**0.006**		**0.0059**	**0.1084**	**< 0.0001**
Model 4	2	**CVDRisk = WC, WC*WT**	**0.58**	**0.04**	**-0.00004**		**0.0352**	**0.1079**	**< 0.0001**
Model 5	3	**CVDRisk = WC WT WC*WT**	**-2.43**	**0.06**	**0.05**	**-0.0004**	**< 0.0001**	**0.1277**	**< 0.0001**
2013-2014									
Model 1	1	**CVDRisk = WC**	**1.03**	**0.03**			**< 0.0001**	**0.1113**	**< 0.0001**
Model 2	1	**CVDRisk = WT**	**2.21**	**0.02**			**< 0.0001**	**0.0965**	**< 0.0001**
Model 3	2	**CVDRisk = WC, WT**	**1.24**	**0.02**	**0.006**		**0.0035**	**0.1122**	**< 0.0001**
Model 4	2	**CVDRisk = WC, WC*WT**	**0.48**	**0.04**	**-0.00004**		**0.0061**	**0.1121**	**< 0.0001**
Model 5	3	**CVDRisk = WC WT WC*WT**	**-2.61**	**0.06**	**0.06**	**-0.0004**	**< 0.0001**	**0.1381**	**< 0.0001**
2015-2016									
Model 1	1	**CVDRisk = WC**	**1.04**	**0.03**			**< 0.0001**	**0.0885**	**< 0.0001**
Model 2	1	**CVDRisk = WT**	**2.08**	**0.02**			**< 0.0001**	**0.0857**	**< 0.0001**
Model 3	2	**CVDRisk = WC, WT**	**1.36**	**0.02**	**0.009**		**< 0.0001**	**0.0920**	**< 0.0001**
Model 4	2	**CVDRisk = WC, WC*WT**	**0.71**	**0.03**	**-0.00003**		**0.1573**	**0.0891**	**< 0.0001**
Model 5	3	**CVDRisk = WC WT WC*WT**	**-3.32**	**0.06**	**0.07**	**-0.0005**	**< 0.0001**	**0.1206**	**< 0.0001**

WC – Waist Circumference, WT – Weight

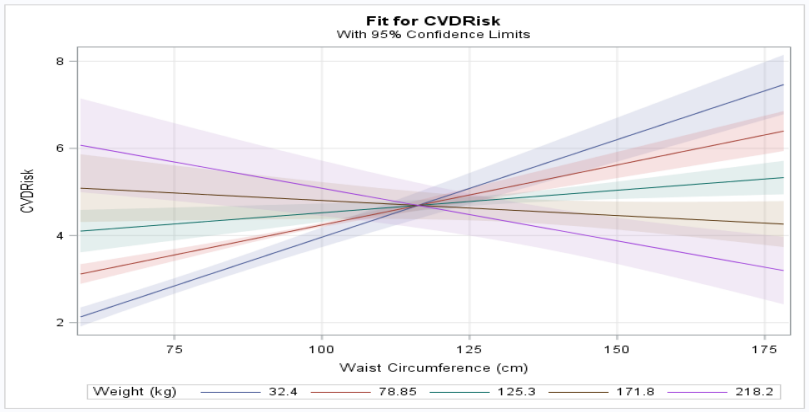

Figure 16: Interactions fit for CVDRisk – 2007-2008 Cohort

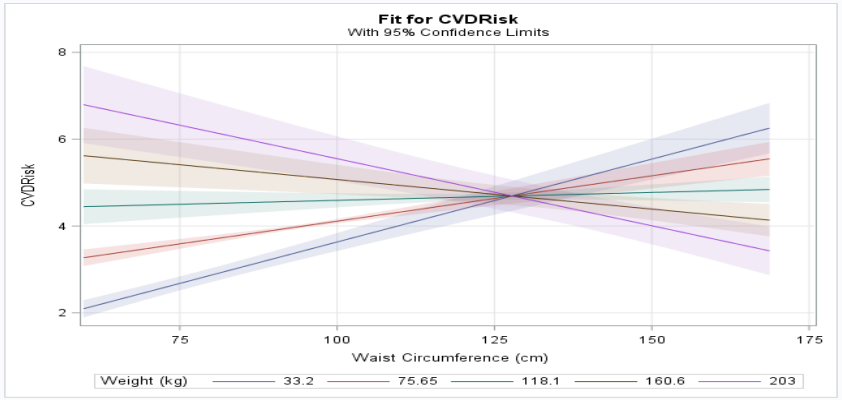

Figure 17: Interaction fit for CVDRisk – 2009-2010 Cohort

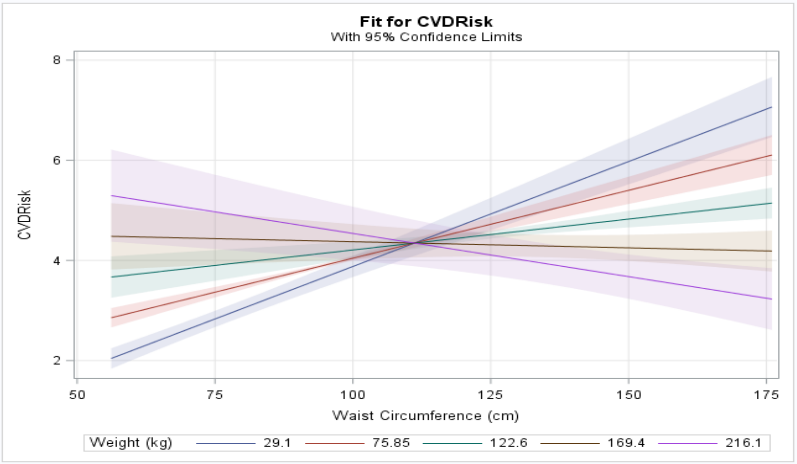

Figure 18: Interaction fit for CVDRisk – 2011-2012 Cohort

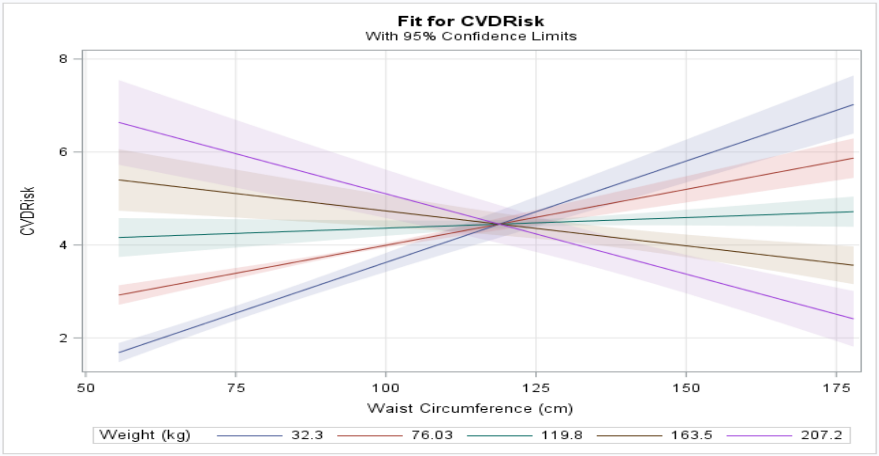

Figure 19: Interaction fit for CVDRisk – 2013-2014 Cohort

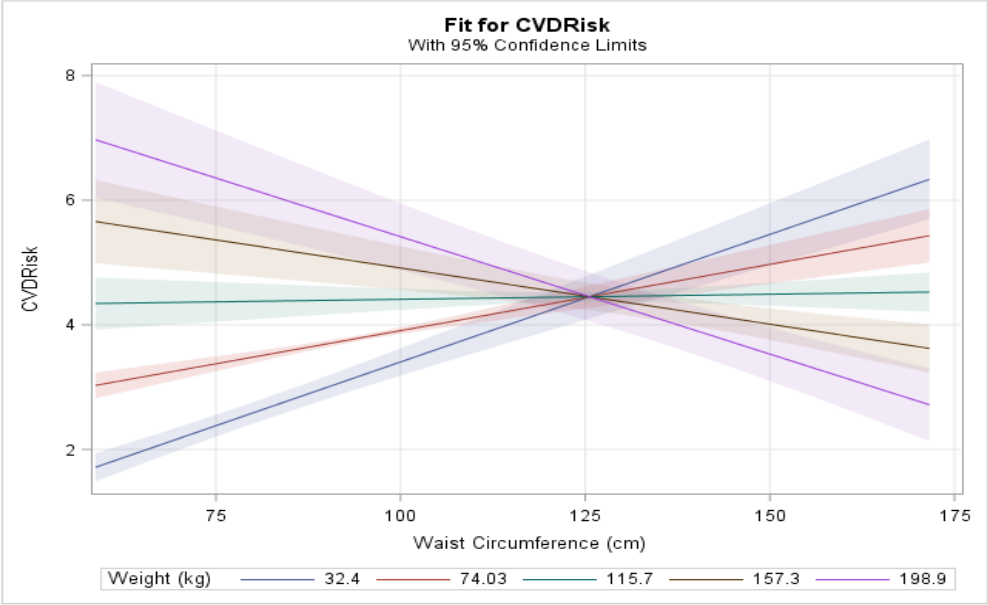

Figure 20: Interaction fit for CVDRisk – 2015-2016 Cohort

After obtaining the model for CVDRisk from its relationship with waist circumference and weight, we adjusted for age, gender, and race/ethnicity. The partial and multiple partial F tests were performed to determine if these demographics contribute to predicting CVDRisk (Table 7). From the analysis, we have sufficient evidence all five cohorts, that is, 2007-2008, 2009-2010, 2011-2012, 2013-2014, and 2015-2016 to conclude that age, gender, and race/ethnicity contributes significantly to the prediction of CVDRisk, over and above waist circumference (WC), weight (WT), and the interaction term WC*WT.

Table 7: CVDRisk model adjusted for age, gender, race/ethnicity

Model	F Value	Pr > F	R^2
2007-2008			
CVDRisk = (WC, WT, WC*WT)	325.31	< 0.0001	0.1302
CVDRisk = (WC, WT, WC*WT), Age, Gender, Race	193.95	< 0.0001	0.1690
CVDRisk = (WC, WT, WC*WT), Age	397.19	< 0.0001	0.1359
CVDRisk = (WC, WT, WC*WT), Gender	232.11	< 0.0001	0.1599
CVDRisk = (WC, WT, WC*WT), Race	242.48	< 0.0001	0.1322
2009-2010			
CVDRisk = (WC, WT, WC*WT)	439.91	< 0.0001	0.1277
CVDRisk = (WC, WT, WC*WT), Age, Gender, Race	353.63	< 0.0001	0.1646
CVDRisk = (WC, WT, WC*WT), Age	306.34	< 0.0001	0.1312
CVDRisk = (WC, WT, WC*WT), Gender	444.49	< 0.0001	0.1574
CVDRisk = (WC, WT, WC*WT), Race	363.31	< 0.0001	0.1299
2011-2012			
CVDRisk = (WC, WT, WC*WT)	190.83	< 0.0001	0.1414
CVDRisk = (WC, WT, WC*WT), Age, Gender, Race	166.20	< 0.0001	0.1727
CVDRisk = (WC, WT, WC*WT), Age	132.71	< 0.0001	0.1440
CVDRisk = (WC, WT, WC*WT), Gender	227.20	< 0.0001	0.1662
CVDRisk = (WC, WT, WC*WT), Race	145.52	< 0.0001	0.1439
2013-2014			
CVDRisk = (WC, WT, WC*WT)	226.11	< 0.0001	0.1381
CVDRisk = (WC, WT, WC*WT), Age, Gender, Race	153.23	< 0.0001	0.1750
CVDRisk = (WC, WT, WC*WT), Age	233.24	< 0.0001	0.1456
CVDRisk = (WC, WT, WC*WT), Gender	180.77	< 0.0001	0.1630
CVDRisk = (WC, WT, WC*WT), Race	178.79	< 0.0001	0.1393
2015-2016			
CVDRisk = (WC, WT, WC*WT)	124.32	< 0.0001	0.1206
CVDRisk = (WC, WT, WC*WT), Age, Gender, Race	135.71	< 0.0001	0.1707
CVDRisk = (WC, WT, WC*WT), Age	96.43	< 0.0001	0.1233
CVDRisk = (WC, WT, WC*WT), Gender	121.47	< 0.0001	0.1626
CVDRisk = (WC, WT, WC*WT), Race	94.34	< 0.0001	0.1228

CHAPTER V

5.0 DISCUSSION

Cardiovascular disease (CVD) linked to high lipid levels and abnormal anthropometrics remain an issue of public health importance. In the United States, the negative challenges of CVDs to health in general and productivity are diverse. Investigating CVDs risk is important for primary prevention and management. For instance, it is well established that higher cardiovascular risk (CVDRisk = TCHOL/HDL) is strongly associated with cardiovascular diseases (Pathak *et al*., 2017; Millan *et al*., 2009; Nam *et al*., 2006; Natarajan *et al*., 2003; Castelli *et al*., 1992; Kannel and Wilson, 1992). In this current study, we estimated the trend of cardiovascular risk from lipid profile measurements and selected anthropometric measurements over five bi-annual years in the US population. After this, the association between CVDRisk and selected anthropometric measurements was determined.

The overall mean BMI of adults ≥ 20 years for the five cohorts was 28.9 kg/m^2 from the analysis. This mean BMI implies that, on average, the US population is predominantly overweight. There was a significant increase of mean BMI from 28.3 kg/m^2 to 29.2 kg/m^2 ($t = 4.61$, $p = 0.0192$). While underweight, normal weight, and overweight declined from the 2007-2008 cohort through 2015-2016, all the three obesity classes saw a steady increase. It is uncertain if individuals in the overweight category are transitioning into the obesity categories as years go by. Analysis of data from succeeding years may confirm this transition. Of the three obesity classes, only the increase in obesity class III was not statistically significant. The linear increase in the three obesity classes is an indication that obesity in the US population is progressing upwards. This presupposes that CVDs influenced by obesity could be elevated in the absence of measures in high-risk groups as an early primary prevention intervention.

Of all the body measurement estimates, waist to height ratio (WHtR) is the most useful because it is easy to estimate and can recognize cardiometabolic risks across all demographics (Savva *et al*., 2013; Ashwell and Hsieh, 2005). For this study, the mean waist circumference (WC) for the population was 98.8 cm, and this increased significantly from 97.8 cm to 99.6 cm across the cohorts ($t = 7.12$, $p = 0.0057$). The overall mean WHtR was estimated to be 0.587. The suggested global threshold for WHtR is < 0.50 (Browning *et al*., 2010). In essence, to prevent cardiovascular diseases and minimize the effects of its events, it will be best to maintain waist circumference at less than half of the standing height. Mean WHtR increased significantly from 0.580 to 0.592 from cohort 0 to cohort 4 ($t = 7.20$, $p = 0.0055$). With the WHtR risk categories, 37.5% of the population had increased risk, while 62.5% had very high risk. While the prevalence of increased risk category declined significantly from 41.7% to 33.1% ($t = 14.38$, $p = 0.0007$) from the beginning of the study to the end, that of the very high risk category increased significantly from 58.3% to 67% ($t = 14.38$, $p = 0.0007$). In this study, every participant was at risk of CVDs (WHtR > 0.5). The WHtR is currently highly acclaimed as being better at discriminating cardiometabolic risks. Therefore, the outcome of this study raises public health concerns for the US population. There is an urgent need to encourage the population to participate in primary prevention activities to reduce their WHtR.

The mean TCHOL in the population decreased significantly over the period under study from 198.1 mg/dL to 189.5 mg/dL ($t = -4.15$, $p = 0.00254$). Although mean LDL and TRIG decreased as well, it was not statistically significant. Reduced mean TCHOL, LDL, and TRIG are protective atherogenic makers, advantageous to the US population. The mean HDL increased from 52.5 mg/dL to 53.2 mg/dL through 2015-2016 but was statistically not significant ($t = 2.16$, $p = 0.1192$). This increase in mean HDL for the population is anti-atherogenic and will potentially

support the abatement of metabolic syndromes and other risk factors associated with CVDs (Ascaso *et al*., 2007). Most of the population (70%) had the desirable TCHOL, LDL, and TRIG and there was no significant change across the years analyzed ($p > 0.05$). Although these desirable levels are protective, these individuals are could be potentially at risk if the necessary primary prevention strategies are not applied. Across the years, a significant proportion of the population was in the healthy level category for HDL. While the percentage of participants with low HDL decreased significantly ($t = 3.27$, $p = 0.0468$), that of the desirable HDL increased but was statistically insignificant ($t = 2.26$, $p = 0.1093$). Although not significant, an increasing percentage of individuals with desirable HDL in the US population is advantageous as it is known to offer strong protection against CVDs (Albrektsen *et al*., 2017).

Aberrations in lipid metabolism account for approximately 50% of the population's attributable risk of CVDs (Yusuf *et al*., 2004). These abnormalities are physiologically measured as the serum lipid profile and its associated calculated estimates. For instance, TCHOL/HDL ratio is deemed the most useful ischemic heart disease index in men. The TCHOL/HDL ratio application dwells on the premise that it is a collective marker of the cluster of metabolic abnormalities identified in persons with high triglycerides and reduced HDL (Lemieux *et al*., 2001). A study involving 32,826 menopausal women found TCHOL/HDL ratio a good predictor of CVD risk regardless of other associated predictors (Shai *et al*., 2004). In this current study, we provide estimates of the distribution of CVDRisk (TCHOL/HDL) categories in the US population and the relationship with selected correlates. The CVDRisk declined significantly by 0.05 annually through the 2015-2016 cohort ($p = 0.0467$). About 0.3% of the population had desirable risk. Approximately 93.1% were in the borderline risk, and 6.6% were in the high-risk category. All the risk classifications for CVDRisk declined across the bi-annual years considered. The percentage

of individuals with desirable CVDRisk decreased from 0.42% to 0.1% ($p = 0.0689$). The percentage of individuals with borderline CVDRisk increased from 90.7% to 93.8% ($p = 0.1176$). As well, that of the high CVDRisk also declined steadily from 8.9% to 6.2% ($p = 0.1464$). The American College of Cardiology (ACC) and the American Heart Association (AHA) guidelines suggests identifying and prescribing primary prevention remedies for low and borderline-risk individuals (Grundy *et al*., 2019). Individuals with borderline CVDRisk have a greater advantage of improving their lipid indices by lifestyle changes, that is, with healthy dieting and physical activity.

The TCHOL/HDL ratio was consistently higher in males than females for all the cohorts ($p < 0.01$) analyzed. Although data on CVDs occurrence is higher in men, information on higher risk associated with TCHOL/HDL is scanty. Available studies are either for only one gender or exclusively for those who are already experiencing a CVD. Comparing the referent age group, that is, 20-29 years for this current study, the prevalence of CVDRisk was significantly higher in all the age groups ($p < 0.01$). The CVDRisk began to heighten at age 30 through 69. After age 70 years, there was a decline when compared with the referent age group. It has long been established that cholesterol concentrations decline with advancement in age (Benfante *et al*., 1994) and this incongruence with findings of this current study where we saw a decline in CVDRisk after age 70. Mexican Americans and other Hispanics had a significant increase in CVDRisk compared to the referent Non-Hispanic Whites. The CVDRisk in Non-Hispanic Blacks reduced significantly compared to the referent Non-Hispanic Whites ($p < 0.01$) in all the cohorts. Comparable to a clinical trial that studied the racial differences in blood lipids, blacks' TCHOL/HDL ratios were significantly lower than their white counterparts ($p < 0.0001$). Regardless, this existing finding and that found in this current study, the overall CVD events are significantly high among blacks than

whites in the United States. This discrepancy suggests other factors beyond racial differences being responsible for CVDs (Saab *et al*., 2015; Kappelle *et al*., 2011).

From this study, waist circumference had a stronger independent association and a better predictor of CVDRisk when used alone, compared to the other anthropometric measurements. A previous study on regional fat localizations by Okosun *et al*. (2006), inferred that increased waist circumference is strongly associated with cardiovascular diseases and related risk conditions. The association between CVDRisk and the anthropometrics found the model involving WC, Weight (WT), and WC*WT to have the highest coefficients of determination for all cohorts. Altogether, WC, WT, and the WC*WT term significantly help to predict CVDRisk after adjusting for age, gender, and race/ethnicity. As well, we found that WT and WC do not operate independently of one another. This current study suggests that for the assessment of CVDRisk from total cholesterol and HDL ratio, the analysis should factor in participants' waist circumference and body weight measurements.

Conclusion

This study's outcome supports the urgency required to initiate or expand preventive efforts on the effects of abnormal plasma lipid levels in adults. We propose the use of TCHOL/HDL ratio in the assessment and preliminary screening for cardiovascular disease risk. We also suggest population-level strategies, lifestyle changes, environmental modifications, as well as socioeconomic status improvement.

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