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Associations of Youth Weight Status Categories and Cholesterol Levels: Analysis of Data from the National Health and Nutrition Examination Survey

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ASSOCIATIONS OF YOUTH WEIGHT STATUS CATEGORIES
AND CHOLESTEROL LEVELS:
ANALYSIS OF DATA FROM THE
NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

by

SANDRA C. METCALF

B.S.N., UNIVERSITY OF NORTH FLORIDA

A Thesis Submitted to the Graduate Faculty
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MASTER OF PUBLIC HEALTH

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APPROVAL PAGE

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April 23, 2012_____
Date

DEDICATION

For my mother,

who has always encouraged me to achieve higher education.

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CHAPTER I
INTRODUCTION

1.1 *Background*

Atherosclerotic cardiovascular disease is the leading cause of death in the United

States. Cardiovascular disease (CVD) events such as a heart attack, stroke and peripheral

arterial disease are the culmination of a disease process that begins at a young age and

spans decades of a person's life (Roger et al., 2012). Although CVD rarely manifests in

childhood, many risk factors and risk behaviors for the development and acceleration of

atherosclerosis begin in childhood (Daniels et al., 2011).

Predominant risk factors for CVD are family history, age, gender, hypertension,

dyslipidemia, overweight/obesity, diabetes, tobacco exposure, diet and physical

inactivity. There is increasing evidence that the number and/or severity of risk factors is

associated with CVD and that reducing risk factors delays disease progression (Berenson

et al., 1992; Magnussen et al., 2011). Thus, the aim of primary prevention for children

and adolescents is to identify and manage those at increased risk due to their identified

risk factors with the ultimate goal of risk reduction and thwarting CVD progression

(Raitakari et al., 2003; Webber, Srinivasan, Wattigney, & Berenson, 1991; Strong et al.,

1999).

Dyslipidemia is a term that describes abnormalities in lipoprotein metabolism and

often includes elevations in total cholesterol (TC), low-density lipoprotein cholesterol

(LDL-C) or triglycerides or deficiencies in high-density lipoprotein cholesterol (HDL-C).

Disorders can be related to genetic conditions and/or multi-factorial with relationship to

1

risk factors as described above (US Preventive Services Task Force, 2007). Non-high-density lipoprotein cholesterol (non-HDL-C) has recently emerged as a significant predictor of atherosclerosis in both children and adults. Non-HDL-C appears to be more predictive than TC, LDL-C or HDL-C for detecting dyslipidemia, atherosclerosis and future CVD events (Frontini et al., 2008; Srinivasan, Frontini, Xu, & Berenson, 2006). Non-HDL-C is especially advantageous in pediatric clinical practice because it can be measured from non-fasting samples. Non-HDL-C is calculated by subtracting HDL-C from TC which can be accurately obtained from non-fasting serum samples. Evidence supports the use of non-HDL-C as a screening measure for dyslipidemia in youth and the most recent screening guidelines include parameters for Non-HDL-C (Daniels et al., 2011).

A series of observational studies exist which clearly demonstrate the correlation of dyslipidemia with atherosclerotic development in youth (Daniels et al., 2011). Postmortem studies on children, adolescents and young adults have found significant associations between abnormal lipid levels and early atherosclerotic development of fatty streaks and fibrous plaque (Berenson et al., 1992; Daniels et al., 2011). Childhood dyslipidemia is also a predictor for increased carotid intima-media thickness, which is a precursor for atherosclerosis (Raitakari et al., 2003).

Pediatric guidelines include targeted dyslipidemia screening for youth at risk beginning at 2 years of age and universal screening between the ages of 17 and 21 years. The primary risk factors used in this targeted approach are a family history of premature CVD or dyslipidemia (Hagan, Shaw, & Duncan, 2008). In December 2011, the American Academy of Pediatrics (AAP) endorsed the *Expert Panel on Integrated*

Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents
(Expert Panel), which added to the existing recommendations, universal screening of all
children once between the ages of 9 and 11 years (Kavey, Simons-Morton, & de Jesus,
2011). This change was made in part, because recent research has shown that using
family history of premature CVD or dyslipidemia as the primary risk factor for pediatric
screening misses 30-60% of children with dyslipidemias (Derinoz et al., 2007). Other
predominant risk factors used to identify youth for targeted screening include
hypertension, diabetes, smoking and overweight. Of these risk factors, overweight
children and adolescents are especially of concern given the preponderance of obesity in
the US and the propensity of obesity itself to accelerate atherosclerosis (McGill et al.,
2001; Ogden, Carroll, Curtin, Lamb, & Flegal, 2010).

The American Academy of Pediatrics (AAP) follows the Centers for Disease
Control and Prevention (CDC) body mass index (BMI) overweight percentile cutoffs to
determine which youth meet the criteria for dyslipidemia screening. In children and
adolescents the preferred screening tool for weight status is the child's BMI percentile
distribution relative to gender and age which is derived from CDC 2000 growth charts
(Kuczmarski et al., 2000; Daniels et al., 2011). Overweight children are defined as those
with BMIs at the 85th percentile or greater and obese youth are those with BMIs at the
95th percentile or greater. Overweight youth, those at the 85th percentile or greater are
considered at risk and dyslipidemia screening is advised (Barlow & the Expert
Committee, 2007).

Extensive research has shown a positive relationship between adiposity status and
CVD risk factors in youth. However studies on the relationship of dyslipidemia and BMI

at the 85th percentile or greater are suggesting a need for additional research. Research conducted on US children has predominantly examined the relationship of obese, not overweight children and the development of atherosclerosis through pathology studies, carotid artery imaging studies or lipid levels. International studies have found positive associations between increasing levels of adiposity and more severe dyslipidemias. However, this research is not readily generalized to the US population because researchers used different classification systems for obesity and some studies were conducted in Asian populations whose diets are dissimilar to American western foods (Flechtner-Mors et al., 2011; Holl et al., 2011; Katzmarzyk, Tremblay, Perusse, Despres, & Bouchard, 2003; Kim Soh Ye, Hong Kyung Hee, Jang Ki Hyo, Kang Soon Ah, & Choue Ryo Won, 2005; Takada et al., 1998; Zhai et al., 2004). Additionally, in a recent study Lee et al. (2009) found BMI did not provide effective discrimination for detecting youth with elevated TC or LDL-C levels.

National expert organizations have designated BMI at the 85th percentile as the screening threshold for youth at risk for dyslipidemia, however additional research to support this cutpoint is needed. Although, the association of childhood obesity and CVD is well documented, studies on US youth specific to the relationship of BMI percentiles and dyslipidemia are lacking. There is a need to improve our understanding of overweight youth and their risk for dyslipidemias.

1.2 *Purpose of Study and Hypothesis*

Although overweight children with BMIs at or greater than the 85th percentile meet the at risk criteria for dyslipidemia screening, there is a scarcity of research on US youth that specifically study this association. Analysis from Bogalusa researchers found

CDC obesity BMI cutoffs to have low sensitivity and high specificity (Freedman, Mei, Srinivasan, Berenson, & Dietz, 2007). This finding is important because sensitivity and specificity respectively, refer to the ability of a test to correctly identify individuals with or without disease. Additionally, a recent study on NHANES subjects using current recommended screening thresholds found that BMI did not adequately identify youth with abnormal TC and LDL-C levels and called into question the current screening recommendations (Lee et al., 2009). Given the prevalence of overweight and obese youth in the United States, screening recommendations based on a threshold of the 85th BMI percentile results in a large number of children and adolescents to receive dyslipidemia screening.

The purpose of this research is to add to the body of knowledge on childhood and adolescent weight categories and their association with dyslipidemia. This research seeks to elucidate whether US youth with BMIs at the 85th percentile or greater are at increased risk for dyslipidemia compared to children and adolescents who are at a healthy weight. The study group will consist of youth 6 to 18 years of age who participated in NHANES during the cycle years from 2007 to 2010. The objective of using sample groups from the latest NHANES surveys is to more closely mirror the current US population. The study hypothesizes that children and adolescents who are overweight are at greater risk for dyslipidemia compared to normal weight youth.

CHAPTER II

REVIEW OF THE LITERATURE

2.1 *Cardiovascular Disease*

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide. In 2008, 17.3 million deaths occurred worldwide due to CVD. Of these deaths, 7.3 million were from heart attacks and 6.2 million from strokes (Mendis, Puska, & Norrving, 2011). In the United States, for the past 90 years CVD has accounted for more deaths than any other cause. Approximately one in three persons in the United States has some form of CVD and one in three deaths are attributed to CVD. Cardiovascular disease causes more deaths each year than cancer, accidents and chronic lower respiratory diseases combined (Lloyd-Jones et al., 2009).

Cardiovascular disease includes diseases of the heart and vascular diseases of the blood vessels to the heart, brain and peripheral arteries. In the adult, acute CVD events, such as myocardial infarction and stroke, occur after the long-term development of atherosclerosis and thrombotic events associated with atherosclerotic plaque instability. In pediatrics, the primary component of this process is the development of atherosclerosis, because CVD thrombosis does not occur in the absence of atherosclerosis. Although CVD in children and adolescents is rare, risk factors and behaviors that contribute to atherosclerosis often begin in childhood and there is increasing evidence that reducing these risk factors can delay progression of atherosclerosis and eventual CVD (Daniels et al., 2011).

2.2 *Expert Guidelines and Recommendations*

To address this health issue, in 2006, an Expert Panel was appointed by the National Heart, Lung, and Blood Institute (NHLBI) to conduct a formal evidence review and to develop cardiovascular health and risk reduction guidelines for pediatric care providers. The Expert Panel's approach to this guideline development was characterized by formal evidence review and integration of multiple major CVD risk factors into one document. The Full Report of the Expert Panel is available on the NHLBI website and these Expert Panel guidelines were endorsed by the American Academy of Pediatrics (AAP) in 2011 (Daniels et al., 2011).

Prior to release of the Expert Panel's report, guidance for dyslipidemia screening in children was primarily presented through two publications, the AAP policy statement *Lipid Screening and Cardiovascular Health in Childhood* and *Bright Futures 3rd Edition Guidelines.* The AAP policy statement, published in 2008, presented three different sets of guidelines to use in determining normal and abnormal lipid levels. One set of guidelines was adapted from the 1992 *National Cholesterol Education Program: Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents.* Another was adopted from the American Heart Association, while a third, percentile ranking table, was adapted from the Lipid Research Clinic Pediatric Prevalence Study. Although the National Cholesterol Education Program (NCEP) and AAP recommend a targeted approach to screen children with certain risk factors (i.e., family history of premature CVD or hypercholesterolemia, diabetes, hypertension and obesity) research to optimize screening protocols has not led to consensus in pediatric screening (Daniels, Greer, & the Committee on Nutrition, 2008).

In 2007, the US Preventive Services Task Force (USPSTF) (2007) concluded that evidence was insufficient to recommend for or against routine screening for dyslipidemia in youth and young adults up to age 20. The USPSTF could not address key questions about screening and treatment of dyslipidemia in children and adolescents because studies were lacking. However, due to the nature of pediatric research, pediatric prevention unfortunately is often based upon less rigorous scientific evidence, and "Insufficient" recommendations from the USPSTF are not uncommon (Daniels, Greer, & Stettler, 2008; Moyer & Nelson, 2008). The lack of studies in this area of pediatric research is due in part because longitudinal studies linking childhood risk factors to CVD would involve extensive periods of time in the range of 50 to 60 years duration and clinical trials of voluntary risk exposure in children are unethical (Daniels et al., 2011).

The recent report of the *Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents* is a comprehensive review and critical appraisal of every relevant study available on the multiple risk factors for CVD development, progression and management. The Expert Panel followed an Evidence Grading System adapted from the American Academy of Pediatrics Steering Committee on Quality Improvement and Management. The Expert Panel assigned the Evidence Review for Lipid Assessment in Childhood and Adolescence a Grade B (strongly recommended). Evidence for a Grade B was based on randomized controlled trials or diagnostic studies with minor limitations, genetic natural history studies, and/or overwhelmingly consistent evidence from observational studies. The definition for a strong recommendation as included in the report is that the benefits clearly exceed the harms and that the quality of the supporting evidence is excellent. In some

circumstances, strong recommendations were made on the basis of lesser evidence when high-quality evidence was impossible to obtain and the anticipated benefits clearly outweighed the harms. Unlike earlier policy statements and guidelines, the Expert Panel Report has integrated the evidence and produced conclusive detailed tables and algorithms to follow for lipid assessment that address age variance. The Expert Panel determined that CV risk reduction in children and adolescents addresses the disease process atherosclerosis, in which the clinical endpoint of manifest CVD occurs much later in life (Daniels et al., 2011).

2.3 *Atherosclerosis*

Atherosclerosis is responsible for a large proportion of cardiovascular diseases. It is an underlying pathological process in the blood vessels that develops over many years. In atherosclerosis, plaque which consists of fatty substances and cholesterol, builds up in arteries. Over time the plaque hardens and the arterial lumen narrows with resultant decreased blood flow and potential clot formation. The atherosclerotic process often leads to disruption of blood supply to vital organs such as the heart and brain, resulting in cardiac and cerebral events (Mendis, Puska, & Norrving, 2011).

The earliest sign of atherosclerosis is the fatty streak, which is an accumulation of lipid-filled macrophages in the intimal layer of the artery. Progression of atherosclerosis occurs with accumulation of smooth muscle cells and fibrous tissue produced by the fat laden smooth muscle cells. Over time the fatty streak evolves into a fibrous plaque, the hallmark of established atherosclerosis. The buildup of plaque restricts blood flow by narrowing arteries, hardening arterial walls and clot formation. Cessation of blood

supply causes lack of oxygen and tissue infarction, which damages the affected tissues or organs (Crowther, 2005; Daniels, Greer, & the Committee on Nutrition, 2008).

2.4 *Childhood Risk Factors for Adult CVD*

Most of the clinical burden of atherosclerosis occurs in middle to older adulthood, but the pathological process of atherosclerosis begins in childhood (Juonala et al., 2010). Pathology studies have confirmed the atherosclerotic process begins at a young age. Autopsy studies of young soldiers killed in the Korean and Vietnam Wars found evidence of atherosclerosis (Enos, Homes, & Beyer, 1953; McNamara, Molot, Stremple, & Cutting, 1971). In the Korean War study, 300 soldiers who were battle casualties were examined for gross lesions in the coronary arteries. The ages of the first 98 soldiers were not recorded, except that the oldest was 33 years of age. The average recorded age of the remaining 200 soldiers was 22 years of age, ranging from 18 to 48 years. Cases with known clinical evidence of coronary disease were excluded from the study. Findings indicated 77% had evidence of atherosclerosis (Enos, Homes, & Beyer, 1953; Le, Zhang, Menees, Chen, & Raghuveer, 2009). In the Vietnam War study, postmortem examination of 105 soldiers with coronary angiography and heart dissection revealed 45% with some evidence of atherosclerosis and 5% with gross evidence of severe coronary atherosclerosis (McNamara et al., 1971).

The study, Pathobiological Determinants of Atherosclerosis in Youth (PDAY) was a multi-institutional study which was initiated to document the natural history of atherosclerosis, its relationship to risk factors, and the pathobiology of lesion development in young subjects (Strong for the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group, 1995). PDAY studies conducted

from 1987 to 1994, examined subjects from 15 to 34 years of age, because this is the age when fatty streaks are prevalent and fibrous plaques begin to appear (Strong et al., 1999). This study included 1079 males and 364 females, black and white, who died from external causes (suicide, homicide and accidents).

PDAY studies have described the effects of age, sex, race, dyslipidemias, smoking, hypertension, diabetes and obesity on the microscopic development of atherosclerosis in youth and young adults. The extent of arterial intima involved with fatty streaks and raised lesions increased with age in both sexes and race groups. Investigators found strong relationships between the degree of atherosclerosis and the extent of known risk factors, including increasing age, increasing levels of non-HDL-C, lower HDL-C, hypertension, impaired glucose tolerance, smoking, and obesity in males. The severity of atherosclerosis was markedly increased in subjects with multiple risks (McGill et al., 2001; Strong for the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group, 1995).

PDAY researchers devised youth risk scores for predicting advanced atherosclerotic lesions using modifiable risk factors of dyslipidemia, tobacco use, hypertension, obesity and hyperglycemia. Subjects with higher risk scores had significantly higher odds ratios for atherosclerotic lesions. The prevalence of advanced atherosclerosis in the high-risk 15 to 19 year olds was nearly the same as low-risk 30 to 34 year old subjects (McMahan et al., 2006).

The Bogalusa Heart Study was a long-term epidemiologic study of cardiovascular disease risk factors in persons from birth through 38 years of age. The study began in 1973 in the biracial community of Bogalusa, Louisiana. Bogalusa investigators

performed autopsy studies on 204 persons, 2 through 39 years of age. The causes of

death varied, but principally were due to accidents and homicide. Subjects were

evaluated for extent of atherosclerotic lesions in the aorta and coronary arteries.

Investigators found the extent of fatty streaks and fibrous plaque increased with age.

This age related trend was especially significant in the coronary arteries where the

prevalence of fibrous plaques increased from 8% in the 2 to 15 year old group, to 69% in

the 26 to 39 year old group (Berenson et al., 1998).

In the Bogalusa study, investigators conducted six cross-sectional surveys which

included over 3,500 children. The first survey examined 5 to 14 year old subjects.

Subsequent surveys were conducted throughout school age and beyond high school.

Findings from Bogalusa report on the positive association of cardiovascular risk factors,

body mass index (BMI), blood pressure, lipid levels and the development of

atherosclerosis in the aorta and coronary arteries (Berenson et al., 1998; Berenson et al.,

1992; Newman et al., 1986).

Two large studies utilized ultrasonography, a non-invasive method, to detect

atherosclerosis by measurement of carotid artery intima-media thickness (IMT), a

surrogate measure for CVD. The validity of using carotid IMT as a reliable marker for

atherosclerosis is well documented (de Groot et al., 2004; Roger et al., 2012). The

Rotterdam Study and the Atherosclerosis Risk in Communities (ARIC) Study found that

carotid IMT correlates positively and significantly with vascular risk factors and

cardiovascular disease. Additionally, in the ARIC study, carotid ultrasonography was

able to determine all stages of atherosclerosis (Bots, Hoes, Koudstaal, Hofman, &

Grobbee, 1997; Heiss et al., 1991.

The Muscatine study was a longitudinal cohort study which began in 1971 with biennial examinations of school children 8 to 18 years of age in Muscatine, Iowa. Ultrasonography was used in the Muscatine study in the 1990s to determine the relationship of higher carotid IMT with cardiovascular risk factors that occurred in childhood and beyond. The study included 725 male and female participants who had previously participated in at least one childhood survey and had reached the age of 33 to 42 years. In this cohort, childhood risk factors measured as early as 8 to 11 years of age and predictive of high adult carotid IMT were TC for both men and women and BMI for women (Davis, Dawson, Riley, & Lauer, 2001).

In the Bogalusa study, investigators measured carotid IMT to evaluate the influence of gender, ethnicity and risk factors on early stages of atherosclerosis. The study included 518 male and female subjects, with a mean age of 32 years. The subjects were overweight, but otherwise healthy, asymptomatic young adults. Cardiovascular risk factors evaluated included obesity, hypertension, dyslipidemia, hyperinsulinemia and smoking. After adjustments for age, race and sex, carotid IMT was associated significantly and positively with waist circumference, systolic blood pressure, diastolic blood pressure, and LDL cholesterol. Carotid IMT was inversely correlated with high-density lipoprotein (HDL) cholesterol levels. Participants with greater numbers of adverse risk factors had stepwise increases in mean carotid IMT levels (Urbina et al., 2002).

Probably the most compelling evidence that childhood dyslipidemia risk factors are related to adult CVD is the manifestation of cardiovascular conditions. Familial hypercholesterolemia (FH) is an autosomal dominant disorder characterized by

abnormally high concentrations of LDL-C. FH is one of the most common inherited

disorders with an estimated worldwide prevalence of 1 in 500 (Austin, Hutter, Zimmern,

& Humphries, 2004). The dyslipidemia associated with FH leads to increased risk for

CVD and death. Risk for coronary heart disease (CHD) and cardiac events is much

higher with 50% of FH men and 25% of FH women experiencing clinical coronary

events by 50 years of age (Neil et al., 2008; Stone, Levy, Fredrickson, & Verter, 1974).

Adding to the evidence of causation, the use of statin medications to reduce dyslipidemia

in FH subjects has been shown to reduce morbidity and mortality (Neil et al., 2008).

Furthermore, the ARIC study found that persons with genetic traits associated with low

cholesterol had conferred protection against CHD and significantly lower measures of

carotid IMT (Cohen, Boerwinkle, & Hobbs, 2006). Collectively these studies helped to

establish the association of childhood dyslipidemia as a risk factor for adult CVD.

2.5 *Childhood Risk Factors Track into Adulthood*

Risk factors for CVD and atherosclerosis can be categorized as life conditions

(e.g., family history, age, gender), pathophysiologic (e.g., hypertension, dyslipidemia,

overweight, diabetes), behavioral (e.g., tobacco exposure, nutrition, physical activity) and

emerging (e.g., metabolic syndrome, inflammatory markers, perinatal factors) (Daniels et

al., 2011). The strongest risk factors include obesity, dyslipidemia, hypertension,

diabetes, and tobacco use (Daniels, Greer, & The Committee On Nutrition, 2008; Wilson

et al., 1998). Research has demonstrated that these pathophysiologic risk factors can be

present at young ages and track into adulthood (Berenson et al., 1998; Juonala et al.,

2005). A detailed review of all risk factors is beyond the scope of this thesis. Obesity

and dyslipidemia, individually, are broad topics. Because obesity and dyslipidemia as

screening indices in childhood are the focus of this study, this literature review will aim to present research findings relevant to childhood overweight/obesity and its' associations with dyslipidemia, although brief mention of other risk factors and related components of overweight/obesity and dyslipidemia may be included.

In epidemiologic studies, tracking describes consistency and longitudinal development of risk factors over time (Magnussen et al., 2011; Twisk, Kemper, & Mellenbergh, 1994). From a pediatric viewpoint, tracking analyses are beneficial because they can predict future values from early life measurements and aid in determining which risk factors to target for primary prevention or treatment. Tracking indicators are generally correlations between repeated measurements of an attribute at different times and the proportion of participants that remain in the group. Due to established associations of dyslipidemia and CVD in adults, blood lipid levels have been studied for tracking in children and adolescents.

A number of prospective studies on the tracking of lipids from youth into adulthood exist. In the Bogalusa Heart Study, a study cohort was derived and monitored for an average of 27 years. There were 1163 subjects, 30% black and 55% female who were 5 to 14 years at baseline. Investigators studied persistence of ranking of non-HDL-C and LDL-C levels in quintile levels from childhood to adulthood. For both cholesterol levels 66% of subjects who were above the 60th percentile in childhood remained above the 60th percentile as an adult. Of the variables studied, baseline levels of non-HDL-C and LDL-C were the best predictors for adult levels with standardized regression coefficients of 0.36 and 0.40 respectively. Change in BMI from childhood to adulthood was the next best predictor for both variables with standardized regression coefficients of

0.20 for non-HDL-C and 0.22 for LDL-C. Children in age-, gender- and race-specific top quartiles of non-HDL-C and LDL-C were compared to those in the bottom quartiles and had odds ratios of 4.5 and 3.5 respectively to develop dyslipidemia (Srinivasan, Frontini, Xu, & Berenson, 2006).

Muscatine investigators found that increased cholesterol values during childhood were associated with increased values as adults. A cohort of 2446 subjects were initially examined at 8 to 18 years of age, then re-examined between 20 to 30 years of age. Eighty one percent of children who had cholesterol values above the 50th percentile remained above the 50th percentile as an adult. Of those that were at or above the 75th percentile, 62% remained at this level as an adult. For the highest level at or above the 90th percentile, 43% remained as adults. Fifty to 87% of children whose cholesterol levels exceeded the 90th percentile were above the 75th percentile as adults. Conversely, if children's cholesterol levels were less than the 90th percentile, 78 – 84% were below the 75th percentile as adults. The 75th percentile cutoff was used in this study because it was the National Cholesterol Education Program recommended benchmark to implement dietary interventions in adults with dyslipidemias (Lauer, Lee, & Clarke, 1989).

In the Cardiovascular Risk in Young Finns Study tracking and predictiveness of lipid measurements of Finnish youth were analyzed over a 12 year period. The cohort included 883 subjects from 3 to 18 years of age with 47% male. Spearman's correlation coefficients for 12–year tracking were as follows: TC 0.48-0.58, LDL-C 0.53-0.58, HDL-C 0.53-0.58, LDL:HDL cholesterol ratio 0.57-0.59 and triglycerides 0.33-0.37. Approximately 50% of participants who were in the extreme quintiles for TC, LDL-C and HDL-C on initial exam remained in the same quintiles after 12 years. In multiple

regression analyses, conducted by Porkka, Viikari, Taimela, Dahl, and Akerblom (1994) childhood obesity, exercise, diet, and smoking habits did not markedly aid the prediction of adult serum lipid values.

Friedman (2006) found a wide range of test agreement values in tracking of lipid abnormalities from childhood to adulthood. The Princeton Lipid Research Clinics Prevalence Program Follow-Up Study was a prospective study to determine sensitivity and specificity of National Cholesterol Education Program (NCEP) pediatric cutoff points during youth for adult lipid status. The derived cohort included children 5 to 19 years of age when initially studied in the Cincinnati Clinic of the Lipid Research Clinics (LRC) Prevalence Study from 1972-1978. Study participants for the Princeton Follow-Up Study (PFS) were students in 1st to 12th grade in public and parochial schools in the Princeton School District. The study group was 73% white, 27% black, 52% male and 48% female. A total of 844 subjects were evaluated for LDL-C tracking and 897 subjects for TC tracking. Guidelines from the NCEP were followed for determining adult elevated TC and LDL-C levels (Friedman, 2006).

Reported overall sensitivities were 43 to 46% and specificities were 82 to 86% for total and low-density lipoprotein cholesterol levels respectively. The positive predictive values were 39% for TC and 31% for LDL-C. Negative predictive values were 88% for TC and 91% for LDL-C. Researchers examined sensitivity and specificity of the entire cohort according to age. Sensitivities ranged from 18% (16 years old) to 63% (11 years old) for TC, and 22% (15 years old) to 69% (9 years old) for LDL-C. The highest sensitivities occurred in the younger age groups between 5 and 11 years of age and the lowest occurred at 14 to 16 years of age. Sensitivities seemed to be increasing in the 17

to 19 year old groups (~49% TC and ~65% LDL-C) to levels similar to the younger ages. The specificities were high ranging from 77 to 96%. This study was especially of merit in delineating the variability in sensitivities at different ages.

Childhood to adult lipid tracking was described in another prospective study by Stuhldreher et al., (1991). In the Beaver County Lipid Study investigators conducted follow-up screening on 295 adults who had initially participated as children in a school-based screening program at the ages of 11 to 14 years. The follow-up phase of the study was conducted 16 years after the baseline study conducted in 1972 -1973 when the subjects had reached a mean age of 28 years. Overall correlation coefficients between the baseline and follow-up study for TC levels were 0.44 ($P<0.0001$). Correlation coefficients for women were higher ($r = 0.51$) compared to men ($r = 0.38$). Based on recommended guidelines, cutoffs for elevated TC levels or positive test results were established at 175 mg/dl in children and 200 mg/dl in adults. Researchers reported sensitivity of 63%, specificity of 67% and a positive predictive value of 47% for screening at 12 years of age and predicting elevated adult TC levels.

For this Beaver study, a false-positive test was a child who was above the cutoff as a child, but not as an adult. A false-negative test was a child who was below the cutoff as a child, but not as an adult. A comparison of test results found that male and female subjects with false-positive results smoked significantly less than those with false-negative results. In addition, false-positive males had a greater improvement between evaluation periods in cholesterol-lowering dietary practices. Comparisons also revealed that female subjects with false-positive results were less overweight and had a lower prevalence of oral contraceptive use. Researchers surmised that although some subjects

were misclassified as a result of childhood screening, some misclassification was associated with adopting changes that would be promoted through a screening and intervention program such as tobacco cessation, achieving healthy weight and dietary changes.

2.6 Childhood Obesity Tracks into Adulthood

Of all the aforementioned pathophysiologic risk factors, obesity tracks from childhood to adulthood the strongest (Daniels et al., 2011). Childhood levels of obesity are epidemic in the US and since 1980 obesity prevalence in school aged children has tripled. Data from the 2007 National Survey of Children's Health and the 2007-2008 NHANES find approximately 32% of youth are overweight and approximately 17% are obese (Odgen, Carroll, Curtin, Lamb, & Flegal, 2010 ; Singh, Kogan, & van Dyck, 2010). Reports from the most recent NHANES survey 2009-2010 indicate no change in childhood obesity prevalence from 2007-2008 (Ogden et al., 2010).

Centers for Disease Control and Prevention (CDC) growth charts with BMI percentiles relative to age and gender are the preferred reference to identify overweight and obesity in youth from 2 to 18 years of age. Expert committee recommendations with representation from 15 national health care organizations, recommend using BMI on individual children in order to assess weight-for-height relationships. BMI as an obesity measure has limitations such as, it does not directly measure body fat, and does not take into account skeletal size or muscle mass (Wilk, 2007). Thus, a very muscular person may have a BMI which falls into an overweight category. Although there are some limitations, BMI is easily calculated, correlates strongly with direct measure of body fat and has acceptable accuracy especially in identifying individuals with higher amounts of

body fat, e.g. those above the 85th percentile. The expert committee convened by the

American Medical Association, the CDC and the Maternal and Child Health Bureau

(MCHB) has defined childhood and adolescent obesity as a BMI at or greater than the

95th percentile and BMIs between the 85th and 94th percentiles as overweight (Barlow &

the Expert Committee, 2007; Daniels et al., 2011).

Investigators from the Bogalusa Heart Study reported that childhood BMI is

associated with adult obesity. In this study with over 2600 participants, 77% of obese

youth (BMI at or greater than the 95th percentile) remained obese (BMI at or greater than

30 kg/m²) as an adult. Children 2 to 17 years of age were re-examined at 18 to 37 years

of age. The mean follow-up time was 17 years. The magnitude of correlations between

childhood and adult obesity increased with age of childhood measurement. The BMIs of

2 to 5 year olds were moderately associated with Spearman's correlation coefficients at

0.50 and 0.45 for males and females respectively. Associations increased with age with

the strongest BMI association occurring in 15 to 17 year old adolescents 0.74 and 0.66

for males and females respectively (Freedman, Khan, Dietz, Srinivasan, & Berenson,

2001; Freedman et al., 2005).

Muscatine researchers report even higher tracking correlations for BMI that range

from 0.58 to 0.91. This study involved 2631 children from 9 to 18 years of age that were

followed into their young adult life and re-examined between the ages of 23 and 33 years.

An interesting finding in this study was that approximately 31% of children in the top

quintile of BMI became adults that fell into a much lower weight category and that

approximately the same percentage of lean children became obese adults. Similar to the

Bogalusa study, Muscatine investigators also found tracking associations increased as

childhood age increased with correlations of adult Quetelet Index (weight divided by height²) lowest at 0.45 in the 7 to 8 year old female group and reaching a maximum of 0.74 in the 13 to 14 year old males (Clarke & Lauer, 1993).

In the National Heart, Lung and Blood Institute Growth and Health Study (NGHS) a cohort of 2379 bi-racial females were examined annually from the age of 9 or 10 through 18 to 19 years of age. NGHS-Wave II was conducted as a follow-up telephone interview when the subjects were between 21 to 23 years of age. There were 2054 participants in NGHS-Wave II which included 991 Caucasians and 1063 African-American girls. Overweight in youth up to 18 years of age was defined by attainment of the 95th percentile for BMI, and for young adults 21 years of age and older BMI was defined as at or greater than 30 kg/m². Study participants who were overweight from age 9 to 18 years were 11 to 30 times more likely to be obese as adults compared to not overweight girls. Investigators noted the limitation that self-reported body measurements in the follow-up study presented, but nonetheless found these strong associations noteworthy (Thompson et al., 2007).

2.7 *BMI as a Predictor for Dyslipidemias*

Bogalusa researchers found that dyslipidemia was associated with increased BMI. In the Bogalusa study, overweight children 5 to 17 years of age compared to normal weight children were 2.4 times as likely to have elevated levels of TC, 3.0 times more likely to have high LDL-C and 3.4 times as likely to have low HDL-C (Freedman, Dietz, Srinivasan, & Berenson, 1999). NGHS researchers found strong associations between obesity and some dyslipidemia markers. Obese females 9 to 18 years of age were 6.3 times more likely to have HDL-C levels less than 50 mg/dl, and 3.3 times more likely to

have triglyceride levels at or greater than 130 mg/dl. Obesity in this cohort was not significantly associated with elevated TC or elevated LDL-C levels. Researchers adjusted for pubertal maturation as there was some association with lipids. In this secondary analysis with adjustment for pubertal maturation, elevated LDL-C levels were significantly associated with obesity with OR = 3.0 (P = .01). Total cholesterol remained not significantly associated (Thompson et al., 2007).

Holl et al. (2011) report on their findings from a large cross-sectional study conducted in Germany on subjects that were analyzed beginning in 2003. The study purpose was to report on the effects of age, gender and obesity category on dyslipidemia components. Participants included 29,711 overweight and obese subjects from the German, Austrian and Swiss APV registry (mean age 12.61 $\pm$ 3.14) and the comparison group of 11,110 normal-weight subjects from the German Health Interview and Examination Survey for Children and Adolescents, KIGGS (mean age 9.8 $\pm$ 4.7). Cutoffs for abnormal lipid values were based on American Heart Association recommendations, and with conversion from mmol/L to mg/dl were approximately TC greater than 200 mg/dl, HDL-C less than 35 mg/dl, LDL-C greater than 130 mg/dl, and triglycerides greater than 150 mg/dl. Weight classifications used were different than the customary US standard, and were based on BMI-SDS values calculated with German normative data. Youth were normal weight with BMI less than the 90th percentile, overweight with BMI from the 90th to 97th percentile, obese with BMI between the 97th to 99.5[th] percentile and extremely obese with BMI greater than the 99.5[th] percentile. Although not a study on a US population, given the size of the cohort and significant

findings which are especially pertinent to the analysis section of this thesis, it is worthy of inclusion in this review.

As BMI categories increased, the prevalence of hypertriglyceridemia and reduced HDL-C increased rapidly. A weaker relationship was present for LDL-C and TC, however still with high significance ($p<0.0001$). Holl et al. (2011) reported at least one abnormal lipid value was found in 13.4% of normal-weight subjects, 24.3% of overweight patients, 27.9% of obese subjects and 31.9% in the extremely obese group ($p<0.0001$). Multiple logistic regression analysis with age and gender as covariates in addition to BMI categories resulted in significant relative risk (RR) increases according to BMI category increases. The RRs in comparison to normal weight subjects were as follows: for reduced HDL-C 1.52 (1.24-1.86) in overweight subjects to 4.39 (2.89-3.97) in extremely obese subjects, for elevated triglycerides 3.21 (1.18-8.75) in overweight subjects to 4.86 (1.79-13.18) in extremely obese subjects, for LDL-C the RR increased to 1.94 (1.76-2.14) and for TC to 1.43 (1.31-1.57). If the criterion of at least one abnormal lipid component was applied the RRs were as follows: 2.07 (1.87-2.28) for overweight subjects, 2.49 (2.33-2.67) for obese subjects and 3.02 (2.83-3.24) for extremely obese subjects (Holl et al., 2011).

2.8 *Lipid Profile Statistics for US Youth*

In an effort to present data that is more relevant to the state of current US youth lipid levels, this review will focus on recent studies that used data from the National Health and Nutrition Examination Survey (NHANES). NHANES conducted by the CDC's National Center for Health Statistics is a population based survey that examines nationally representative samples of the US non-institutionalized civilian population.

Data from NHANES is used to produce national estimates of US health and nutrition status. Previous National Health and Nutrition Examination Survey (NHANES) studies have found prevalence of dyslipidemias in children and adolescents of approximately 10% for TC, 26% for triglycerides, 6.6% for LDL-C and 19% for HDL-C (Ford, Li, Zhao, & Mokdad, 2009; Johnson et al., 2009; Li et al., 2010).

Li and colleagues (2010) compared statistics from a large national insurance claims database and NHANES 1999-2004 survey data. In analysis of data from the NHANES cohort an estimated 7.4 million children out of 30 million US children (weighted frequency with fasting weights, unweighted n=585) had laboratory-defined dyslipidemia. Laboratory defined dyslipidemia was identified by subjects having at least one abnormal lipid measure regardless of fasting status. The dyslipidemic measurements were as follows: TC $\geq$ 200 mg/dl, HDL-C < 35 mg/dl, LDL-C $\geq$ 130 mg/dl, Triglycerides $\geq$ 130 mg/dl, Apolipoprotein A-I, (Apo-A) < 110 mg/dl, or Apolipoprotein B (Apo-B) $\geq$ 100 mg/dl. With application of mobile examination center (MEC) and fasting weights this yielded a prevalence of approximately 19.9% (95% CI: 18.3-21.6) to 23.9% (95% CI: 21.60-26.27) respectively.

Children from 10 to 18 years of age with laboratory defined dyslipidemia were defined from the Integrated Healthcare Information Services (IHCIS) database for the years from 2003-2006. The IHCIS database contained 273,064 children with at least one laboratory lipid value. Of these children 22.9% (n=62451) had laboratory defined dyslipidemia. A comparison cohort of 10 to 18 year old children was derived from NHANES survey years 1999-2004. Prevalence for the IHCIS and NHANES cohorts were similar for triglycerides at 13.2% and 14.2% respectively. Although prevalence of

overall dyslipidemia was similar, the prevalence for TC, HDL-C and LDL-C was lower in the IHCIS cohort (TC 9.6% vs. 7.7%, HDL-C 6.7% vs. 4.1%, and LDL-C 7.2% vs. 3.2%). Several theories for this were suggested by the researchers, such as insured status, health status, interventions and selection bias (Li et al., 2010).

The occurrence of dyslipidemias differed by age and gender amongst the two cohorts. In the NHANES cohort 10 to11 year old boys displayed the highest prevalence (58%) of TC compared to 16-18 year old boys with the lowest prevalence (27%). Whereas TC prevalence for girls in the NHANES group was 45% in the 12 to 13 year old group and increased to 63% in the 16 to 18 year old girls. The same trends were seen in the IHCIS cohorts for boys and girls.

For HDL-C, age-related dyslipidemia was reversed, with 10 to 11 year old boys in the NHANES group at the lowest prevalence (24%) compared to 16 to 18 year boys with the highest prevalence (57%). This same trend was found in the IHCIS cohort, with the boys steadily increasing prevalence of dyslipidemic HDL-C with age. There were differences between the cohorts for girls with dyslipidemic HDL-C. In the NHANES cohort, dyslipidemic HDL-C decreased as the girls increased in age, whereas in the IHCIS girl's cohort this did not occur.

For dyslipidemic triglycerides no age-related changes were found in the NHANES groups, whereas in the IHCIS cohort boys demonstrated an age-related increase. LDL-C dyslipidemias were highest in the NHANES 10 to 13 year old boys at 37% compared to prevalence of 23% in the 16 to 18 year group. Smaller age-related increases were also found in the IHCIS boys. Girls in both cohorts experienced age-related increases (J. Li et al., 2010).

IHCIS cohort data shows a decrease in TC dyslipidemia prevalence in the 12 to 13 year old female group and 14 to 15 year old male group which then begins to rebound with increasing age. This same trend occurs for LDL-C. Detailed data on the NHANES cohort was not available for comparison. This change in dyslipidemic TC and LDL-C prevalence at pubertal ages is consistent with other reported research where TC and LDL-C levels decreased by 10 to 20% during puberty (Berenson, Srinivasan, Cresanta, Foster, & Webber, 1981; Kwiterovich et al., 1997).

Hickman et al. (1998) report on lipid distributions of NHANES data (1988-1994) which demonstrate similar trends for TC and HDL-C. Children in the 9 to 11 year old group had the highest mean TC values (171 mg/dl). Females had higher mean TC (167 mg/dl) than males (163 mg/dl). Among racial groups non-Hispanic blacks had significantly higher mean TC values (170 mg/dl) than non-Hispanic whites (164 mg/dl) or Mexican Americans (164 mg/dl). Consistent with research on pubertal changes, boys mean TC levels were significantly less in the 12 to 15 year old group compared to boys 9 to 11 years of age ($P < 0.0001$). Hickman and colleagues report that mean TC levels among adolescents decreased by 7 mg/dl ($P<0.0001$) from 1966 to 1994. This same trend had previously been reported in adults and is believed to have contributed to the decrease in mortality from CHD during the same period of time.

HDL-C levels were relatively constant across all age groups, except that boys mean HDL-C levels decreased significantly from the 9 to 11 age group to the 12 to 15 year old group ($P < 0.0001$). Overall, the means for HDL-C were similar for both sexes. Although in females the mean steadily increased with age, whereas in boys the mean was highest in the 9 to 10 year old group then steadily decreased. Non-Hispanic blacks had

the highest mean HDL-C levels (55 male, 56 female) compared to non-Hispanic whites

(48 male, 50 female) and Mexican Americans (51 male, 52 female).

The Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk

Reduction in Children and Adolescents include in their report that differences exist

according to race and ethnicity according to geography and that these differences could

be explained in part by socioeconomic status. However, the Expert Panel also points out

"that no group in the U.S. is without a significant prevalence of risk" (Kavey, Simons-

Morton, & de Jesus, 2011, p. S4). Several longitudinal cohort studies have included

biracial populations, but longitudinal studies that include Hispanic, Asian and Native

American youth are lacking.   The Expert Panel acknowledges that differences exist in

risk factor prevalence according to gender and race and that low socioeconomic status

alone confers substantial risk. However, the "evidence is not adequate" for the Expert

Panel to make recommendations specific to racial or ethnic groups or socioeconomic

status (Kavey et al., 2011, p. S4).

2.9 *Reliability of BMI at 85th percentile as a Risk Factor*

As previously described, a number of prospective studies have reported tracking of

lipid levels from childhood into adulthood. These studies have found that youth to adult

levels correlate in the range of 0.4 (Daniels et al., 2011). However, Magnussen et al.

(2008) report on the instability of the classification of blood lipid levels in youth, to

predict dyslipidemias in adults. The results of their study show that 60% of youth who

were identified with high risk LDL cholesterol levels did not have abnormal levels as

adults and that most adults who developed low HDL-C did not have dyslipidemic HDL-C

as youth. These findings contribute to the uncertainty surrounding the approach to and utility of screening for pediatric dyslipidemias (Magnussen et al., 2011, p. 68).

There is a volume of research that has examined the relationship between adiposity status and CVD risk factors in youth and which demonstrate positive correlations. However studies are lacking which assess relationships with dyslipidemia and BMI at the 85th percentile or greater, the AAP screening criteria in youth. The majority of research on US children has examined the relationship of obese, not overweight children and atherosclerosis development through pathology studies, sub-clinical measures or lipid levels. There are a number of international studies that have found positive associations between increasing levels of adiposity and more severe dyslipidemias (Flechtner-Mors et al., 2011; Katzmarzyk, Tremblay, Perusse, Despres, & Bouchard, 2003; Kim Soh Ye, Hong Kyung Hee, Jang Ki Hyo, Kang Soon Ah, & Choue Ryo Won, 2005; Takada et al., 1998; Zhai et al., 2004). These studies however, are not readily generalized to the US pediatric population because many studies were conducted in Asian populations whose diets are often dissimilar to western foods and because they used different classification systems for childhood obesity making them difficult to compare (Cole, Bellizzi, Flegal, & Dietz, 2000).

In a more recent US study Lamb, Ogden, Carroll, Lacher, and Flegal (2011), analyzed National Health and Nutrition Examination Survey data (1999-2004) for associations between childhood adiposity and lipid levels. However, due to concern about the accuracy of BMI as an adiposity measure, researchers instead measured body fat percentage by dual-energy X-ray absorptiometry. A recent study by Lee and colleagues (2009) found BMI did not perform well in detecting youth with elevated TC

or LDL-C levels and called into question the current screening recommendations. The study population was a NHANES cohort from 1999-2004 survey years. Children 3 to 18 years of old were evaluated for TC and HDL-C levels and 12 to 18 years of age for LDL-C and triglycerides. The researchers used receiver operating characteristic (ROC) curves to evaluate the performance of specific BMI percentiles in predicting dyslipidemias. ROC analysis for BMIs at the 85th percentile produced area under the curve values of 0.60 for TC, 0.63 for LDL-C, 0.69 for HDL-C and 0.72 for triglycerides.

Lee et al. (2009) also calculated sensitivity, specificity, positive predictive values (PPVs), and negative predictive values (NPVs) for each lipid factor at different BMI percentile thresholds. BMI at the 85th percentile as a threshold screening test for TC dyslipidemia resulted in sensitivity and specificity levels of 53% and 63% respectively, PPV (14%) and NPV (93%). BMI at the 85th percentile as a screening test for HDL-C dyslipidemia resulted in sensitivity and specificity of 63% and 65% respectively, PPV (11%) and NPV (97%).

National expert guidelines recommend BMI at the 85th percentile as the screening threshold for children and adolescents at risk for dyslipidemia, although research to support this cutpoint is unclear. Even the Expert Panel Guidelines, with their extensive research review, do not include studies on this specific relationship. The association of childhood obesity and cardiovascular disease is well documented. However, additional research is needed on the relationship of overweight youth and dyslipidemia prevalence. Cardiovascular disease primary prevention goals for youth address two main areas: prevention of the development of risk factors and prevention to recognize and manage youth at risk due to identified risk factors. National expert bodies have developed

guidelines which delineate children at risk who should receive targeted screening. Screening guidelines include recommendations to perform serum lipid evaluations on overweight children. The objective of this thesis is to add to the body of knowledge concerning the relationship between youth with BMIs at the 85th percentile or greater and dyslipidemias of TC, HDL-C and non-HDL-C.

CHAPTER III
METHODOLOGY

3.1 *Subjects*

The data source for this study is the National Health and Nutrition Examination Survey (NHANES) 2007-2008 and 2009-2010 survey years. NHANES is conducted through the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC). The survey program began in the 1960s and since has evolved into a continuous program that is conducted every two years. NHANES is highly regarded as the most comprehensive study of the health and nutrition status of adults and children in the US. Strict confidentiality is maintained throughout the process. De-identified survey data are publicly available through the NHANES website. The survey combines interview and physical examination data from a nationally representative sample of approximately 5,000 persons each year. The NHANES interview is conducted in the sample person's home and includes demographic, socioeconomic, nutrition and health-related questions. The examination section is conducted in the mobile examination center (MEC) by physicians and highly trained medical personnel. The examination includes medical, dental, and physiological measurements and laboratory tests (Centers for Disease Control and Prevention, 2012).

NHANES is conducted according to strict protocol and informed consent is obtained from participants. For each survey cycle, NHANES undergoes National Center for Health Statistics (NCHS) Research Ethics Review Board Approval. Manuals developed for interviewer and examiner training are available for public viewing on the

NHANES website. These manuals contain exact details on all policies, procedures and standards for conducting NHANES survey components (Centers for Disease Control and Prevention, 2011). Georgia State University Institutional Review Board approval was granted for this study under Protocol Type H12278, Exempt Review, Category 4.

NHANES uses a complex, multistage, probability sampling design in an effort to select participants that are representative of the civilian, non-institutionalized US population. Certain subgroups are oversampled in order to produce reliable statistics. NHANES oversamples the elderly, Hispanics, African-Americans and low income persons. In the first stage primary sampling units (PSUs) are selected, which are mostly single counties or less often groups of contiguous counties. These PSUs are selected from strata defined by geography and proportions of minority populations. In the second stage, PSUs are divided into segments such as city blocks. In stage 3, households are randomly selected from each segment. In stage 4, individuals are randomly chosen to participate from all persons residing in the household, which results in approximately 1.6 persons per household. Each sample person is assigned a sample weight. This weight is used to produce an unbiased national estimate (Centers for Disease Control and Prevention, n.d.).

The original 2007-2008 survey consisted of 10149 sample persons and the 2009-2010 survey had 10537 sample persons. Complete body measurements were available on 8088 sample persons from the 2007-2008 survey and 8608 sample persons from the 2009-2010 survey. Of these 7387 and 7846 sample persons in the 2007-2008 and 2009-2010 respective surveys had TC and HDL-C laboratory values. In these survey years, total cholesterol and HDL-C measurements were conducted on participants beginning at

6 years of age. The subset for the present study consists of males and females 6 through 18 years of age who had complete body measurements, TC and HDL-C measurements. The final data set of combined survey cycles contains 3888 participants of which 2016 are male and 1872 are female.

Beginning in 2007 NHANES employed a new sampling methodology, whereby other Hispanics were oversampled, not just Mexican-Americans. For example in the 2005-2006 cycle other Hispanics comprised 3.3% of the unweighted sample size, whereas in 2007-2008 this unweighted sample consisted of 11.7% and 10.8% in 2009-2010. The like percentages for Mexican-Americans were as follows: 2005-2006 (27.5%), 2007-2008 (21.1%) and 2009-1010 (22.5%). The non-Hispanic black unweighted sample decreased from 26.3% in 2005-2006, to 21.9% in 2007-2008 and finally 18.6% in 2009-2010. The non-Hispanic white and other race/ethnicity categories both had small increases overall. Beginning with the 2007 year survey, changes in the age domains led to a decrease in the number of participants under 20 years old and an increase in the number of participants 40 years of age or greater. Also beginning with the 2007-2008 survey, pregnant women were no longer oversampled.

NHANES has been in existence for over 50 years and is renowned as a comprehensive, national data source for health research interests. NHANES is highly regarded for adhering to rigorous sampling and data collection processes. Although the researchers are highly trained and protocols are followed, there is always the possibility for human and/or technical error. For NHANES in general, selection bias can be present as subjects are invited to participate and are paid for their participation. As a result, the cohort of subjects who elect to participate may differ from those that do not. In addition,

participants do not have to complete all components of the survey. For example

questions may not be answered and laboratory tests refused.   The interview component

relies on self-reported information thus lending itself to error with recall or information

bias. There is limitation of race/ethnicity groups. The sampling methodology of

NHANES produces three main groups, Mexican-American, non-Hispanic black and non-

Hispanic white. The 2007 sampling change has enlarged the other Hispanic sample

group, which allows for stronger analysis of this group. There is no distinct Asian group.

Parameters for exam, laboratory analysis and interview questions vary especially

by age. For example TC and HDL-C testing begins at age 6 years, but triglyceride and

LDL-C testing begins at age 12 years and is restricted to fasting individuals. Since all

participants may not adhere to fasting instructions or falsely report their fasting time, this

could affect the reliability of these lab values. In addition, because a fasting state was

required, noncompliance would further decrease the number of participants who would

be eligible for this component of the exam. In another example, history of hypertension

was initially considered for inclusion in the present study, as a possible confounder, but

was not, because blood pressure interview questions in NHANES are only asked of

participants who are at least 16 years of age.

3.2 *Definition of Terms*

The variables used in this study are gender, age, race/ethnicity, income, cotinine,

BMI percentile, TC, HDL-C and non-HDL-C. Age is measured in months at the time of

MEC. The study cohort includes youth from 72 through 227 months of age. The lower

threshold of 72 months was selected because this is the minimum age for NHANES

participants to receive TC and HDL-C laboratory analysis. The first age category is 6 to

8 years of age. The second age category is 9 to 11 years, because this group is recommended to receive universal screening. The third category is 12 to 15 years of age, in an effort to capture the pubertal years. The last age category is 16 to 18 years. The selection of 18 year olds as the upper limit was somewhat arbitrary. The present study is on children and adolescents. The literature review revealed an assortment of ages studied including adolescents 18 and 19 years of age. Universal lipid screening is recommended for persons 18 to 21 years of age and with the guidelines published in December 2011, the age for universal screening was lowered to 17 years, hence a 17 or 18 year old could receive lipid screening without having other risk factors. All other age categories consisted of at least three progressive age years. Including 17 and 18 year olds in the oldest age category enabled this group to have three progressive years and more closely resemble the other groups in size.

NHANES uses five race/ethnicity categories: non-Hispanic white, non-Hispanic black, Mexican-American, other Hispanic and other. The present study is comprised of four race/ethnicity categories. Three categories are comprised of the same NHANES subjects for non-Hispanic white, non-Hispanic black, and Mexican-American. The fourth race/ethnicity category is a merged "other" category derived from the NHANES other Hispanic and other groups. This fourth merged other category resulted in a subset of 723 persons out of a total sample group of 3888.

The total household income variable was used as a socioeconomic indicator variable. Income was divided into five categories by merging NHANES categories. The resulting five income levels ranged from very low at $0 to $19,999 to high at $100,000 or greater.

Tobacco exposure was accounted for by including the laboratory value for cotinine. According to CDC literature, cotinine levels less than 1 ng/ml indicate non-tobacco exposure. A person with cotinine levels ranging from 1 to 10 ng/ml is environmentally exposed and levels above 10 ng/ml represent tobacco use.

As the focus of the present study is to analyze associations between BMI categories used in the current guidelines and dyslipidemia, it was imperative to use the same BMI categories. BMI percentile rankings are categorized according to CDC 2000 pediatric growth chart rankings for obese, overweight, normal and underweight children and adolescents. The 85th to 94th percentile is the overweight category and threshold for lipid screening in youth. Children with BMI percentiles at the 95th percentile or greater are considered obese. Normal or healthy weight children range in the 5th to 84th BMI percentile and underweight children are less than the 5th BMI percentile.

Three lipid values are used in this analysis, total cholesterol (TC), high-density lipid cholesterol (HDL-C) and non-high-density lipid cholesterol (non-HDL-C). For categorical analysis values are categorized into two variables. Total cholesterol less than 200 mg/dl is 'Acceptable to Borderline'. Total cholesterol at or greater than 200 mg/dl is 'High'. With HDL-C, the lower values are abnormal, thus a value less than 40 mg/dl is 'Low' and values at or greater than 40 mg/dl are 'Acceptable to Borderline-Low'. Non-HDL-C is not included in NHANES surveys, but is easily calculated by subtracting HDL-C from TC. Non-HDL-C is 'High' with values at or greater than 145 mg/dl and 'Acceptable to Borderline-High' if less than 145 mg/dl. The definitions used in this study for TC, HDL-C and non-HDL-C are consistent with expert panel guidelines from major national organizations (Kavey, Simons-Morton, & de Jesus, 2011).

3.3 *Statistical Analysis*

SAS 9.2 was used for all analysis in this study (SAS Institute Inc., 2012). Survey documentation for both NHANES two year cycles 2007-2008 and 2009-2010 were thoroughly reviewed to select needed variables. Data from two 2-year cycles was combined in order to produce estimates with greater statistical reliability. All of the selected variables from both 2-year cycles have the same names and definitions hence data files were appended directly. The appended dataset was sorted by sequence number and Demographic, Examination and Laboratory data files were merged.

Triglyceride and LDL-C data were considered for inclusion in this study. However, in NHANES triglycerides and LDL-C lab values are only computed on participants who are fasting and at least 12 years of age and older. As a result approximately 76% of the study sample did not have these lab values. Non-HDL-C is gaining recognition as an important risk marker and could be calculated for inclusion in this study. Non-HDL-C includes LDL-C and triglycerides, thus considering the possibility and benefits of including Non-HDL-C in the present study and deficit of a smaller sample size for triglycerides and LDL-C, triglycerides and LDL-C were not included in the present study.

Diabetes history was considered, but not included as a covariate. In NHANES, the interview question for diabetes history and laboratory exam for glycohemogloblin, a diabetes indicator, are implemented in subjects beginning at 12 years of age. Thus like triglycerides and LDL-C mentioned above, inclusion of this covariate would substantially reduce the sample size for this study. It was also noted that there were only 22 positive responses from subjects in the sample indicating they had a history of diabetes.

Considering the factors of low diabetes prevalence and that inclusion would necessitate a

substantial reduction in sample size, the decision was made not to include a diabetes

covariate. Pregnancy history questions and laboratory pregnancy testing data are only

available in NHANES on women beginning at 20 years of age, thus pregnant subjects are

not accounted for in this study.

NHANES files were reviewed to check for skip patterns in regards to the variables

selected and none were found. Univariate analysis was conducted for continuous

variables TC, HDL-C, LDL- C and triglycerides to check the distribution and identify

outliers. Although there were some outliers, no outliers were removed for this study,

primarily because their impact was germane to the present study, i.e., extremely high TC

or non-HDL-C or low HDL-C. Multivariate regression analysis was conducted with and

without the inclusion of one extremely low TC variable (TC = 66 mg/dl) and the results

were effectively unchanged, hence this outlier was left in the study sample. The variable

for non-HDL-C was created. The SAS program for CDC Growth Charts was conducted

in order to add the BMI percentile variable to the dataset. Data was recoded into

categorical variables as described in Definition of Terms above.

Descriptive statistics of the study sample are shown in Tables 1, 2 and 3. The

independent-samples t-test is conducted to test equality between mean lipid values for

males and females (Table 4). The sample sizes for males (n=2016) and females (n=1872)

are represented fairly evenly. The large sample size n=3888 compensates for violations

of normality assumption. For all three lipid factors, the F value is small, but significant

to reject equal variances, and both the Pooled (equal) and Satterthwaite (unequal) t-

statistics are not significant for mean differences. Satterthwaite t-statistics are included in

Table 4. Analysis of variance (ANOVA) was completed to examine mean differences of lipid values for all other categorical variables and results are presented in Tables 5, 6 and 7. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of BMI percentile risk factor agreement with dyslipidemias were calculated for the entire sample and stratified by age category with results presented in Tables 8, 9 and 10. Because the focus of this study is the overweight category of children, in contrast to obese, only the overweight category children were included as positive tests. For negative tests, only healthy weight children were included.

Simple logistic regression analyses were completed for each covariate and lipid factor and the results are presented in Table 11. Multiple logistic regression was completed including all categorical independent variables for each lipid factor and the results are presented in Table 12.

CHAPTER IV
RESULTS

4.1 *Study Sample Demographics*

There are 3888 subjects overall in this study sample who comprised the age range of 6 through 18 years and who had measures for BMI percentile, TC and HDL-C. Descriptive statistics for the covariates of gender, age, race ethnicity, income, cotinine levels and BMI percentages are presented in Tables 1, 2 and 3 for each lipid factor studied. Males represent 52% (n= 2016) and females 48% (n= 1872). The four age categories (6-8 years, 9-11 years, 12-15 years and 16-18 years) are fairly evenly divided. There are higher proportions of non-Hispanic whites (31%) and Mexican-Americans (28%) compared to Non-Hispanic blacks (22%) and other (19%) race ethnic groups. Household income is categorized into five levels. This subset of the study group is somewhat smaller at n=3625. The low income group ($20,000 to $44,999) is the largest at 33%. The moderately high income group ($75,000 to $99,999) is the smallest at 9%. The subset for cotinine level analysis is slightly smaller at n=3865. Approximately 5% of the subset are tobacco users and 11% are environmentally exposed.

Twenty-two percent (n=840) of the sample is obese. Overweight youth comprise 17% of the study population (n=652). Fifty-nine percent (n=2283) of the sample are a healthy weight and 3% (n=113) are underweight. As depicted in Table 2 dyslipidemic HDL-C is the most prevalent abnormal lipid factor with 52% of obese children and adolescents at abnormal levels. Although underweight youth have lower levels of dyslipidemia, they do not always have the lowest prevalence per lipid factor. The lowest

prevalence for dyslipidemias occurs for non-HDL-C in the underweight group (4%), but for TC and HDL-C the lowest prevalence is in the healthy weight group at 6% and 18% respectively. Abnormality of lipid prevalence progressively increases as BMI percentile categories transition from healthy weight to obese for all three lipid factors.

Table 1

Total Cholesterol (TC) Values Descriptive Statistics of Study Sample

Variables	Acceptable to Borderline-High <200 mg/dl	High >=200 mg/dl	Total
Gender (N=3888)			
Male	1851 (91.82%)	165 (8.18%)	2016 (51.85%)
Female	1739 (92.90%)	133 (7.10%)	1872 (48.15%)
Total	3590 (92.34%)	298 (7.66%)	3888
Age (N=3888)			
6-8 years	844 (91.74%)	76 (8.26%)	920 (23.66%)
9-11 years	916 (90.60%)	95 (9.40%)	1011 (26.00%)
12-15 years	1038 (94.36%)	62 (5.64%)	1100 (28.29%)
16-18 years	792 (92.42%)	65 (7.58%)	857 (22.04%)
Total	3590 (92.34%)	298 (7.66%)	3888
BMI Percentiles (N=3888)			
Underweight <5th Percentile	103 (91.15%)	10 (8.85%)	113 (2.91%)
Healthy Weight 5th – 84th Percentile	2148 (94.09%)	135 (5.91%)	2283 (58.72%)
Overweight 85th – 94th Percentile	593 (90.95%)	59 (9.05%)	652 (16.77%)
Obese >=95th Percentile	746 (88.81%)	94 (11.19%)	840 (21.60%)
Total	3590 (92.34%)	298 (7.66%)	3888
Race Ethnicity (N=3888)			
Non-Hispanic white	1116 (92.69%)	88 (7.31%)	1204 (30.97%)
Non-Hispanic black	804 (91.99%)	70 (8.01%)	874 (22.48%)
Mexican-American	1012 (93.10%)	75 (6.90%)	1087 (27.96%)
Other	658 (91.01%)	65 (8.99%)	723 (18.60%)
Total	3590 (92.34%)	298 (7.66%)	3888
Household Income (N=3625)			
$0 to $19,999	771 (92.56%)	62 (7.44%)	833 (22.98%)
$20,000 to $44,999	1105 (91.78%)	99 (8.22%)	1204 (33.21%)
$45,000 to $74,999	692 (93.01%)	52 (6.99%)	744 (20.52%)
$75,000 to $99,999	303 (92.10%)	26 (7.90%)	329 (9.08%)
$100,000+	478 (92.82%)	37 (7.18%)	515 (14.21%)
Total	3349 (92.39%)	276 (7.61%)	3625
Cotinine Levels (N=3865)			
Non-Tobacco Exposure <1 ng/ml	3012 (92.42%)	247 (7.58%)	3259 (84.32%)
Environmental Tobacco Exposure 1 to 10 ng/ml	386 (92.12%)	33 (7.88%)	419 (10.84%)
Tobacco User >10 ng/ml	170 (90.91%)	17 (9.09%)	187 (4.84%)
Total	3568 (92.32%)	297 (7.68%)	3865

Table 2

High-Density Lipoprotein Cholesterol (HDL-C) Values Descriptive Statistics of Study Sample

Variables	Acceptable to Borderline-Low >=40 mg/dl	Low <40 mg/dl	Total
Gender (N=3888)			
Male	1446 (71.73%)	570 (28.27%)	2016 (51.85%)
Female	1377 (73.56%)	495 (26.44%)	1872 (48.15%)
Total	2823 (72.61%)	1065 (27.39%)	3888
Age (N=3888)			
6-8 years	726 (78.91%)	194 (21.09%)	920 (23.66%)
9-11 years	746 (73.79%)	265 (26.21%)	1011 (26.00%)
12-15 years	787 (71.55%)	313 (28.45%)	1100 (28.29%)
16-18 years	564 (65.81%)	293 (34.19%)	857 (22.04%)
Total	2823 (72.61%)	1065 (27.39%)	3888
BMI Percentiles (N=3888)			
Underweight <5th Percentile	92 (81.42%)	21 (18.58%)	113 (2.91%)
Healthy Weight 5th – 84th Percentile	1875 (82.13%)	408 (17.87%)	2283 (58.72%)
Overweight 85th – 94th Percentile	450 (69.02%)	202 (30.98%)	652 (16.77%)
Obese >=95th Percentile	406 (48.33%)	434 (51.67%)	840 (21.60%)
Total	2823 (72.61%)	1065 (27.39%)	3888
Race Ethnicity (N=3888)			
Non-Hispanic white	851 (70.68%)	353 (29.32%)	1204 (30.97%)
Non-Hispanic black	710 (81.24%)	164 (18.76%)	874 (22.48%)
Mexican-American	747 (68.72%)	340 (31.28%)	1087 (27.96%)
Other	515 (71.23%)	208 (28.77%)	723 (18.60%)
Total	2823 (72.61%)	1065 (27.39%)	3888
Household Income (N=3625)			
$0 to $19,999	584 (70.11%)	249 (29.89%)	833 (22.98%)
$20,000 to $44,999	857 (71.18%)	347 (28.82%)	1204 (33.21%)
$45,000 to $74,999	539 (72.45%)	205 (27.55%)	744 (20.52%)
$75,000 to $99,999	248 (75.38%)	81 (24.62%)	329 (9.08%)
$100,000+	409 (79.42%)	106 (20.58%)	515 (14.21%)
Total	2637 (72.74%)	988 (27.26%)	3625
Cotinine Levels (N=3865)			
Non-Tobacco Exposure <1 ng/ml	2404 (73.76%)	855 (26.24%)	3259 (84.32%)
Environmental Tobacco Exposure 1 to 10 ng/ml	295 (70.41%)	124 (29.59%)	419 (10.84%)
Tobacco User >10 ng/ml	107 (57.22%)	80 (42.78%)	187 (4.84%)
Total	2806 (72.60%)	1059 (27.40%)	3865

Table 3

Non-High-Density Lipoprotein-Cholesterol (Non-HDL-C) Values Descriptive Statistics of Study Sample

Variables	Acceptable to Borderline-Low >=40 mg/dl	Low <40 mg/dl	Total
Gender (N=3888)			
Male	1816 (90.08%)	200 (9.92%)	2016 (51.85%)
Female	1717 (91.72%)	155 (8.28%)	1872 (48.15%)
Total	3533 (90.87%)	355 (9.13%)	3888
Age (N=3888)			
6-8 years	856 (93.04%)	64 (6.96%)	920 (23.66%)
9-11 years	906 (89.61%)	105 (10.39%)	1011 (26.00%)
12-15 years	1012 (92.00%)	88 (8.00%)	1100 (28.29%)
16-18 years	759 (88.56%)	98 (11.44%)	857 (22.04%)
Total	3533 (90.87%)	355 (9.13%)	3888
BMI Percentiles (N=3888)			
Underweight <5th Percentile	108 (95.58%)	5 (4.42%)	113 (2.91%)
Healthy Weight 5th – 84th Percentile	2160 (94.61%)	123 (5.39%)	2283 (58.72%)
Overweight 85th – 94th Percentile	582 (89.26%)	70 (10.74%)	652 (16.77%)
Obese >=95th Percentile	683 (81.31%)	157 (18.69%)	840 (21.60%)
Total	3533 (90.87%)	355 (9.13%)	3888
Race Ethnicity (N=3888)			
Non-Hispanic white	1073 (89.12%)	131 (10.88%)	1204 (30.97%)
Non-Hispanic black	816 (93.36%)	58 (6.64%)	874 (22.48%)
Mexican-American	989 (90.98%)	98 (9.02%)	1087 (27.96%)
Other	655 (90.59%)	68 (9.41%)	723 (18.60%)
Total	3533 (90.87%)	355 (9.13%)	3888
Household Income (N=3625)			
$0 to $19,999	752 (90.28%)	81 (9.72%)	833 (22.98%)
$20,000 to $44,999	1080 (89.70%)	124 (10.30%)	1204 (33.21%)
$45,000 to $74,999	686 (92.20%)	58 (7.80%)	744 (20.52%)
$75,000 to $99,999	303 (92.10%)	26 (7.90%)	329 (9.08%)
$100,000+	474 (92.04%)	41 (7.96%)	515 (14.21%)
Total	3295 (90.90%)	330 (9.10%)	3625
Cotinine Levels (N=3865)			
Non-Tobacco Exposure <1 ng/ml	2972 (91.19%)	287 (8.81%)	3259 (84.32%)
Environmental Tobacco Exposure 1 to 10 ng/ml	381 (90.93%)	38 (9.07%)	419 (10.84%)
Tobacco User >10 ng/ml	158 (84.49%)	29 (15.51%)	187 (4.84%)
Total	3511 (90.84%)	354 (9.16%)	3865

Table 4 depicts the Independent-Samples t-test analysis to compare mean values of the three lipid factors studied among males and females. There are no significant differences in the mean values for any of the three lipids between males and females.

Table 4
Lipid Factors Independent-Samples *t*-Test (N=3888)

Lipid Variable	Mean (95% CI)	t Value	Pr > [t]
Total Cholesterol		-1.27	0.2037
Male	158.7 (157.5, 159.9)		
Female	159.8 (158.6, 161.0)		
HDL-C		-0.26	0.7975
Male	52.6 (52.0, 53.2)		
Female	52.7 (52.1, 53.2)		
Non-HDL-C		-1.17	0.2430
Male	106.1 (104.9, 107.4)		
Female	107.1 (106.0, 108.3)		

Male (N=2016)
Female (N=1872)

Tables 5, 6 and 7 are an ANOVA analysis to examine the differences of the mean lipid values for each multi-categorical independent variable. ANOVA analysis for total cholesterol mean values is presented in Table 5. There are significant mean differences of TC values according to age and BMI percentile categories. Children 6 to 8 years of age have mean TC values approximately 6 mg/dl higher than youth in the 12 to 15 year age group. Youth in the 9 to 11 year old group have mean levels of TC significantly higher than both older groups. The mean TC value for healthy weight children is approximately 3 mg/dl lower than overweight children and approximately 5 mg/dl lower than obese youth.

Table 5

Total Cholesterol (TC) Analysis of Variance

Variable Categorical Comparisons	Difference Between Means (95% CI)	F Value	Pr > F
BMI Percentiles (N=3888)		8.91	<.0001
Healthy Weight – Underweight	-2.7069 (-9.5156, 4.1018)		
Healthy Weight – Overweight	-3.4511 (-6.5883, -0.3139)***		
Healthy Weight – Obese	-5.4068 (-8.2579, -2.5558)***		
Overweight – Underweight	0.7442 (-6.4549, 7.9433)		
Overweight – Obese	-1.9557 (-5.6432, 1.7318)		
Obese – Underweight	2.6999 (-4.3792, 9.7790)		
Age (N=3888)		13.70	<.0001
Age 6-8 years - Age 9-11 years	-1.159 (-4.373, 2.054)		
Age 6-8 years - Age 12-15 years	5.891 (2.741, 9.042)***		
Age 6-8 years - Age 16-18 years	2.770 (-0.578, 6.118)		
Age 9-11 years - Age 12-15 years	7.051 (3.978, 10.123)***		
Age 9-11 years - Age 16-18 years	3.930 (0.655, 7.204)***		
Age 12-15 years - Age 16-18 years	-3.121 (-6.334, -0.092)		
Race Ethnicity (N=3888)		1.07	0.3586
Non-Hispanic white - Non-Hispanic black	0.324 (-2.825, 3.473)		
Non-Hispanic white - Mexican-American	1.197 (-1.768, 4.162)		
Non-Hispanic white – Other	-1.145 (-4.480, 2.189)		
Non-Hispanic black - Mexican-American	0.873 (-2.346, 4.093)		
Non-Hispanic black – Other	-1.469 (-5.031, 2.093)		
Mexican-American – Other	-2.342 (-5.743, 1.059)		
Household Income (N=3625)		1.81	0.1246
0 to $19,999 - $20,000 to $44,999	-2.333 (-5.722, 1.056)		
0 to $19,999 - $45,000 to $74,999	0.280 (-3.513, 4.074)		
0 to $19,999 - $75,000 to $99,999	-2.813 (-7.709, 2.084)		
0 to $19,999 - $100,000+	-1.916 (-6.132, 2.300)		
$20,000 to $44,999 - $45,000 to $74,999	2.613 (-0.894, 6.120)		
$20,000 to $44,999 - $75,000 to $99,999	-0.480 (-5.158, 4.199)		
$20,000 to $44,999 - $100,000+	0.417 (-3.543 4.377)		
$45,000 to $74,999 – $75,000 to $99,999	-3.093 (-8.072, 1.886)		
$45,000 to $74,999 - $100,000+	-2.196 (-6.507, 2.115)		
$75,000 to $99,999 - $100,000+	0.897 (-4.411, 6.204)		
Cotinine Levels (N=3865)		2.37	0.0937
Non-Tobacco –Environmental Tobacco	1.7298 (-1.6272, 5.0867)		
Non-Tobacco - Tobacco User	3.9416 (-0.9223, 8.8055)		
Environmental Tobacco – Tobacco User	2.2118 (-3.4766, 7.9003)		

***comparisons significant at the 0.05 level

As depicted in Table 6, all five multi-categorical covariates examined for HDL-C mean differences have significant findings as described to follow. Six to 8 year olds have higher mean HDL-C values than 12 to 18 year olds. HDL-C mean values of 16 to 18 year old adolescents are lower than youth 9 through 15 years of age. There are significant differences in HDL-C mean values according to participant BMI percentiles, which paralleled increasing weight categories. The most extreme is a decrease of 12 mg/dl in obese compared to underweight youth. The mean HDL-C of non-Hispanic whites and Mexican-Americans is approximately 5 mg/dl lower than non-Hispanic blacks. The other race ethnicity group has a mean HDL-C value that is approximately 4 mg/dl lower than non-Hispanic blacks. Study youth in households at the lowest income have lower HDL-C mean levels when compared to study participants in the higher income groups. The mean values of HDL-C are 4 mg/dl lower in tobacco users compared to those environmentally exposed to tobacco, and 5 mg/dl lower in tobacco users in comparison to non-tobacco users.

Table 6
High-Density Lipoprotein Cholesterol (HDL-C) Analysis of Variance

Variable Categorical Comparisons	Difference Between Means (95% CI)	F Value	Pr > F
BMI Percentiles (N=3888)		161.13	<.0001
Healthy Weight – Underweight	-2.0747 (-5.0581, 0.9088)		
Healthy Weight – Overweight	4.8203 (3.4456, 6.1950)***		
Healthy Weight – Obese	10.2800 (9.0308, 11.5293)***		
Overweight – Underweight	-6.8950 (-10.0495, -3.7404)***		
Overweight – Obese	5.4598 (3.8439, 7.0756)***		
Obese - Underweight	-12.3547 (-15.4567, -9.2527)***		
Age (N=3888)		16.41	<.0001
Age 6-8 years - Age 9-11 years	-1.2487 (-0.2376, 2.7351)		
Age 6-8 years - Age 12-15 years	2.4499 (0.9924, 3.9073)***		
Age 6-8 years - Age 16-18 years	4.0192 (2.4705, 5.5679)***		
Age 9-11 years - Age 12-15 years	1.2012 (-0.2201, 2.6224)		
Age 9-11 years - Age 16-18 years	2.7705 (1.2558, 4.2852)***		
Age 12-15 years - Age 16-18 years	1.5693 (0.0830, 3.0556)***		
Race Ethnicity (N=3888)		34.30	<.0001
Non-Hispanic white - Non-Hispanic black	-4.9946 (-6.4345, -3.5548)***		
Non-Hispanic white - Mexican-American	0.1752 (-1.1804, 1.5309)		
Non-Hispanic white - Other	-1.1225 (-2.6470, 0.4019)		
Non-Hispanic black - Mexican-American	5.1698 (3.6978, 6.6419)***		
Non-Hispanic black - Other	3.8721 (2.2432, 5.5010)***		
Mexican-American - Other	-1.2978 (-2.8527, 0.2572)		
Household Income (N=3625)		3.03	0.0166
0 to $19,999 - $20,000 to $44,999	-1.1062 (-2.6724, 0.4599)		
0 to $19,999 - $45,000 to $74,999	-1.2174 (-2.9704, 0.5355)		
0 to $19,999 - $75,000 to $99,999	-2.2689 (-4.5316, 0.0061)***		
0 to $19,999 - $100,000+	-2.0847 (-4.0327, -0.1368)***		
$20,000 to $44,999 - $45,000 to $74,999	-0.1112 (-1.7317, 1.5094)		
$20,000 to $44,999 - $75,000 to $99,999	-1.1626 (-3.3244, 0.9992)		
$20,000 to $44,999 - $100,000+	-0.9785 (-2.8082, 0.8512)		
$45,000 to $74,999 – $75,000 to $99,999	-1.0514 (-3.3522, 1.2494)		
$45,000 to $74,999 - $100,000+	-0.8673 (-2.8593, 1.1247)		
$75,000 to $99,999 - $100,000+	0.1841 (-2.2685, 2.6367)		
Cotinine Levels (N=3865)		15.18	<.0001
Non-Tobacco –Environmental Tobacco	1.1539 (-0.3932, 2.7010)		
Non-Tobacco - Tobacco User	5.1123 (2.8706, 7.3539)***		
Environmental Tobacco – Tobacco User	3.9583 (1.3367, 6.5800)***		

***comparisons significant at the 0.05 level

ANOVA analysis for non-HDL-C value mean differences is presented in Table 7. Significant findings are in the age, BMI percentile and race ethnicity groups as follows. Children 12 to 15 years old have lower non-HDL-C mean values in comparison to all the other age groups. Non-HDL-C mean values are progressively higher in parallel to increasing BMI percentile groups for all comparisons, except the underweight to healthy weight comparison which lacks significance. Non-Hispanic black participants have mean values approximately 4 to 5 mg/dl lower than all other race ethnicity study groups.

Table 7
Non-High-Density Lipoprotein Cholesterol (Non-HDL-C) Analysis of Variance

Variable Categorical Comparisons	Difference Between Means (95% CI)	F Value	Pr > F
BMI Percentiles (N=3888)		77.10	<.0001
Healthy Weight – Underweight	-0.6322 (-7.1869, 5.9225)		
Healthy Weight – Overweight	-8.2714 (-11.2916, -5.2512)***		
Healthy Weight – Obese	-15.6869 (-18.4316, -12.9421)***		
Overweight – Underweight	7.6392 (0.7086, 14.5698)***		
Overweight – Obese	-7.4155 (-10.9654, -3.8655)***		
Obese – Underweight	15.0546 (8.2396, 21.8697)***		
Age (N=3888)		9.14	<.0001
Age 6-8 years - Age 9-11 years	-2.408 (-5.587, 0.771)		
Age 6-8 years - Age 12-15 years	3.441 (0.324, 6.558)***		
Age 6-8 years - Age 16-18 years	-1.249 (-4.561, 2.063)		
Age 9-11 years - Age 12-15 years	5.849 (2.810, 8.889)***		
Age 9-11 years - Age 16-18 years	1.159 (-2.080, 4.399)		
Age 12-15 years - Age 16-18 years	-4.690 (-7.869, -1.511)***		
Race Ethnicity (N=3888)		7.85	<.0001
Non-Hispanic white - Non-Hispanic black	5.318 (2.216, 8.420)***		
Non-Hispanic white - Mexican-American	1.022 (-1.899, 3.942)		
Non-Hispanic white - Other	-0.023 (-3.307, 3.261)		
Non-Hispanic black - Mexican-American	-4.297 (-7.468, -1.126)***		
Non-Hispanic black - Other	-5.341 (-8.850, -1.832)***		
Mexican-American - Other	-1.044 (-4.394, 2.305)		
Household Income (N=3625)		1.19	0.3121
0 to $19,999 - $20,000 to $44,999	-1.227 (-4.576, 2.122)		
0 to $19,999 - $45,000 to $74,999	1.498 (-2.251, 5.246)		
0 to $19,999 - $75,000 to $99,999	-0.544 (-5.383, 4.295)		
0 to $19,999 - $100,000+	0.169 (-3.997, 4.334)		
$20,000 to $44,999 - $45,000 to $74,999	2.724 (-0.741, 6.190)		
$20,000 to $44,999 - $75,000 to $99,999	0.683 (-3.940, 5.306)		
$20,000 to $44,999 - $100,000+	1.395 (-2.517, 5.308)		
$45,000 to $74,999 – $75,000 to $99,999	-2.041 (-6.962, 2.879)		
$45,000 to $74,999 - $100,000+	-1.329 (-5.589, 2.931)		
$75,000 to $99,999 - $100,000+	0.713 (-4.532, 5.957)		
Cotinine Levels (N=3865)		0.27	0.7666
Non-Tobacco –Environmental Tobacco	0.5758 (-2.7415, 3.8932)		
Non-Tobacco - Tobacco User	-1.1707 (-5.9772, 3.6359)		
Environmental Tobacco – Tobacco User	-1.7465 (-7.3679, 3.8749)		

***comparisons significant at the 0.05 level

4.2 *Test Agreement*

Agreement between the overweight BMI category (85th to less than the 95th percentile) as a test/predictor and dyslipidemia of the three lipid factors is presented in Tables 8, 9 and 10. The results for TC dyslipidemia as the positive outcome/disease are depicted in Table 8. The sensitivity of overweight children as positive testers is low and ranges from 26.19 to 36.84%. The highest sensitivity (36.84%) is in the 9 to 11 year old age group. The specificity is moderate at 78.37%. The PPV is low with the highest PPV in the 9 to 11 year old group at 12.07%. The NPV is high at 94.09%.

Table 8

Agreement between Overweight BMI Percentile as a Risk Factor and Dyslipidemia of Total Cholesterol in study participants (N = 2935)

Overweight BMI Percentile Risk Factor	Total Cholesterol Dyslipidemia		Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
	6 to 18 years old					
	Positive³	*Negative⁴*				
Positive¹	59	593	30.41%	78.37%	9.05%	94.09%
Negative²	135	2148	(0.240, 0.374)	(0.768, 0.799)	(0.070, 0.115)	(0.930, 0.950)
	6 to 8 years old					
	Positive³	*Negative⁴*				
Positive¹	14	114	27.45%	82.57%	10.94%	93.59%
Negative²	37	540	(0.159, 0.417)	(0.794, 0.854)	(0.061, 0.177)	(0.913, 0.955)
	9 to 11 years old					
	Positive³	*Negative⁴*				
Positive¹	21	153	36.84%	77.73%	12.07%	93.68%
Negative²	36	534	(0.245, 0.507)	(0.744, 0.808)	(0.076, 0.179)	(0.914, 0.955)
	12 to 15 years old					
	Positive³	*Negative⁴*				
Positive¹	11	183	26.19%	76.84%	5.67%	95.14%
Negative²	31	607	(0.139, 0.420)	(0.737, 0.797)	(0.029, 0.099)	(0.932, 0.967)
	16 to 18 years old					
	Positive³	*Negative⁴*				
Positive¹	13	143	29.55%	76.56%	8.33%	93.78%
Negative²	31	467	(0.168, 0.452)	(0.730, 0.799)	(0.045, 0.138)	(0.913, 0.957)

[1]Overweight BMI = 85th to <95th percentile
[2]Healthy Weight BMI = 5th to < 85th percentile
[3]Total Cholesterol values >= 200 mg/dl
[4]Total Cholesterol values <200 mg/dl

Test agreement statistics for HDL-C are presented in Table 9. Sensitivity is highest in the 12 to 15 year old children at 38.76%. Although the PPV (30.98%) is still low for this lipid factor, it is much higher than TC and non-HDL-C. The highest PPV is with the 16 to 18 year old group at 37.82%. Specificity and NPV is approximately 80% overall.

Table 9

Agreement between Overweight BMI Percentile as a Risk Factor and Dyslipidemia of High Density Lipoprotein-Cholesterol (HDL-C) in study participants (N = 2935)

Overweight BMI Percentile Risk Factor	HDL-C Dyslipidemia		Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
	6 to 18 years old					
	Positive[5]	*Negative[6]*				
Positive[1]	202	450	33.11%	80.65%	30.98%	82.13%
Negative[2]	408	1875	(0.294,	(0.790,	(0.275,	(0.805,
			0.370)	0.822)	0.347)	0.837)
	6 to 8 years old					
	Positive[5]	*Negative[6]*				
Positive[1]	23	105	21.50%	82.44%	17.97%	85.44%
Negative[2]	84	493	(0.141,	(0.792,	(0.117,	(0.823,
			0.304)	0.854)	0.257)	0.882)
	9 to 11 years old					
	Positive[5]	*Negative[6]*				
Positive[1]	51	123	35.17%	79.47%	29.31%	83.51%
Negative[2]	94	476	(0.274,	(0.760,	(0.227,	(0.802,
			0.435)	0.826)	0.367)	0.865)
	12 to 15 years old					
	Positive[5]	*Negative[6]*				
Positive[1]	69	125	38.76%	80.89%	35.57%	82.92%
Negative[2]	109	529	(0.316,	(0.777,	(0.288,	(0.798,
			0.463)	0.838)	0.427)	0.858)
	16 to 18 years old					
	Positive[5]	*Negative[6]*				
Positive[1]	59	97	32.78%	79.54%	37.82%	75.70%
Negative[2]	121	377	(0.260,	(0.756,	(0.302,	(0.717,
			0.402)	0.831)	0.459)	0.794)

[1]Overweight BMI = 85th to <95th percentile

[2]Healthy Weight BMI = 5th to < 85th percentile

[5]HDL-C values <40 mg/dl

[6]HDL-C values >=40 mg/dl

Table 10 includes results of test agreement between children in the overweight BMI percentile and dyslipidemia of non-HDL-C. Nine to 11 year old children have the highest sensitivity (41.51%) and PPV (12.64%). The specificity and NPV are 78.77% and 94.61% respectively.

Table 10

Agreement between Overweight BMI Percentile as a Risk Factor and Dyslipidemia of Non-High Density Lipoprotein Cholesterol (Non-HDL-C) in study participants (N = 2935)

Overweight BMI Percentile Risk Factor	Non-HDL Dyslipidemia		Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
6 to 18 years old						
	Positive⁷	*Negative⁸*				
Positive¹	70	582	36.27%	78.77%	10.74%	94.61%
Negative²	123	2160	(0.295, 0.435)	(0.772, 0.803)	(0.085, 0.134)	(0.936, 0.955)
6 to 8 years old						
	Positive⁷	*Negative⁸*				
Positive¹	14	114	41.18%	83.01%	10.94%	96.53%
Negative²	20	557	(0.247, 0.593)	(0.800, 0.858)	(0.061, 0.177)	(0.947, 0.979)
9 to 11 years old						
	Positive⁷	*Negative⁸*				
Positive¹	22	152	41.51%	78.00%	12.64%	94.56%
Negative²	31	539	(0.281, 0.559)	(0.747, 0.810)	(0.081, 0.185)	(0.924, 0.963)
12 to15 years old						
	Positive⁷	*Negative⁸*				
Positive¹	18	176	36.00%	77.49%	9.28%	94.98%
Negative²	32	606	(0.229, 0.508)	(0.744, 0.804)	(0.056, 0.143)	(0.930, 0.965)
16 to18 years old						
	Positive⁷	*Negative⁸*				
Positive¹	16	140	28.57%	76.59%	10.26%	91.97%
Negative²	40	458	(0.173, 0.422)	(0.730, 0.799)	(0.060, 0.161)	(0.892, 0.942)

¹Overweight BMI = 85th to <95th percentile

²Healthy Weight BMI = 5th to < 85th percentile

⁷Non-HDL-C values >=145 mg/dl

⁸Non-HDL-C values <145 mg/dl

4.3 *Simple Logistic Regression*

Univariate logistic regression for each covariate is presented in Table 11. Analysis for dyslipidemic TC reveals two covariates, age and BMI percentiles have significant findings. Twelve to 15 year old youth are at decreased risk (OR= 0.7) for dyslipidemic TC in comparison to 6 to 8 year old children. Overweight and obese children are respectively 1.6 and 2.0 times more likely to have abnormal TC values compared to healthy weight youth.

Significant findings for dyslipidemic HDL-C are numerous. As children progress into higher age categories their odds ratios (OR= 1.3 to 1.9) for dyslipidemic HDL-C increase. Overweight and obese youth are at increased risk (OR= 2.1 and 4.9 respectively) for abnormal HDL-C. Non-Hispanic blacks have less risk (OR= 0.6) in comparison to non-Hispanic whites. Children from households in the highest income group are 40% less likely to have dyslipidemic HDL-C than those from the lowest income category. Lastly, tobacco users have 2.1 times the risk for abnormal HDL-C compared to those not exposed to tobacco.

There are four covariates with significant findings for dyslipidemic non-HDL-C, age, BMI percentiles, race ethnicity and tobacco exposure. Two age categories of children, 9 to 11 year olds and 16 to 18 year olds are at increased risk (OR = 1.6 and 1.7 respectively) for abnormal non-HDL-C. The overweight and obese youth again display increased risk (OR = 2.1 and 4.0 respectively) in comparison to normal weight children. The race ethnicity category of non-Hispanic black demonstrates a protective effect (OR = 0.6) for non-HDL-C dyslipidemia. Tobacco users have 1.9 times the risk for abnormal non-HDL-C.

Table 11

Simple Logistic Regression for Dyslipidemias

Categorical Variables	Total Cholesterol OR (95% CI)	HDL-C OR (95% CI)	Non-HDL-C OR (95% CI)
BMI Percentiles (N=3888)			
Healthy Weight[1] (Ref)			
Underweight[2]	1.55 (0.79, 3.03)	1.05 (0.65, 1.71)	0.81 (0.33, 2.03)
Overweight[3]	1.58 (1.15, 2.18)***	2.06 (1.69, 2.51)***	2.11 (1.55, 2.87)***
Obese[4]	2.01 (1.52, 2.64)***	4.91 (4.13, 5.84)***	4.04 (3.14, 5.19)***
Gender (N=3888)			
Male (Ref)			
Female	0.86 (0.68, 1.09)	0.91 (0.79, 1.05)	0.82 (0.66, 1.02)
Age (N=3888)			
6 to 8 years (Ref)			
9 to 11 years	1.15 (0.84, 1.58)	1.33 (1.08, 1.64)***	1.55 (1.12, 2.14)***
12 to 15 years	0.66 (0.47, 0.94)***	1.49 (1.21, 1.83)***	1.16 (0.83, 1.63)
16 to 18 years	0.91 (0.65, 1.29)	1.94 (1.57, 2.40)***	1.73 (1.24, 2.40)***
Race Ethnicity (N=3888)			
Non-Hispanic white (Ref)			
Non-Hispanic black	1.10 (0.80, 1.53)	0.56 (0.45, 0.69)***	0.58 (0.42, 0.80)***
Mexican-American	0.94 (0.68, 1.29)	1.10 (0.92, 1.31)	0.81 (0.62, 1.07)
Other	1.25 (0.90, 1.75)	0.97 (0.80, 1.19)	0.85 (0.63, 1.16)
Household Income (N=3625)			
$0 to $19,999 (Ref)			
$20,000 to $44,999	1.11 (0.80, 1.55)	0.95 (0.78, 1.15)	1.07 (0.79, 1.43)
$45,000 to $74,999	0.93 (0.64, 1.37)	0.89 (0.72, 1.11)	0.79 (0.55, 1.12)
$75,000 to $99,999	1.07 (0.66, 1.72)	0.77 (0.57, 1.03)	0.80 (0.50, 1.26)
$100,000+	0.96 (0.63, 1.47)	0.61 (0.47, 0.79)***	0.80 (0.54, 1.19)
Tobacco Exposure (N=3865)			
Non-Exposed[5] (Ref)			
Environmental Exposure[6]	1.04 (0.71, 1.52)	1.18 (0.95, 1.48)	1.03 (0.72, 1.47)
Tobacco User[7]	1.22 (0.73, 2.04)	2.10 (1.56, 2.84)***	1.90 (1.26, 2.88)***

***ORs significant at the 0.05 level

Note: Dyslipidemias are defined as TC >=200 mg/dl, HDL-C < 40 mg/dl, and non-HDL-C >=145 mg/dl

[1] Healthy Weight = BMI 5th – 84th percentile

[2] Underweight =BMI <5th percentile

[3] Overweight = BMI 85th to 94th percentile

[4] Obese = BMI >= 95th percentile

[5] Non-Tobacco Exposure = Cotinine level <1 ng/ml

[6] Environmental Tobacco Exposure = Cotinine level 1 to 10 ng/ml

[7] Tobacco User = Cotinine level > 10 ng/ml

4.4 *Multivariate Logistic Regression*

Multiple logistic regression analysis is conducted with inclusion of all independent covariates as depicted in Table 12. There are 3605 participants in the sample who have data elements for all dependent and independent variables. For TC dyslipidemia the same covariates remain significant with essentially no change in their odds ratios. There is also very little change in the ORs of independent variables in the regression analysis for HDL-C dyslipidemia, with the exception of cotinine. After controlling for all other categorical variables, tobacco users risk for dyslipidemic HDL-C decreases from 110 to 62%.

Analyses for non-HDL-C dyslipidemia reveal a small increase in the ORs from the univariate to the multiple regression for obese youth, 4.0 to 4.3 respectively. Mexican-American youth are 30% less likely (OR = 0.7) to have abnormal non-HDL-C in the multiple regression, whereas in the univariate analysis this OR was not significant. Also after controlling for other variables, the protective effect of non-Hispanic black race ethnicity status is increased slightly from OR= 0.6 to 0.5.   The increased risk associated with tobacco use is no longer significant in the multiple regression analysis. All other significant ORs for non-HDL-C dyslipidemia remain essentially the same.

Table 12

Multiple Logistic Regression for Dyslipidemias (N = 3605)

Categorical Variables	Total Cholesterol OR (95% CI)	HDL-C OR (95% CI)	Non-HDL-C OR (95% CI)
BMI Percentiles			
Healthy Weight[1] (Ref)			
Underweight[2]	1.63 (0.83, 3.22)	0.93 (0.55, 1.55)	0.81 (0.32, 2.03)
Overweight[3]	1.53 (1.09, 2.16)***	1.98 (1.60, 2.44)***	2.19 (1.59, 3.04)***
Obese[4]	2.11 (1.58, 2.81)***	5.04 (4.19, 6.07)***	4.28 (3.28, 5.58)***
Gender			
Male (Ref)			
Female	0.86 (0.67, 1.11)	0.97 (0.83, 1.13)	0.85 (0.67, 1.08)
Age			
6 to 8 years (Ref)			
9 to 11 years	1.18 (0.85, 1.65)	1.33 (1.05, 1.68)***	1.60 (1.13, 2.27)***
12 to 15 years	0.66 (0.46, 0.95)***	1.52 (1.21, 1.90)***	1.22 (0.85, 1.74)
16 to 18 years	0.86 (0.59, 1.26)	2.01 (1.57, 2.57)***	1.66 (1.15, 2.41)***
Race Ethnicity			
Non-Hispanic white (Ref)			
Non-Hispanic black	1.08 (0.77, 1.53)	0.41 (0.32, 0.52)***	0.48 (0.34, 0.68)***
Mexican-American	0.92 (0.65, 1.30)	0.92 (0.75, 1.14)	0.67 (0.49, 0.92)***
Other	1.14 (0.79, 1.65)	0.80 (0.64, 1.01)	0.74 (0.53, 1.05)
Household Income			
$0 to $19,999 (Ref)			
$20,000 to $44,999	1.14 (0.81, 1.59)	0.86 (0.70, 1.06)	1.03 (0.76, 1.40)
$45,000 to $74,999	0.98 (0.66, 1.44)	0.90 (0.71, 1.14)	0.78 (0.54, 1.13)
$75,000 to $99,999	1.06 (0.65, 1.75)	0.73 (0.53, 1.00)	0.73 (0.45, 1.18)
$100,000+	1.11 (0.71, 1.72)	0.61 (0.45, 0.80)***	0.81 (0.53, 1.23)
Tobacco Exposure			
Non-Exposed[5] (Ref)			
Environmental Exposure[6]	1.33 (0.75, 2.39)	1.25 (0.97, 1.61)	0.93 (0.63, 1.37)
Tobacco User[7]	1.05 (0.70, 1.57)	1.62 (1.14, 2.31)***	1.48 (0.91, 2.39)

***ORs significant at the 0.05 level

Note: Dyslipidemias are defined as TC >=200 mg/dl, HDL-C < 40 mg/dl, and non-HDL-C >=145 mg/dl

[1]Healthy Weight = BMI 5th – 84th percentile

[2]Underweight =BMI <5th percentile

[3]Overweight = BMI 85th to 94th percentile

[4]Obese = BMI >= 95th percentile

[5]Non-Tobacco Exposure = Cotinine level <1 ng/ml

[6]Environmental Tobacco Exposure = Cotinine level 1 to 10 ng/ml

[7]Tobacco User = Cotinine level > 10 ng/ml

CHAPTER V
DISCUSSION AND CONCLUSION

5.1 *Study Purpose*

BMI at the 85th percentile is the threshold to designate children and adolescents at risk for dyslipidemia and screening is recommended by the Expert Panel. Although research has demonstrated a positive relationship between obesity and dyslipidemia and CVD, research specific to the relationship of overweight rather than obese youth and dyslipidemias is lacking. The purpose of this study was to examine associations between BMI at the 85th percentile or greater and dyslipidemias of total cholesterol, high-density lipoprotein cholesterol and non-high-density lipoprotein cholesterol in children and adolescents 6 through 18 years of age.

5.2 *Descriptive Data*

For the three lipid factors studied, mean value differences between males and females are not significant. The present study found that the mean concentration of TC among 6 to 18 year old youth is 158.7 mg/dl for males and 159.8 mg/dl for females. An elevated TC is found in 7.7% of the study participants. This is lower than published findings from other NHANES studies where approximately 10% of children ranging from 6 to 18 years of age had elevated TC levels. Consistent with earlier studies children in the younger age groups, 6 to 11 years of age have significantly higher mean values of TC in comparison to those 12 to 18 years old. There is no significant difference found among race/ethnicity groups for TC in this study. Whereas NHANES 1999-2006 analysis conducted by Ford, Li, Zhao, and Mokdad (2009) found blacks had higher

concentrations of TC in comparison to whites and Mexican-Americans. TC mean levels are significantly lower in healthy weight children compared to overweight (-3.45 [95% CI: -6.59, -0.31]) and obese children (-5.41 [95% CI: -8.26, -2.56]). There are no significant differences in the mean TC values of participants based on household income or tobacco exposure.

The most obvious finding in the descriptive analysis is the high prevalence of HDL-C dyslipidemia. In the present study dyslipidemic HDL-C values are found in 27.4% of the participants. This prevalence is much higher than another NHANES study from the 2001–2006 cycles, with published prevalence rates of approximately 19% for HDL-C at or below 40 mg/dl (Johnson et al., 2009).

In all but one age comparison group, the mean values of HDL-C decrease with age, most with significance. The exception is an increase in mean HDL-C value from the 6 to 8 year old group to the 9 to 11 year old children. Decreasing HDL-C values as children age into adolescence may indicate that dyslipidemia is increasing in this study group. This is consistent with reports by Li et al. (2010) who found a much higher prevalence (57%) of HDL-C abnormality in adolescents, in comparison to 10 to 11 year old boys (24%). In the present study, non-Hispanic blacks have significantly higher levels of mean HDL-C in comparison with all other race/ethnic groups. This positive finding is also reflected in this group's dyslipidemia prevalence. Non-Hispanic blacks have the lowest HDL-C dyslipidemia (18.8%) compared to all other race ethnic groups (28.8 – 31.3%). This finding of racial difference is consistent with an earlier NHANES' study by Johnson et al. (2009).

In the present study, HDL-C demonstrates significant mean differences for income and cotinine categories. Participants from households at the lowest income level have mean HDL-C values approximately 2.17 mg/dl lower than the highest two income categories. In regards to dyslipidemia development, it is reasonable to expect a socioeconomic effect. Low-income groups are disadvantaged because they have less access to healthful foods, fewer physical activity options and generally experience stress related to their life condition, which can contribute to obesity development. Study results for tobacco exposure are more dramatic, the changes in mean values of HDL-C decrease by a mean value of 5.11 md/dl for a tobacco user versus a non-tobacco user. These findings concur with known risk factors for low HDL-C, which include smoking, lack of physical activity, excess body weight, and a diet high in refined carbohydrates (Harvard University, 2012).

Of all the variables analyzed for mean differences the most profound difference is found in the BMI percentile for HDL-C. Mean HDL-C values consistently decrease, inversely to BMI percentile category increases, all with significance except for the underweight and healthy weight group. Although not significant, the mean HDL-C value for the healthy weight group is still lower than the underweight group.

Non-HDL-C mean values are 106.1 for males and 107.1 for females. In this study population 9.1% have abnormal non-HDL-C levels. Significant results for mean values of this lipid factor involve age groups, race ethnicity and BMI percentile findings. In regards to age groups, 12 to 15 year old children have significantly lower mean values than all other age groups. Although specific research on non-HDL-C is lacking, this seems to be consistent with dyslipidemia studies in general that have found decreases in

cholesterol levels during puberty. In this study sample, non-Hispanic blacks have considerably lower non-HDL-C values than all other groups studied ranging from 4.3 to 5.3 mg/dl less. The results for BMI percentile categories and resulting difference among non-HDL-C mean values is significant for all combinations, except the healthy weight and underweight comparison. In all cases, higher BMI percentile categories have higher mean non-HDL-C values in comparison to lower BMI percentile groups.

5.3 *Test Agreement*

Predictiveness of BMI percentile overweight category (85th through 94th percentile) at detecting dyslipidemia is evaluated by constructing two by two tables and calculating sensitivity, specificity, PPV and NPV for each of the three lipid factors. A true positive test is defined as an overweight, but not obese child, who also has a positive lipid abnormality. A false positive test is defined as an overweight, but not obese child with a negative test for lipid abnormality. A true negative test is defined as a healthy weight (5th through 84th percentile BMI) child, who also has a negative test for lipid abnormality. A false negative test is defined as a healthy weight child with a positive lipid abnormality.

Overall sensitivity for all three lipid factors is poor ranging from a low of 30.4% for TC to 36.3% for non-HDL-C. Specificity in comparison is in a much more acceptable range of 78.4 to 80.7%. The overall PPVs are very low at 9.1% for TC and 10.7% for HDL-C. The PPV for HDL-C demonstrates the most discrimination, but is low at 31.0%. Test agreement statistics stratified by age categories produces interesting results. For both TC and non-HDL-C, the 9 to 11 year old group has the highest sensitivity and PPVs. Sensitivity for HDL-C increases commensurate with increasing

age categories, but the 12 to 15 year old group has the highest sensitivity (38.8%), whereas the 16 to 18 year olds has the highest PPV (37.8%). The NPVs are high ranging from 82.1 to 94.7% and consistent with earlier research by Lee et al.

Test agreement analyses from previous research is not entirely consistent with the present study, however parameters used also differ which make them difficult to compare. In the Project HeartBeat study, results included similar sensitivity and specificity levels, but higher PPV values for TC (26%) and HDL-C (24%) (Eissa, Wen, Mihalopoulos, Grunbaum, & Lararthe, 2009). Lee et al., (2009) studied NHANES data from earlier years and reported much higher sensitivities, 51% for TC and 64% for HDL-C and different PPVs 14% for TC and 11% for HDL-C.

The PPV for TC (9.1%) in the present study is lower than results (14%) from Lee and colleagues (2009). The PPV for HDL-C (31.0%) is much higher than 11% found in the earlier study by Lee et al. This may be a function of disease prevalence, as this study has a higher prevalence of HDL-C positive dyslipidemia than earlier research. Positive predictive values increase in accuracy with increasing disease prevalence. In the present study, prevalence of TC is 7.7% and for HDL-C 27.4%. In contrast, Lee et al. reported higher TC prevalence (males 8.2%, females 10.2%) and much lower HDL-C prevalence (males 7.9%, females 5.4%). The study by Lee et al. was on subjects from NHANES cycle years 1999-2004. What is alarming here are the indications that HDL-C dyslipidemia prevalence may be substantially higher in US youth today compared to levels from only one decade ago.

5.4 *Logistic Regression*

The variables of BMI percentile and age dominate the associations found in both the simple and multivariate models. The most profound results are in the BMI percentile categories. For all three lipid factors, as children increase from overweight to obese categories their ORs for dyslipidemia increase. These findings remain significant after controlling for gender, age, race ethnicity, income and tobacco exposure. The risk for dyslipidemias among obese children is about two times that of overweight children (TC 1.5 to 2.1; HDL-C 2.0 to 5.0; non-HDL-C 2.1 to 4.2). These findings are consistent with studies that have shown increasing relative risk for dyslipidemias as BMI weight status categories increased (Freedman, Dietz, Srinivasan, Berenson, 1999; Holl et al., 2011).

Age related risk differences were found in this study. The protective effect of the pubertal years is especially noted for TC with a significant OR = 0.7 for children 12 to 15 years of age. This value remains unchanged in the multiple logistic regression model after controlling for all other independent covariables. Significant findings in the age categories for HDL-C and non-HDL-C also remain essentially unchanged in the multiple logistic regression model compared to the univariate analyses. HDL-C odds ratios are higher as age categories increase (OR = 1.3 to 2.0). For non-HDL-C, the OR for the 12 to 15 year old group is less than the other age categories, but this finding is not significant. These study findings are consistent with lipid value changes in relation to pubertal maturation also found by Bogalusa researchers and Kwiterovich et al., 1977 (Berenson, Srinivasan, Cresanta, Foster, & Webber, 1981).

Although a number of large studies exist that have found increased TC values among black children in comparison to white children, this study did not find significant

differences among race ethnic groups for TC dyslipidemia (Freedman, Lee, Byers, Kuester, & Sell, 1992; Frerichs, Srinivasan, Webber, & Berenson, 1976; Webber et al., 1991). Study results for TC are also inconsistent with a study by Resnicow and colleagues who found significantly higher TC values for both black and Hispanic children in comparison to white children (1989). This study's logistic regression analysis revealed significant findings in the race ethnicity categories for HDL-C and non-HDL-C dyslipidemias. Non-Hispanic black subjects demonstrate a protective effect against HDL-C (OR = 0.4) and non-HDL-C (OR = 0.5) dyslipidemia in simple and multivariate logistic regression. After controlling for gender, age, BMI percentile, income and tobacco exposure, Mexican-Americans also have a significant decreased risk for non-HDL-C dyslipidemia (OR = 0.7).

Prior research and statistics exist which agree with this study's findings in regards to the protective effect of non-Hispanic black race and HDL-C dyslipidemia. NGHS researchers found decreased risk for African-American girls to exhibit unhealthful HDL-C and 2012 Heart Disease and Stroke Statistics report much higher HDL-C mean values in non-Hispanic blacks compared to non-Hispanic whites and Mexican American boys and girls (Roger et al., 2012; Thompson et al., 2007). However there are some inconsistencies with this study's findings and prior research. Bogalusa investigators found that non-HDL-C values were similar in black and white children, and Tortolero and colleagues found Mexican American boys had slightly lower HDL-C levels than non-Hispanic white boys (Srinivasan, Myers, & Berenson, 2002; Tortolero et al., 1997).

In adults, socioeconomic status strongly predicts CVD risk factors. A study of NHANES subjects from 1999-2008 found 6 to 17 year olds from low-income families

have higher prevalence of obesity, sedentary behavior and tobacco exposure, all of which are risk factors for abnormal low HDL-C levels (Ali et al., 2011). In the present study, household income is included to account for socioeconomic influence on the outcome variables. HDL-C is the only lipid factor with a significant finding. Youth from homes with the highest income, greater than $100,000 a year, have 40% less risk for HDL-C dyslipidemia than children from the lowest income households. This significant finding remains unchanged after controlling for BMI percentile, gender, age, race ethnicity and tobacco exposure.

In the present study, tobacco use risk demonstrates the most change between simple and multiple logistic regression analyses. Tobacco users in simple logistic regression are at greater risk for HDL-C (OR = 2.1) and non-HDL-C (OR = 1.9) dyslipidemia. This is consistent with previous studies that have found unfavorable changes in plasma lipids, including HDL-C, amongst youth who smoke tobacco (Clarke et al., 1986; Craig, Palomaki, Johnson, & Haddow, 1990; Glueck, Heiss, Morrison, Khoury, & Moore, 1981). In the multivariate logistic regression, tobacco users risk for HDL-C abnormality reduces to OR = 1.6, but remains significant. For non-HDL-C dyslipidemia, the risk from tobacco use is no longer significant (OR = 1.4 [95% CI: 0.9, 2.4]) after controlling for all other covariables, BMI percentile, age, gender, race ethnicity, and income.

5.5 *Public Health Implications*

Atherosclerotic CVD is the leading cause of death in the US and many risk factors that contribute to development of atherosclerosis begin in childhood. The basis for screening children at risk for dyslipidemia is a function of primary prevention with the

goal to identify children at increased risk and to prevent CVD development by effectively

managing risk factors. Pediatric guidelines include targeted screening of children with

BMIs at or greater than the 85th percentile, but studies are lacking on associations of the

overweight BMI category children and dyslipidemia.

Findings from this study have contributed to the body of knowledge concerning

the relationship of youth BMI percentiles and dyslipidemias of TC, HDL-C and non-

HDL-C. The results of this study provide additional statistics on the current prevalence

of lipid levels in US youth in the context of gender, race, age, income, tobacco exposure

and BMI percentiles. Further information is presented on test agreement and association

of BMI at the 85th percentile and dyslipidemias of TC, HDL-C and non-HDL-C. This

study has contributed to the body of knowledge of BMI percentiles and relationships with

abnormal levels of TC, HDL-C and non-HDL-C by examining a large sample of US

youth. Overall, results from this study can be used as a reference for additional studies

and for planning intervention programs that aim to reduce the burden of CVD.

5.6 *Strengths and Limitations*

The major strengths of this study are related to the source of the data NHANES.

NHANES surveys are conducted in a manner that uphold the highest research standards

and result in a high quality, comprehensive data bank of health information from a

national representative sample of the US population. Another major strength of this

study is the relatively large sample size, which lends itself to greater statistical

significance and representation from three distinct race/ethnicity groups. Also due to the

comprehensive nature of NHANES, it was possible to include considerable details related

to the participants and to include non-HDL-C in the study.

Limitations of this study are that not all race/ethnic groups could be represented. In particular, NHANES does not have a separate category for Asians and it would have been informative to include this group in the analysis. In some regards, it was difficult to include confounders due to nuances of NHANES. Thus the study does not include variables related to hypertension and diabetes, which are known high risk factors for atherosclerosis development. There were limitations in the selection of lipid factors selected for the study. Triglycerides and low density lipoprotein-cholesterol are not included because this would have decreased the sample size and limited the age of the study sample to those over 12 years. NHANES is a cross sectional survey and there was only one laboratory value for each lipid factor. Individual lipid levels can vary and evaluation should not be based on a single laboratory test. Thus, a limitation is that only one value per lipid factor was available for this study.

5.7 *Recommendations*

Obesity is clearly established as a CVD risk factor, however studies on overweight youth and dyslipidemia are lacking. This study has contributed to the body of knowledge of youth risk for dyslipidemias according to BMI weight status categories. Results of this study support continued screening of children and adolescents in the overweight category, as both overweight and obese youth were found to be at increased risk for dyslipidemias. Although targeted screening of overweight children was not supported by results of the test agreement analysis, these analyses may have been problematic due to the multifactorial basis for dyslipidemia and low dyslipidemia prevalence found in the sample. Further research on associations of pediatric overweight, obesity and

dyslipidemia, and specifically studies on the effectiveness of BMI at the 85th percentile as a predictor of dyslipidemias in youth are warranted.

In regards to race and ethnicity, most studies have been conducted on non-Hispanic whites and non-Hispanic blacks. Additional research on a broader range of race/ethnic groups is needed, especially in US Hispanic and Asian populations. Further studies are needed to assess the relationship of tobacco use and dyslipidemias. Tobacco use is a known risk factor for dyslipidemias, however in this study the multivariate regression analysis revealed significant findings only for HDL-C.

It is important to continue surveillance of distinct dyslipidemia prevalence among our youth. Full lipid profiles are more revealing. Results of the present study found differences in TC, HDL-C and non-HDL-C dyslipidemia prevalence, as well as differences in dyslipidemias according to age and race ethnicity groups. The prevalence of HDL-C was alarming, as it was much higher in this study cohort than had been reported in earlier research. These findings validate the importance of monitoring lipid factors and dyslipidemia prevalence in our youth.

The obesity epidemic is of utmost concern and the evidence base is strong that obesity is a major risk factor for CVD, as well as other risk factors for CVD such as dyslipidemias and diabetes. Additional studies on the effects of physical inactivity and diet in regards to dyslipidemias could add valuable information for both risk conditions. Further studies may reveal a genetic component related to ethnic origin and responses to diet or physical activity levels. For example, some groups may have less tolerance for fat intake or respond more positively to physical activity.

Studies that analyze the effects of screening youth and detecting dyslipidemias, which may lead to identifying additional family members with dyslipidemias, could reveal a secondary benefit from screening youth, in that we could ameliorate the health consequences of CVD in two generations simultaneously. This could also lead to studies that examine the relationship of a mother's or father's dyslipidemia status and those of their children. Prospective studies on children through adulthood, which examine their CVD risk status, how risk status changes over time, if knowledge of risks effects behavior, the effects of intervention and incidence of CVD, would ultimately offer the most credible information on CVD screening in youth and planning CVD prevention programs.

5.8 *Conclusion*

This study has provided further evidence that not only obese, but overweight children are at greater risk for dyslipidemias of TC, HDL-cholesterol and non-HDL-cholesterol. Findings show the importance of analyzing individual lipid factors, especially HDL-C in contrast to only obtaining a TC value, as the components offer a much better picture of the individual's lipid status and each lipid factor seems to be affected by risk factors differently. As in earlier reported research, BMI at the 85th percentile did not provide good discrimination in detecting children and adolescents with dyslipidemia. Thus despite this study's findings that overweight children are at increased risk for dyslipidemias, overweight status and perhaps even obesity, may not be strong enough risk factors individually, to translate into a good screening indice for youth dyslipidemia. Use of BMI at the 85th percentile as a threshold for dyslipidemia screening in youth warrants further consideration. Considering age-related prevalence and the lack

of predictiveness of major screening criteria, such as family history and BMI at the 85th percentile, the recent change in recommendations by the Expert Panel to include universal screening of 9 to 11 year old children is affirmed and may obviate the need to target screen overweight children for dyslipidemia.

Atherosclerotic cardiovascular disease is the leading cause of death in the US and CVD is a chronic condition that begins in youth. Public health primary prevention goals aim to reduce the burden of CVD by reducing risk factors early in life. The high prevalence of overweight and obese US youth is a public health concern for the development of chronic diseases, including CVD. The results of this study, and other research, have demonstrated that overweight and obese youth are at increased risk for dyslipidemias. It is important to continue public health efforts to reduce obesity prevalence, as well as other risk factors, which lead to adult CVD. Public health surveillance and study of lipid levels in youth and risk behaviors that can lead to dyslipidemias, atherosclerosclerosis and CVD is vital, in the effort to better understand this disease process, promote prevention programs and ultimately to reduce the burden of cardiovascular disease.

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