MAJOR DEPRESSION AND INSULIN RESISTANCE AMONG NONDIABETIC U.S. ADULTS AGED 20-39 YEARS: THE ROLES OF GENDER AND RACE/ETHNICITY

BY

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ABSTRACT

The relationship between depression and insulin resistance has been evaluated in previous studies but with conflicting results. No study was found that investigates the role of race/ethnicity in the relationship between depression and insulin resistance. The purpose of this study was to: 1) determine the prevalence of major depression and insulin resistance among nondiabetic young adults aged 20-39 years in the United States, 2) examine the relationship between major depression and insulin resistance among nondiabetic young adults aged 20-39 years in the United States, and 3) determine whether this relationship varies by gender, race/ethnicity, or measure of depression.

Analyses of cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) 1999-2008 were performed. The study sample consisted of 1,054 (46.5%) men and 1,211 (53.5%) women who were nondiabetic and aged 20-39 years (N = 2,265). Major depression was measured by the Composite International Diagnostic Interview in NHANES 1999-2004 and by the Patient Health Questionnaire-9 in NHANES 2005-2008. Insulin resistance was measured by the homeostasis model assessment for insulin resistance.

The prevalence of major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years in the study was 3.7% (n = 84; weighted % = 3.8) and

25.7% (*n* = 582; weighted % = 22.7) respectively. No significant association was found between major depression and insulin resistance in bivariate logistic regression analysis. However, a significant interaction effect between gender and major depression was observed. For men, major depression was negatively associated with insulin resistance after adjusting for age, race/ethnicity, systolic blood pressure, triglyceride level, high-sensitivity C-reactive protein, obesity, leisure time physical activity, smoking, and alcohol consumption. In contrast, no significant association between major depression and insulin resistance among women was found. There was no significant interaction between race/ethnicity and major depression. No significant variations in the relationship between major depression and insulin resistance by measure of depression were revealed. Study findings provide support for a significant positive relationship between insulin resistance and 1) systolic blood pressure, 2) triglyceride level, 3) and obesity as measured by body mass index or waist circumference among nondiabetic young adults aged 20-39 years.

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CHAPTER I INTRODUCTION

Insulin Resistance and Depression

Insulin resistance is causally linked to the development of type 2 diabetes (Fonseca, 2007). Clinical abnormalities, such as hypertension, elevated triglyceride and low-density-lipoprotein cholesterol (LDL-C), or decreased high-density-lipoprotein cholesterol (HDL-C), that are associated with insulin resistance and its accompanying hyperinsulinemia also contribute to an increased risk for cardiovascular disease (Reaven, 2005a; Saely et al., 2005). Given advances in modernization and current sedentary lifestyles, the prevalence of insulin resistance has significantly increased (Lloyd-Jones et al., 2010). The adverse effects of insulin resistance are latent but detrimental (Jellinger, 2007; Lebovitz, 2006; Reaven, 1988). Without intervention, insulin resistance can progress to type 2 diabetes and accompanying negative sequelae, such as hypertension, dyslipidemia and other cardiovascular disease.

According to the 2007 National Diabetes Fact Sheet, 7.8% of the United States population, or about 23.6 million people have diabetes. Approximately 90-95% of those affected have type 2 diabetes. Another estimated 57 million people have prediabetes; a condition when blood glucose levels are higher than normal but do not meet the diagnostic criteria of diabetes that includes impaired fasting glucose [IFG]

and impaired glucose tolerance [IGT]. About 1.6 million new cases of diabetes are diagnosed in adults aged 20 years and older every year (CDC, 2008).

The costs associated with diabetes are high. In 2007, the estimated total national cost of diabetes in the United States was approximately $174 billion (CDC, 2008; National Institute of Diabetes and Digestive and Kidney Diseases, 2008). According to current national diabetes cost statistics, this $174 billion included $116 billion direct costs related to medical expenditures and $58 billion indirect costs associated with increased absenteeism, reduced productivity and lost productive capacity (American Diabetes Association, 2008b; CDC, 2008; National Institute of Diabetes and Digestive and Kidney Diseases, 2008). The average medical expenditures of individuals with diagnosed diabetes is $11,744 per year (American Diabetes Association, 2008b).

The rate of diabetes related complications also is increasing. It is reported that the death rate of heart disease among people with diabetes is two to four times higher than those without diabetes (Lloyd-Jones, et al., 2010). In addition, diabetes is the leading cause of new cases of blindness and kidney failure. More than 60% of nontraumatic lower-limb amputations occur in diabetic patients. According to the latest available data, diabetes was the seventh leading cause of death listed on United States death certificates in 2006, which contributed to a total of 233,619 deaths in 2005 (CDC, 2008).

Depression also is a major cause of morbidity and mortality in the United States. It has substantial negative impact on patients' quality of life, physical and mental well-being, and social functioning, which can lead to increased disability and reduced work productivity (Halfin, 2007). The economic burden of depression on society and individuals is enormous. In 2000, the estimated total cost of depression in the United States was $83.1 billion (Greenberg et al., 2003; Wade & Haring, 2010). This included $26.1 billion (31%) (equivalent to $32 billion in 2008) for direct medical costs, $51.5 billion (62%) (equivalent to $63 billion in 2008) for indirect costs, and $5.4 billion (7%) for suicide-related mortality costs (Greenberg, et al., 2003; Wade & Haring, 2010). In Sweden, the total cost of depression for 2005 was 3.5 billion Euros, including 500 million Euros (16%) of direct medical costs, 3 billion Euros (86%) of indirect costs and 100 million Euros of drug cost (3%) (Sobocki, Lekander, Borgstrom, Strom, & Runeson, 2007). At the individual level, it was reported that patients with depression had 50-100% higher medical expenditures than comparable patients without depression (Halfin, 2007). Moreover, workers with depression were on short term disability an average of 1.5 to 3.2 days longer in a one-month period than those without depression, translating into an average salary loss of $182 to $395 person/month (Kessler et al., 1999).

Studies have found an increased prevalence of depression among patients with diabetes, and other chronic diseases such as asthma, cancer, cardiovascular disease, and obesity (Chapman, Perry, & Strine, 2005). It was reported that about 50% of patients with asthma experienced clinically significant depressive symptoms (Di

Marco, Santus, & Centanni, 2010; Mancuso, Peterson, & Charlson, 2000). Moreover, depression may play an important role in the etiology and pathogenesis of these chronic diseases. The overall relative risk for developing coronary heart disease among patients with depression was 1.64 (95% confidence interval [CI] = 1.29-2.08) based on a meta-analysis (Rugulies, 2002). Similar findings were observed in a recent prospective cohort study among 23,282 Finnish adults aged 20-54 years (Nabi et al., 2010). A positive bidirectional association between depression and type 2 diabetes also has been well established. Results from two meta-analyses demonstrated that individuals with depression had a 37% increased risk of developing type 2 diabetes (Knol et al., 2006) and patients with type 2 diabetes had a 24% increased risk of developing depression (Nouwen et al., 2010). Women with diabetes had significantly higher prevalence of depression than men (23.8% vs 12.8%) (Ali, Stone, Peters, Davies, & Khunti, 2006). Although insulin resistance is the underlying mechanism for type 2 diabetes, the relationship between depression and insulin resistance is far less studied and remains unclear with conflicting results reported from previous studies.

Prevalence of Insulin Resistance

Insulin resistance can be present in apparently healthy appearing persons. The reported prevalence of insulin resistance in the general population ranges from 21.5% (Do, Lohsoonthorn, Jiamjarasrangsi, Lertmaharit, & Williams, 2010) to 59% (Petersen et al., 2006) and varies by racial/ethnic groups. Among adults aged 20 years and older with euglycemia, the reported prevalence of insulin resistance was 32.2%

(Ioannou, Bryson, & Boyko, 2007). The prevalence of insulin resistance was even higher among patients with metabolic syndrome and chronic diseases. In a recent study conducted among 1,453 U.S. eighth-grade students, those with highest quintiles (20%) of the homeostasis model assessment for insulin resistance (HOMA-IR), a surrogate of insulin resistance, were almost 200 times more likely to have metabolic syndrome than those with the lowest quintile of HOMA-IR (Jago et al., 2008). An estimated 40.2% of women with polycystic ovary syndrome (PCOS) had insulin resistance (Vrbikova et al., 2007). About 50% of patients with primary hypertension were insulin resistant, regardless of their treatment status (treated or untreated) (Lima, Abbasi, Lamendola, & Reaven, 2009). Overall, the variations in reported prevalence rates may result from the methods used to measure insulin resistance and the cutoff value to define insulin resistance.

Prevalence of Depression

Depression is a mood disorder. As defined by the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) (American Psychiatric Association, 1994), depression can be further classified as major depressive disorder (MDD), also known as major depression, dysthymic disorder, and depressive disorder not otherwise specified (NOS), or minor depression. Their definition and clinical diagnostic criteria are discussed in detail in a later section.

Estimates of the prevalence of depression in the United States vary across studies, depending on the operational definition of depression (clinical diagnosis of depression or depressive symptoms), measurements (structured clinical diagnostic interview or self-report depression questionnaire/inventory), and studied populations (general population or diseased populations). The prevalence of lifetime depression in the general population ranges from 15.7% to 16.2%. A more detailed discussion on prevalence of depression across age, gender, and race/ethnic groups can be found in Chapter II of this dissertation.

Statement of the Problem

A limited number of studies have been conducted to examine the relationship between depression and insulin resistance. Based on the fact that depression is highly prevalent among patients with type 2 diabetes and insulin resistance precedes development of type 2 diabetes, it was hypothesized that depression and insulin resistance are positively associated. However, the relationship between depression and insulin resistance remains unclear as the limited number of studies conducted report mixed results. A detailed discussion of these previous studies is included in Chapter II of this dissertation. Moreover, all these studies were conducted in Europe, Australia, or Asia and most were limited to middle- and older-aged adults. Only two studies explored the relationship between depression and insulin resistance in young males and only one study compared this relationship in young males and females. Study methodologies further limit the generalizability of their results. No known

study was found that investigates the relationship between depression and insulin resistance by race/ethnicity.

Significance

Investigation of the relationship between depression and insulin resistance among young adults is essential to understanding how insulin resistance may be influenced by depression among what is generally considered a healthy population. With identification of persons who are at risk of developing insulin resistance in primary care clinics, preventive interventions can be developed to intervene at an early stage. Knowing the impact of depression on young adults' health will encourage health care professionals to recognize depression in the clinical settings and provide appropriate treatment. Prompt intervention may help delay or prevent the progression of insulin resistance to type 2 diabetes. Improving the state of insulin resistance at an early age can not only delay the onset of type 2 diabetes, but also may decrease the morbidity and mortality rate of chronic diseases associated with insulin resistance later in life as well as health care costs.

Purpose

The purpose of this study, using data from the National Health and Nutrition Examination Survey (NHANES), was to: 1) determine the prevalence of major depression and insulin resistance among nondiabetic young adults aged 20-39 years in the United States, 2) examine the relationship between major depression and

insulin resistance among nondiabetic young adults aged 20-39 years in the United States, and 3) determine whether the relationship between major depression and insulin resistance varies by gender, race/ethnicity, and measure of depression.

Assumptions

The study was based on the following assumptions:

1. The clinical guidelines on metabolic syndrome from the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) (NCEP ATP III, 2002) and World Health Organization (WHO) (Alberti & Zimmet, 1998) provide evidence based support for factors closely associated with insulin resistance.

2. The phenomenon of insulin resistance was measureable by established methods such as the homeostasis model assessment for insulin resistance.

3. Physiological variables included in this study were measureable by suitable laboratory equipment and assays.

4. Behavioral or demographic variables in this study were measurable through self-report.

5. Participants selected in NHANES 1999-2008 to represent the U.S. civilian, non-institutionalized population actually represented the U.S. civilian, non-institutionalized population.

6. The depression instruments of the Composite International Diagnostic Interview (CIDI) and the Patient Health Questinnaire-9 (PHQ-9) measured major depression in the same way, using the diagnostic criteria established by the *American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*. However, this assumption was examined in the analyses.

Conceptual Schema

A conceptual schema was constructed to provide a theoretical basis for the study. The clinical guidelines from NCEP ATP III (NCEP ATP III, 2002) and WHO (Alberti & Zimmet, 1998) on metabolic syndrome provided the basis for selecting covariates for the study. Figure 1 demonstrates the factors that are associated with insulin resistance supported by these two scientific bodies and review of the literature in Chapter II of this dissertation. Factors associated with insulin resistance were categorized as demographic, physiological, and lifestyle factors. The relationship between depression, as a psychological factor, and insulin resistance and whether this relationship varied by gender and race/ethnicity were examined in the study. Factors that are italicized in the conceptual schema were not tested. These factors and their relationship with insulin resistance are discussed in detail in Chapter II.

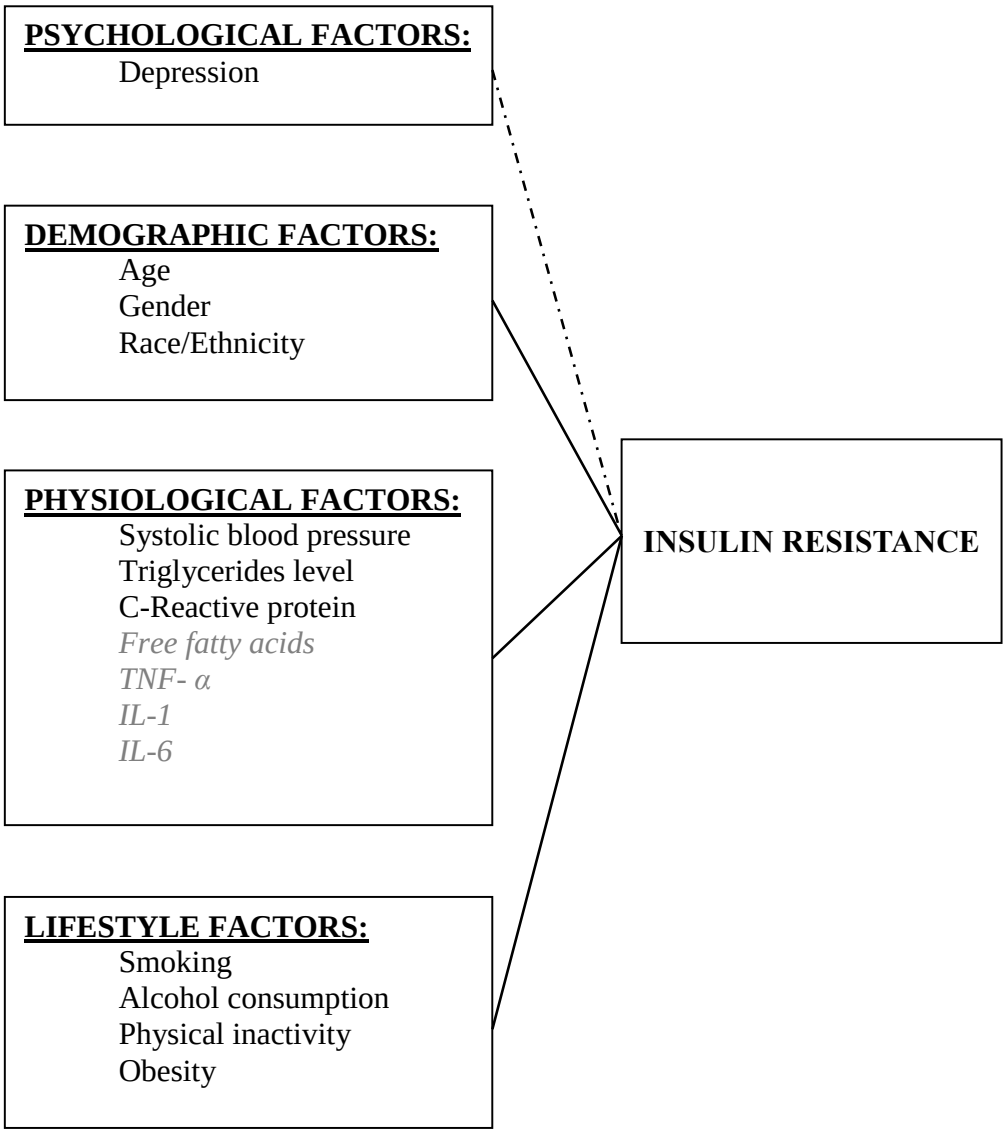


Figure 1. Conceptual schema of factors thought to be associated with insulin resistance.

(Synthesized from NCEP ATP III. (2002). Third report of the expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (ATP III final report). Retrieved from http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3_rpt.htm)

Research Questions

The following were the research questions that were explored in this study:

1. What is the overall prevalence of major depression among nondiabetic U.S. adults aged 20-39 years?

2. What is the overall prevalence of insulin resistance among nondiabetic U.S. adults aged 20-39 years?

3. What is the relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years?

    a) What is the unadjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years?

    b) What is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by gender, adjusting for age, race/ethnicity, systolic blood pressure, triglyceride, high-sensitivity C-reactive protein (hs-CRP), obesity (body mass index [BMI] or waist circumference), physical activity, smoking status, and alcohol consumption?

        b1) Is there an interaction between gender and major depression in the relationship with insulin resistance among nondiabetic U.S. adults aged 20-39 years?

b2) If the interaction between gender and major depression is significant, what is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by gender, adjusting for age, race/ethnicity, systolic blood pressure, triglyceride, hs-CRP, obesity (BMI or waist circumference), physical activity, smoking status, and alcohol consumption?

b3) If the interaction between gender and major depression is not significant, what is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years, adjusting for age, gender, race/ethnicity, systolic blood pressure, triglyceride, hs-CRP, obesity (BMI or waist circumference), physical activity, smoking status, and alcohol consumption?

c) What is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by race/ethnicity, adjusting for age, gender, systolic blood pressure, triglyceride, hs-CRP, obesity (BMI or waist circumference), physical activity, smoking status, and alcohol consumption?

c1) Is there an interaction between race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, and other) and major depression in the association with insulin resistance among nondiabetic U.S. adults aged 20-39 years?

c2) If the interaction between race/ethnicity and major depression is significant, what is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by race/ethnicity, adjusting for age, gender, systolic blood pressure, triglyceride, hs-CRP, obesity (BMI or waist circumference), physical activity, smoking status, and alcohol consumption?

c3) If the interaction between race/ethnicity and major depression is not significant, what is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years, adjusting for age, gender, race/ethnicity, systolic blood pressure, triglyceride, hs-CRP, obesity (BMI or WC), physical activity, smoking status, and alcohol consumption?

4. What is the relationship between major depression and insulin resistance by types of depression measure among nondiabetic U.S. adults aged 20-39 years?

a) What is the unadjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by types of depression measure?

b) What is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by types of depression measure, adjusting for age, gender, race/ethnicity, systolic

blood pressure, triglyceride, hs-CRP, obesity (BMI or waist circumference), physical activity, smoking status, and alcohol consumption?

Definitions of Terms

The definitions of the terms used in this study are provided below. The operational definitions of the terms also are specified.

Nondiabetic U.S. adults aged 20-39 years

Conceptual definition. Nondiabetic U.S. adults aged 20-39 years are defined as U.S. adults aged 20-39 years who do not have diabetes.

Operational definition. Operationally, this was defined as: 1) U.S. adults aged 20-39 years who participated in the NHANES 1999-2008, 2) who denied having diabetes, and 3) had a fasting glucose < 126 mg/dl at the time of NHANES participation.

Insulin Resistance

Conceptual definition. Insulin resistance occurs, when a higher than normal amount of insulin is required to maintain euglycemia. Clinically, insulin resistance is defined as “the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal

population" (Lebovitz, 2001, p. S136). Although insulin has various actions, it is its effect on glucose uptake and utilization that defines insulin resistance. This is the basis for all the techniques that apply the relationship between insulin supply and glucose uptake and utilization to quantify insulin resistance. Insulin exerts its actions by binding to insulin receptors on cellular membrane and induces a conformational change in the receptors that triggers two major cascades of protein-protein interactions. Any factor that intervenes in the process can impair insulin action, particularly glucose uptake.

Operational definition. Insulin resistance was measured by the homeostasis model assessment for insulin resistance (HOMA-IR) in this study. It was operationally defined as a HOMA-IR score ≥ 75 percentile of HOMA-IR scores in the nondiabetic population aged ≥ 20 years. Study subjects whose HOMA-IR scores were above the top 25% were defined as insulin resistant individuals. The rest were defined as non-insulin resistant. The HOMA-IR is discussed in detail in the Chapter III of this dissertation.

Depression

Conceptual definition. Depression is a mood disorder that is defined as recurrent disturbances or alterations in mood that cause psychological distress and behavioral impairment.

Operational definition. The operational definition of depression for this study was a diagnosis of major depression by the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) in the NHANES 1999-2004 or a diagnosis of major depression by the Patient Health Questionnaire-9 (PHQ-9) in the NHANES 2005-2008.

Prevalence

Conceptual definition. Prevalence of a disease is defined as the total number of cases of the disease in the population at a given time and is calculated by dividing the total number of cases with the disease by the total number of individuals in the population.

Operational definition. In this study, the prevalence of insulin resistance was defined as the proportion of the total number of nondiabetic young adults aged 20-39 years who had insulin resistance. The prevalence of depression was defined as the proportion of the total number of nondiabetic young adults aged 20-39 years who had major depression.

Interaction

Conceptual definition. An interaction exists when an independent variable interacts with the independent variable of interest and affects the strength and/or direction of the association between the independent variable of interest and an

outcome variable. In other words, the association of the independent variable of interest with the outcome variable depends on the level of another independent variable (Bennett, 2000).

Operational definition. In this study, interaction was defined as an interaction term (gender*depression or race/ethnicity*depression) with a p-value $\leq .05$ in the multivariate logistic regression analyses.

CHAPTER II REVIEW OF THE LITERATURE

Insulin resistance is a significant risk factor for many diseases, especially for type 2 diabetes and cardiovascular disease. Estimates of the incidence and prevalence of insulin resistance have increased dramatically over the last two decades. Research has examined a number of factors, including depression that are associated with insulin resistance; however, the relationship between depression and insulin resistance remains unclear. This chapter reviews and summarizes the major studies on insulin resistance and depression to provide a conceptual basis for the study. Specifically, this chapter discusses the literature related to the pathogenesis of insulin resistance, factors associated with insulin resistance, and the negative impact of insulin resistance on health. The definition of depression and its classification and prevalence, the relationship between depression and insulin resistance, and the possible pathophysiological mechanisms underlying this relationship also are addressed.

Insulin Resistance

Insulin resistance is defined as attenuated insulin-stimulated glucose uptake with a normal quantity of insulin that is sufficient to produce normal glucose uptake in a normal healthy individual (Lebovitz, 2001). The concept of insulin resistance was first introduced by Himsworth (1936) about 70 years ago, when he observed that many patients with diabetes are “insulin insensitive”. With the development of advanced techniques to measure insulin activity, the phenomenon of insulin resistance

has gained substantial attention. Insulin resistance has become an increasingly common abnormality (Lebovitz, 2001), which exists not only in patients with impaired glucose tolerance and type 2 diabetes, but also in at least 25% of normal population with euglycemia (Reaven, 1988, 2005b). According to Ioannou, Bryson, and Boyko (2007), the prevalence of insulin resistance is 32.2% among normoglycemic persons and 31.1% among persons with impaired fasting glucose or undiagnosed diabetes in the United States. To better understand insulin resistance, normal insulin action is briefly reviewed.

Normal Insulin Action

Insulin plays a critical role in many metabolic processes including the regulation of glucose uptake and controlling gene transcription and cell proliferation (White & Myers, 2001). The main metabolic effects of insulin are to: 1) stimulate glucose uptake in insulin-sensitive cells such as skeletal muscle cells, adipocytes, and the liver; and 2) suppress hepatic glucose production and increase very-low-density lipoprotein (VLDL) (Yki-Jarvinen, 2003). During glucose homeostasis, insulin binds to the insulin receptors on the membranes of insulin-sensitive cells to activate tyrosine kinase, which stimulates a cascade of protein kinases to move glucose transporters 4 (GLUT 4) positioned in the membrane vesicles within the cytosol of cells to the cell surface. The presence of GLUT 4 on the cell membrane allows the transport of glucose into the cells (Barrett, 2005). Other metabolic effects of insulin include

inhibition of the release of free fatty acids from adipose tissue and facilitation of protein synthesis from amino acid (Eckel, Grundy, & Zimmet, 2005).

Insulin is considered to have anti-atherogenic effects (Yki-Jarvinen, 2003). Montagnani, Ravichandran, Chen, Esposito, and Quon (2002) found that insulin can increase the production of nitric oxide (NO) in endothelial cells of blood vessels. NO stimulates vasodilation. Insulin also can inhibit type-1 plasminogen activator inhibitor (PAI-1) (Juhan-Vague, Alessi, & Vague, 1996) and platelet aggregation (Trovati & Anfossi, 1998). In addition, insulin is thought to be a growth factor that stimulates vascular cell proliferation and synthesis of matrix proteins (Feener & King, 1997; McFarlane, Banerji, & Sowers, 2001).

Pathogenesis of Insulin Resistance

Interference with insulin's normal action can occur at any point along the complex signaling pathway. Accordingly, there are multiple possible mechanisms that can account for the development of insulin resistance. Insulin resistance occurs when its action on glucose uptake is impaired. Specifically, significantly lower glucose transport across the entire physiological range of insulin concentrations is characteristic of insulin resistance. The resulting higher circulating levels of glucose stimulate pancreatic beta cells to produce more insulin and a larger fraction of the insulin receptors must be occupied in order to maintain euglycemia (Barrett, 2005). Therefore, compensatory hyperinsulinemia is commonly present in insulin resistant individuals.

Although it is still controversial, some researchers proposed that excessive free fatty acids are implicated in the pathogenesis of insulin resistance (Eckel, et al., 2005). Free fatty acids also are believed to induce insulin resistance in muscles by impairing the insulin-signaling pathway, thus the movement of GLUT 4 to the cell membrane for glucose uptake (Boden & Laakso, 2004). The study conducted by Boden et al. (1991) showed that insulin resistance appeared two to four hours after an acute increase in plasma free fatty acid concentration and disappeared after plasma free fatty acid levels returned to normal among nondiabetic men. Similar results were found in nondiabetic women (Homko, Cheung, & Boden, 2003). However, it is known that one action of insulin is to suppress adipose tissue lipolysis and promote hepatic uptake of free fatty acids, then suppress the level of free fatty acids. Insulin resistance in liver tissue may interfere with hepatic uptake of free fatty acids thus contribute to elevated plasma free fatty acid levels (Boden & Laakso, 2004). This seemingly conflicting information makes it difficult to differentiate the direction of the relationship between insulin resistance and excessive free fatty acids. It is known that they are highly correlated with each other. In addition, excessive free fatty acids increase the level of oxidative stress (Ceriello, 2000). The reactive oxygen species generated by increased oxidative stress also may contribute to the pathogenesis of insulin resistance (Itani, Ruderman, Schmieder, & Boden, 2002). Other proposed mechanisms include genetic abnormalities in the insulin signaling pathways and fetal malnutrition (Lebovitz, 2001). Further discussion on factors associated with insulin resistance and their potential roles in the pathogenesis of insulin resistance follows.

Factors Associated With Insulin Resistance

Clinical guidelines NCEP ATP III (NCEP ATP III, 2002) and WHO (Alberti & Zimmet, 1998) identify factors associated with insulin resistance, which were delineated in research on metabolic syndrome, including hypertension, dyslipidemia, and obesity. These two scientific bodies provided the basis for selecting covariates for this study. Other covariates were identified through a review of the literature on the topic and include age, gender, race/ethnicity, C-reactive protein (CRP), physical inactivity, smoking, and alcohol consumption.

Age. The prevalence of impaired glucose tolerance and type 2 diabetes increases with age. Compared to young people, elderly adults also are more subject to insulin resistance. Fujita et al (2009) found an aged-related defect in muscle protein anabolism among healthy older adults that resulted from age-related insulin resistance as evidenced by the fact that muscle protein synthesis and anabolic signaling increased under supraphysiological hyperinsulinemia. However, the pathogenesis underlying this increasing age-associated insulin resistance is not fully understood and studies investigating the relationship between insulin resistance and age report inconsistent results. In some studies, insulin sensitivity was found to be lower among older adults than in younger people, while other studies found no significant association between insulin resistance and age, after controlling for body fat distribution or weight. For example, Karakelides, Irving, Short, O'Brien and Nair (2010) compared insulin sensitivity and skeletal muscle mitochondrial ATP

production rates (MAPRs) across 12 young lean, 12 young obese, 12 elderly lean, and 12 elderly obese adults. They found that obesity had significant effect in reducing insulin sensitivity, independent of age; while age had no independent effect on insulin sensitivity. In addition, the elderly participants had lower muscle MAPRs than the young participants, independent of obesity and insulin sensitivity. They concluded that aged-related reductions in insulin sensitivity were likely due to an aged-related increase in adiposity rather than a consequence of advanced chronological age. Similar findings were observed by Sakurai et al. (2010) among 812 Japanese elderly with type 2 diabetes aged 65 or above and by Qiao et al. (2005) in a large European population-based study with 6,314 men and 6,393 women aged 30-88 years. Although increased insulin resistance may not directly result from age *per se*, age is usually considered as an important factor to control for in studies involving insulin resistance.

Gender. Studies have shown that gender is closely related to insulin resistance with females being more insulin resistant than males from birth throughout adulthood. This phenomenon can be attributed to intrinsic genetic and hormonal differences between females and males (Wilkin & Murphy, 2006). At birth, girls were found to have significantly higher concentration of insulin and/or its precursor peptides (i.e., proinsulin and split proinsulin) and were lighter weight than boys (Ibanez et al., 2008; Shields et al., 2007). Insulin plays a major role in fetal growth; however, a higher concentration of insulin is associated with smaller body weight among girls, indicating girls are insulin resistant in uterus and at birth. This observation was

persistent among 357 children aged 10-14 years undergoing puberty (Moran et al., 1999).

Race/Ethnicity. Genetic differences plus environmental factors exert their effects on insulin resistance through the role of race/ethnicity. Research found that the etiologies and prevalence of insulin resistance vary among different racial/ethnic groups. The Caucasian population is the most studied group followed by African and Hispanic groups. Other ethnic groups such as Asian are less well studied. Lovejoy, de la Bretonne, Klemperer, and Tulley (1996) observed that African American women (n = 37) had a lower insulin sensitivity index measured by the minimal model than Caucasian women (n = 22) matched for age, BMI, and waist to hip ratio (WHR), even though they had smaller visceral fat area measured by computed tomographic scan (CT). In the later study by Karim, Wang, Hale, and Elbein (2005), African American men and women, when compared with Caucasians, were found to have significant genetic variants in the beta-cell specific transcription factor insulin promoter factor 1 gene that is important for the development of pancreas and maintenance of beta-cell mass. These genetic variants may increase African Americans' risk of developing insulin resistance and type 2 diabetes. In a recent review by Reimann, Schutte, and Schwarz (2007), other factors such as central obesity, variations in adipokines secretion, glucose metabolism, and urbanization also may contribute to the ethnic differences in insulin resistance.

Hispanics are another racial/ethnic group with a higher prevalence of diagnosed diabetes than non-Hispanic Whites among people aged 20 years or older (10.4% vs 6.6%), after adjusting for population age differences (American Diabetes Association, 2008a). Results may be related to their insulin resistance state. For example, healthy and nondiabetic Mexican American women (n = 14) were found to be more insulin resistant and hyperinsulinemic than non-Hispanic Whites (n = 19) with matched age and BMI (Aguirre, Jones, Pei, Villa, & Reaven, 1997).

Type 2 diabetes is reported highly prevalent among American Indians, compared to the U.S. general population. In a cross-sectional study involving 4,549 American Indians aged 45-74 years recruited from Arizona, Oklahoma, and South and North Dakota, the age-adjusted rate of type 2 diabetes ranged from 33% in South and North Dakota men to 72% in Arizona women (Lee et al., 1995). A diabetes-specific quantitative trait loci for body weight on chromosome 1 has been identified among American Indians (Franceschini et al., 2008). These genes could influence distribution of body fat, thus may explain the high susceptibility to obesity, insulin resistance and type 2 diabetes among the American Indians.

Hypertension. A positive relationship between insulin resistance and hypertension has been established in previous studies. Patients with untreated hypertension were found to be hyperinsulinemic (Ferrannini et al., 1987; Zavaroni et al., 1992). The co-existence of glucose intolerance and hyperinsulinemia among these patients with hypertension strongly suggests that insulin-stimulated glucose uptake is impaired and

insulin resistance is present in this group of patients. At least one-half of patients with hypertension are estimated to be insulin resistant (Lima, et al., 2009).

Several possible mechanisms have been proposed to explain the role of insulin resistance in hypertension (Manrique, Lastra, Gardner, & Sowers, 2009). Studies have found that there is a strong positive relationship between insulin resistance and increased activity of the renin angiotensin aldosterone system (RAAS) and the sympathetic nervous system, independent of any change in plasma glucose concentration (Christensen et al., 1980; Grassi et al., 2005; Lembo et al., 1992; Rowe et al., 1981). Moreover, vasodilation induced by NO is impaired because of endothelial dysfunction in an insulin resistant state that is associated elevation of free fatty acids (Montagnani, et al., 2002; Tripathy et al., 2003). In addition, insulin can act on the proximal tubule of the kidneys to increase sodium retention, thus induce hypertension in hyperinsulinemia (Sarafidis & Bakris, 2007; Song et al., 2006).

Dyslipidemia. Dyslipidemia, the most common complication of type 2 diabetes, also is implicated in insulin resistance (Avramoglu, Basciano, & Adeli, 2006; Palaniappan et al., 2007). Petersen et al. (2007) investigated the role of insulin resistance in promoting atherogenic dyslipidemia among 24 young and healthy adults (12 were insulin resistant and 12 were non-insulin resistant). They found that net hepatic triglyceride synthesis increased significantly in insulin resistant subjects accompanied by a 20% decrease in high-density lipoprotein cholesterol (HDL-C) level, when compared to non-insulin resistant individuals. Findings may be explained

by excessive plasma free fatty acids associated with insulin resistance that results in an increased production of glucose, triglycerides, and an increased secretion of very-low-density lipoprotein (VLDL) (Jellinger, 2007).

C-reactive protein. C-reactive protein (CRP) is a biomarker for systemic inflammation and is found to be positively associated with insulin resistance among different populations, such as 2,514 nondiabetic U.S. adults aged 20 years and older (Meng et al., 2007), 1,525 Peruvian adults with a mean age of 39 years (Gelaye et al., 2010), 1,624 nondiabetic Japanese aged 40-69 years (Nakanishi, Shiraishi, & Wada, 2005), and 574 middle aged nondiabetic Taiwanese (Chou et al., 2010). CRP may cause insulin resistance by impairing the insulin signaling pathway (D'Alessandris, Lauro, Presta, & Sesti, 2007; Xu, Morita, Ikeda, Miki, & Yamori, 2007). There also is increasing evidence showing that elevated CRP levels, particularly, high sensitivity CRP (hs-CRP,) (i.e., hs-CRP > 3.0 mg/L), is an independent and significant risk factor for type 2 diabetes and cardiovascular disease such as myocardial infarction and ischemic stroke (Devaraj, Singh, & Jialal, 2009; Jeppesen et al., 2008; Ridker, 2007; Rifai & Ridker, 2001). Different from standard CRP test, hs-CRP is measured by high-sensitivity assay that can detect a range of 0.02-10 mg/L concentrations of CRP. According to a scientific statement from the Centers for Disease Control and Prevention (CDC) and American Heart Association (AHA), plasma levels of hs-CRP are categorized as low (< 1.0 mg/L), moderate (1.0 to 3.0 mg/L), and high (> 3.0 mg/L), indicating low, average, or high relative cardiovascular risk respectively (Pearson et al., 2003).

Obesity. Numerous studies have shown that obesity is the most significant risk factor for insulin resistance. However, the operational definition of obesity varies across studies. Body mass index (BMI) is widely used to identify persons with weight problems and is calculated by dividing an individual's body weight in kilograms by the square of height in meters (kg/m^2). According to the WHO, a BMI < 18.5 is defined as underweight, a BMI of between 18.5 and 24.9 is defined as normal weight, while a BMI from 25 to 29.9 is defined as overweight and a BMI ≥ 30 is defined as obesity (WHO, 2000). Although it is popular and convenient to use, many researchers have identified the limitations of using BMI in studies on insulin resistance. BMI is based on weight and height and does not consider the distribution of fat, muscle and bone mass. Research also has shown that BMI may overestimate fat tissues for those with more lean body mass and underestimate adiposity on those with less lean body mass. For example, Romero-Corral et al. (2008) evaluated the accuracy of BMI in diagnosing obesity, using cross-sectional nationally representative data (N = 13,601) from the Third National Health and Nutrition Examination Survey (NHANES III). They found that the prevalence of obesity defined by BMI ≥ 30 kg/m^2 was 19.1% and 24.7% for men and women respectively, while the rate of obesity defined by body fat percent (BF% > 25% for men and > 35% for women) was much higher for both men (43.9%) and women (53.3%).

Because of these limitations, other measures such as waist circumference were recommended and have become more popular in research and clinical settings. Waist circumference is the distance around the abdomen between the lower rib cage and

hips and is measured by placing a tape around the waist at the upper point of the iliac crest with minimal inspiration. Increased waist circumference is a strong indication for central obesity, which is defined as >35 inches (88 cm) for women and > 40 inches (102 cm) for men (NCEP ATP III, 2002). Waist circumference also has been identified as a better predictor for multiple health risks (e.g., type 2 diabetes and cardiovascular disease) than BMI (Han, Sattar, & Lean, 2006).

Researchers continue to investigate the relationship between BMI and insulin resistance. In a cross-sectional study conducted among a cohort of 1,194 female twins aged 18-74 years, Skidmore et al. (2008) investigated the relationship of birth weight, adult BMI, and change in size between birth and adulthood to insulin resistance, using linear regression analyses. There was no significant association between birth weight and insulin resistance, but a significant positive relationship between adult BMI and insulin resistance was found (a 26% increase in insulin resistance per SD increase in BMI with a confidence interval [CI] of 22.6-29.5%). Farin, Abbasi, and Reaven (2006) conducted a study among 330 healthy nondiabetic adults (191 women and 139 men with mean age of 50 years) to compare the effectiveness of waist circumference and BMI in identifying insulin-resistant individuals. They found that BMI and waist circumference correlated well with each other ($r = .78$, $p < .001$) and with the steady-state plasma glucose (SSPG) concentration in the insulin-suppression test, which is a direct measure of the ability of insulin to mediate glucose disposal at a given load ($r = .58$, $p < .001$ for BMI; $r = .57$, $p < .001$ for waist circumference). Participants who were abdominally obese (waist circumference > 88cm for women

and > 102 cm for men) had significantly higher SSPG concentrations than those with a normal waist circumference within the overweight BMI category. When stratified by waist circumference, subjects in the overweight BMI category had greater SSPG concentrations than subjects who had a normal BMI within normal waist circumference category. For those who were abdominally obese, participants with BMI ≥ 30 had higher SSPG concentrations than those with overweight BMI. The authors concluded that both waist circumference and BMI accounted for about 30% variations in the SSPG concentrations but did not find evidence to suggest that waist circumference was superior to BMI for identifying insulin resistance. Therefore, no matter which obesity index is used, it is clear that obesity contributes to insulin resistance.

Central obesity is a main component of metabolic syndrome. The role of central obesity in the development of insulin resistance is through various adipokines secreted by adipose tissue, such as tumor necrosis factor (TNF)-α, interleukin (IL)-6, resistin, leptin, and adiponectin (Boden & Laakso, 2004). Adiponectin is one of the adipokines that have anti-inflammatory effect and is likely to improve insulin sensitivity by stimulating fatty acid oxidation and decreasing plasma triglycerides (Boden & Laakso, 2004). Among 783 young men aged 20-29 years, it was found that with increased subcutaneous adipose tissue, the level of adiponectin decreases accompanying a higher HOMA-IR level, an indication of insulin resistance (Frederiksen et al., 2009). The reduced release of adiponectin in obesity may contribute to insulin resistance and the development of type 2 diabetes. Although the

mechanism by which obesity leads to decreased adiponectin level is unclear, Boden & Laakso (2004) proposed that adiponectin is inhibited by hyperinsulinemia and enhanced TNF-α caused by obesity-induced insulin resistance. Excess free fatty acids in obesity also can induce insulin resistance by impairing the insulin-signaling pathway (Boden & Laakso, 2004; Homko, et al., 2003).

Physical inactivity. The beneficial effects of exercise in preventing chronic diseases are well known. Alternatively, lack of exercise or physical inactivity itself may contribute to the development of chronic diseases, although this relationship is mediated by the interaction between genetically controlled biochemical processes and a myriad of bio-cultural influences-lifestyle factors, including nutrition, exercise, and exposure to noxious substances (Booth, Laye, Lees, Rector, & Thyfault, 2008). Physical inactivity refers to not engaging in any regular pattern of physical activity beyond daily functioning (CDC, 2010c). Research has focused on the underlying mechanisms exerted by physical inactivity on the development of insulin resistance. A reduction in skeletal muscle insulin sensitivity (Kump & Booth, 2005) and a rapid expansion of intra-abdominal fat storage are the two major biological consequences of the shift from high physical activity to a sedentary condition (Booth, et al., 2008). It was hypothesized that decreased utilization of energy-producing substrates by skeletal muscle from physical inactivity signals a reduced need for additional uptake of glucose, which diminishes insulin sensitivity for glucose uptake.

Smoking. Studies have found that smoking contributes to greater accumulation of visceral fat and greater insulin resistance and that smoking is associated with increased risk of metabolic syndrome and type 2 diabetes (Chiolero, Faeh, Paccaud, & Cornuz, 2008). Cross-sectional studies show that smokers have higher waist-to-hip ratio (WHR), an indicator of central obesity, than nonsmokers in a review by Chiolero et al. (2008). This can be attributed to the increased cortisol level, an imbalance between male (testosterone) and female sex hormones (estrogen) in female smokers and a decrease in testosterone in male smokers. The combined effect of weight gain and increased WHR associated with smoking can lead to insulin resistance.

The relationship between smoking and insulin resistance has been investigated in previous studies. Male smokers with impaired glucose tolerance (IGT) or diabetes were found to be more insulin resistant than non-smokers with IGT or diabetes (Ko, Tong, So, Cockram, & Chan, 2007). This significant association was consistent with findings from studies among Japanese patients with type 2 diabetes (Anan et al., 2006), college students (Bergman et al., 2009), and aboriginal people in rural British Columbia, Canada (Daniel & Cargo, 2004). Anan et al. (2006) also observed that insulin levels were higher among smokers than nonsmokers. Interestingly, Daniel and Cargo (2004) found that current smokers had the highest β cell function, followed by non-smokers and former smokers. In contrast, no significant association between active smoking and insulin sensitivity was found in a study by Henkin et al. (1999)

among 1,481 participants aged 40-69 years or among participants with normal glucose tolerance (Ko, et al., 2007).

Smoking may exert its detrimental effects on health through the influence of nicotine and carbon monoxide (Campbell, Moffatt, & Stamford, 2008). Nicotine binds to various receptors, causing the release of acetylcholine, norepinephrine, dopamine, serotonin, and vasopressin. These neurotransmitters promote sympathetic stimulation and vasoconstriction of the arteries, thus increase heart rate and blood pressure (Campbell, et al., 2008). In addition, decreased insulin action might be explained by increased insulin receptor substrate (IRS)-1 Ser^{636} phosphorylation that can inhibit insulin signaling among smokers when compared to nonsmokers (Bergman, et al., 2009).

Alcohol consumption. Moderate alcohol consumption has been associated with lower risk for both cardiovascular disease and type 2 diabetes. However, the exact mechanism by which alcohol consumption improves insulin sensitivity is not known and conflicting results have been reported. A study by Kim, Abbasi, Lamendola, and Reaven (2009) showed that 8 weeks of moderate alcohol consumption (30g of alcohol per day) had minimal impact on enhancing insulin sensitivity in 20 nondiabetic but insulin-resistant individuals with a mean age of 54 years. Although the SSPG concentrations decreased by approximately 8% in the total group, it was not statistically significant. There were no statistically significant changes in fasting plasma glucose, insulin and surprisingly, triglyceride concentrations after 8-weeks of

moderate alcohol consumption in this study. Findings contradict those from a meta-analysis that identified moderate alcohol consumption (30g per day) can increase level of triglycerides by 5.9% from baseline (Rimm, Williams, Fosher, Criqui, & Stampfer, 1999). Heavy drinking is usually associated with increased triglyceride levels (Brinton, 2010; Foerster et al., 2009).

In contrast, Hong, Smith, Harvey, and Nunez (2009) examined the effects of alcohol consumption on insulin sensitivity in the controlled animal study on male mice with three different body weight phenotypes and found that alcohol did not affect glucose tolerance test (GTT) in any of the body weight phenotypes; however, alcohol consumption promoted insulin sensitivity in mice consuming both the low fat and high fat diets. They concluded that alcohol consumption increased insulin sensitivity without affecting body fat levels in male mice. Similarly, improved insulin sensitivity was observed among 36 postmenopausal women after 6 weeks of consumption of 250 ml white wine (~ 25g alcohol per day), along with an increase in HDL levels, a decrease in LDL levels and a decrease in fasting triacylglycerol (Joosten, Beulens, Kersten, & Hendriks, 2008). The proposed hypothesis suggests that alcohol has effects on: (1) inhibiting gluconeogenesis; (2) decreasing inflammation; (3) increasing the production of factors that improve insulin sensitivity (i.e., adiponectin); and (4) increasing the production of insulin by the pancreas (Hong, et al., 2009).

Impact of Insulin Resistance on Health

Insulin resistance is not considered a disease, but it is not a benign state (Reaven, 2005b). Many studies have been conducted during the last two decades to investigate the role of insulin resistance and hyperinsulinemia in the pathogenesis of metabolic, endocrine, and cardiovascular diseases (Avramoglu, et al., 2006; Despres et al., 1996; Fontbonne et al., 1991; Hsueh & Law, 1998). These studies provide solid evidence for a strong association between insulin resistance and many clinical diseases or abnormalities such as type 2 diabetes, hypertension, dyslipidemia, hyperuricemia, metabolic syndrome, and cardiovascular diseases (Lebovitz, 2001; Stern, 1997). When beta cells are able to secret higher levels of insulin to compensate insulin resistance, euglycemia is maintained. When beta cells fail to maintain hyperinsulinemia, type 2 diabetes develops with significant hyperglycemia. The relative risk of developing type 2 diabetes in 8 years among individuals with insulin resistance is increased as much as 13 fold compared to those without insulin resistance (Stern, 1997). Insulin resistance can induce hypertension by the possible mechanisms of activating sympathetic nervous system (Grassi, et al., 2005; Lembo, et al., 1992), reducing the production of NO (Montagnani, et al., 2002), and increasing sodium retention in the renal system (Sarafidis & Bakris, 2007; Song, et al., 2006). Insulin resistance also is associated with hyperuricemia (Bonora et al., 2008). The elevated free fatty acids concomitant with insulin resistance can lead to increased production of triglycerides, LDL-C, VLDL and decreased HDL-C (Jellinger, 2007). In addition, hypercoagulability among patients with insulin resistance results from

impaired fibrinolysis that is due to increased concentration of plasminogen activator inhibitor 1 (PAI-1) associated with hyperinsulinemia (Meigs et al., 2000). Insulin resistance is proposed as a fundamental component of the metabolic syndrome (Reaven, 2005b) and a risk factor for cardiovascular disease (Fonseca, Desouza, Asnani, & Jialal, 2004). Detailed discussion of the adverse impact of insulin resistance on health can be found in an unpublished review (Shen, 2008).

Depression

Definition of Depression

As mentioned previously in Chapter I, depression is a type of mood disorder. According to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV) (American Psychiatric Association, 1994), mood disorders are defined as recurrent disturbances or alterations in mood that cause psychological distress and behavioral impairment. The diagnosis of depression is based on subjective experience of mood and the presence of a certain number of other depressive symptoms including psychological and physical, which can be evaluated by a structured or standardized clinical interview (Davidson, Rieckmann, & Rapp, 2005). The presence of depressive symptoms also can be measured by self-reported depression questionnaires or inventory.

Classification of Depression

Depression or depressive disorder is one of the five categories of mood disorders. The other four categories are bipolar disorders, mood disorder caused by a general medical condition, substance – induced mood disorder, and mood disorder not otherwise specified (NOS) (American Psychiatric Association, 1994). The three sub-categories of depressive disorders include major depressive disorder (MDD), single or recurrent episodes; dysthymic disorder; and depressive disorder NOS. MDD also is known as major depression and is defined as one or more major depressive episodes. The DSM-IV diagnostic criteria for MDD are: 1) either a depressed mood or a loss of interest in nearly all activities that must be present for at least 2 weeks; and 2) four of seven additional symptoms that must be present for at least 2 weeks including significant appetite/weight change, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, excessive guilt or feelings of worthlessness, diminished ability to think or concentrate or indecisiveness, and suicidal ideation. In contrast, dysthymic disorder is a milder but more chronic form of MDD in that the depressed mood is present for most days for at least 2 years plus two of seven additional symptoms. Depressive disorder NOS includes disorders with depressive features that do not meet all the criteria of MDD or dysthymic disorder.

Prevalence of Depression

Estimates of the prevalence of depression in the United States vary across studies, depending on the definition of depression, measure of depression (structured clinical

diagnostic interview or self-report depressive symptom inventory), and studied populations (general population or patient population). The prevalence of lifetime depression (defined as depression at any point along individuals' lifetime) in general population ranges from 15.7% to 16.2%. Kessler et al. (2003) examined nationally representative data on household residents aged 18 years or older available from National Comorbidity Survey Replication (NCS-R) and found the prevalence of lifetime MDD measured by the WHO Composite International Diagnostic Interview (CIDI) was 16.2% and the prevalence of 12-month MDD measured by the CIDI was 6.6%. In a recent study by Strine et al. (2008), the authors analyzed data on 217,379 participants in 38 states, the District of Columbia, Puerto Rico, and the U.S. Virgin Islands from the 2006 Behavioral Risk Factor Surveillance Survey (BRFSS) and reported that the overall prevalence of current depressive symptoms, when measured by the eight-item Patient Health Questionnaire [PHQ-8] and defined as PHQ-8 $\geq$ 10, was 8.7% (ranges from 5.3% [Alaska] - 13.7% [West Virginia], by state and territory). These authors also found that the prevalence of a lifetime diagnosis of depression, when measured by a question "Has a doctor ever told you that you have a depressive disorder (including depression, major depression, dysthymia, or minor depression)?", was 15.7% (ranges from 6.8 % [the U.S. Virgin Islands] - 21.3 % [Oregon], by state and territory). The prevalence rate of depression measured by the PHQ-9 was 7% among adults aged 20 and above (Pratt & Brody, 2010). A higher rate of depression was reported among special patient populations, such as Asian women with breast

cancer (26%) (Chen et al., 2009), those with type 1 diabetes (32.1%) (Gendelman et al., 2009), and individuals with type 2 diabetes (56%) (Kahn et al., 2008).

Prevalence of depression across age. The prevalence of depression varies across the adult life-span and has been found to be higher among young adults and decrease as people age. For example, one study reported that the prevalence rate of a diagnosed current DSM-IV mental disorder was about 23.8% among young adults aged 20 - 24 years in Finland (Aalto-Setala, Marttunen, Tuulio-Henriksson, Poikolainen, & Lonnqvist, 2001). Moreover, depressive disorders were the most prevalent among all other mental disorders with an overall rate of 10.8% (7.4% in males and 12.7% in females). Similarly , Gwynn et al. (2008) evaluated the 12-month prevalence of MDD among a representative sample of 1,817 community-based New York City adults. MDD was diagnosed by the WHO's CIDI. They found that the overall 12-month prevalence of MDD was 8%. Adults aged 20 - 39 years had highest prevalence of MDD (9%) in this study, compared to adults aged 40 - 59 years (7%) or those aged 60 years and above (5%). This age-related decrease in prevalence of depression may be explained by decreased emotional responsiveness, increased emotional control, and developed resistance to repeatedly exposed adverse or stressful life events as people are getting older (Jorm, 2000). In comparison, the overall 12-month prevalence of MDD was 6.7% among U.S. adults aged 18 or above (Kessler, Chiu, Demler, Merikangas, & Walters, 2005). MDD was measured by WHO World Mental Health (WMH) Survey version of the CIDI (WMH-CIDI) in this study. In contrast, a higher

prevalence rate (11.19%) of any type of depression was reported among 851 Americans aged 71 years or older (Steffens, Fisher, Langa, Potter, & Plassman, 2009) Depression was measured by the CIDI short form.

Prevalence of depression across gender. Females have a higher prevalence rate of depression than males. This might be explained by gender differences in genetic predisposition, hormonal, and responses to adverse life events (CDC, 2010b). In the community-based study of New York adults (Gwynn, et al., 2008), the prevalence of depression among females was 9%, which was significantly higher than the rate of depression in men (6%). McGuire et al. (2008) estimated the prevalence of depression in 14,425 older U.S. women aged 65 and older, using data from 2006 Behavioral Risk Factor Surveillance Survey (BRFSS). The reported prevalence of current depression and lifetime diagnosis of depression was 5.9% and 12.3% respectively. In contrast, no significant differences in prevalence rate of depression were found between American men (10.2%) and women (11.4%) aged 71 and above (Steffens, et al., 2009).

Prevalence of depression across race/ethnicity. The prevalence of depression varies across race/ethnicity, as do the relative differences between groups. Some studies found that racial/ethnic minorities had significantly higher rates of depression than Whites, some studies reported Whites had higher rate of depression, while others reported no racial/ethnic differences in depression rates. Among community-based New York adults aged 20 years and older, black Americans were found to have the highest prevalence of MDD (9%), followed by Whites (8%), Hispanics (7%) and

Asian (5%) (Gwynn, et al., 2008). Similarly, McKnight-Eily et al. (2009) reported a much higher prevalence of current depressive symptoms (13.8%) and lifetime diagnosis of a depressive disorder (14.9%) among African American women aged 18 to 64 years. In contrast, among a group of Americans aged 71 year or older, non-Hispanic White American (11.7%) and Hispanics (12.5%) were reported to have the highest prevalence rate of depression, followed by African Americans (4.1%) (Steffens, et al., 2009). In a recent meta-analysis by Mendelson et al. (2008), the authors compared the prevalence of MDD and depressive symptoms among Latinos with non-Latino Whites in the U.S. and found Latinos reported more depressive symptoms than non-Latino Whites, but findings were not clinically significant. No significant group differences in the lifetime prevalence of MDD were found between Latinos and non-Latino Whites. A higher prevalence rates of depressive disorders (16.2%) and MDD (9.2%) were found among 513 Chinese patients aged 18 years or above hospitalized in general hospitals (Zhong et al., 2010).

The Relationship between Depression and Insulin Resistance

Research has established a positive association between depression and type 2 diabetes (Musselman, Betan, Larsen, & Phillips, 2003) that is more commonly found among women than men (Ali, et al., 2006). A meta-analysis reported that adults with depression (either clinical diagnosed depression or depressive symptoms) had a 37% increased risk of developing type 2 diabetes (Knol, et al., 2006) and the prevalence of depression was twice as high among adults with type 2 diabetes than those without

diabetes (Anderson, Freedland, Clouse, & Lustman, 2001). However, the relationship between depression and insulin resistance is not clear as studies that have examined this association report conflicting results (Adriaanse et al., 2006; Lawlor et al., 2005; Lawlor, Smith, & Ebrahim, 2003; Pan et al., 2008; Pearson et al., 2010; Roos et al., 2007; Timonen et al., 2005; Timonen et al., 2006; Timonen et al., 2007). Table 1 provides an overview of these studies, including study subjects, instruments used for depression and insulin resistance, covariates, and significant findings.

A Positive Association

A positive relationship between depressive symptoms and insulin resistance was found in several cross-sectional population-based studies (Adriaanse, et al., 2006; Pan, et al., 2008; Pearson, et al., 2010; Timonen, et al., 2005; Timonen, et al., 2006; Timonen, et al., 2007). Three of the studies focused on young adults (Pearson, et al., 2010; Timonen, et al., 2006; Timonen, et al., 2007); while the other three investigated the association among middle- or older-aged adults (Adriaanse, et al., 2006; Pan, et al., 2008; Timonen, et al., 2005).

Timonen et al. (2006) studied a birth cohort of 2,069 Finnish young men who were born between January 1st and December 31st, 1966 and aged 31 years old at the time data were collected. They found that the means of the QUICKI values (Qualitative Insulin Sensitivity Check Index, QUICKI), a measure of insulin sensitivity, decreased with the increased severity of depressive symptoms measured

Table 1
Studies on the Relationship between Depression and Insulin Resistance

Authors (Year)	Subjects	Measures on depression	Measure on IR	Covariates	Findings
Timonen, Rajala, Jokelainen, Keinanen-Kiukaanniemi, Meyer-Rochow, & Rasanen (2006)	A birth cohort of 2,069 Finnish young men aged 31 years	HSCL-25	QUICKI IR: lowest quartile lowest quintile lowest decile	Socio-economic status, BMI, smoking, alcohol intake, physical inactivity, CRP, fasting serum level of cholesterol and hospital treated physical disease	A positive association between severe depressive symptoms and IR (in all three definitions)
Timonen, Salmenkaita, Jokelainen, Laakso, Harkonen, Koskela, Meyer-Rochow, Peitso, & Keinanen-Kiukaanniemi (2007)	1,054 healthy Finnish male military conscripts aged 18-28 years	Finnish modification of the 13-item Beck Depression Inventory No depression: 0-4 Mild: 5-7 Moderate: 8-15 Severe: ≥ 16	HOMA-IR IR: highest quartile highest decile	Waist circumference, smoking, alcohol consumption, physical inactivity, and education	A positive association between moderate-to-severe depressive symptoms and IR (defined as the highest decile of the HOMA-IR)
Pearson, Schmidt, Patton, Dwyer, Blizzard, Otahal, & Venn (2010)	1,732 Australian aged 26-36 years	CIDI Depression: mild, moderate, or severe depressive disorder	Updated HOMA2-IR (www.dtu.ox.ac.uk) IR: HOMA2-IR used as a continuous variable	Smoking, alcohol consumption, physical activity, education, fish consumption, PCOS (for women), use of oral contraceptives (for women) Mediators: waist circumference	A positive association between depressive disorder and IR

Table 1 continued

Authors (Year)	Subjects	Measures on depression	Measure on IR	Covariates	Findings
Timonen, Laakso, Jokelainen, Rajala, Meyer-Rochow, & Keinanen-Kiukaanniemi (2005)	491 Finnish men and women aged 61-63 years	Beck's Depression Inventory 21	QUICKI	BMI, smoking, alcohol consumption, physical inactivity, sex, and basic education	QUICKI scores were negatively associated with depression scores
Pan, Ye, Franco, Li, Yu, Zou, Zhang, Jiao & Lin (2008)	3,285 Chinese aged 50-70 years	CES-D Depressive symptoms: CES-D ≥ 16	Updated HOMA2-IR (www.dtu.ox.ac.uk) IR: the highest quartile	Socio-demographic (age, gender, geographic location, residential region, education level), BMI, smoking status, alcohol consumption, physical activity level, comorbidity.	A positive association between depressive symptoms and IR (OR = 1.54, 95% CI = [1.17, 2.04]
Adriaanse, Dekker, Nijpels, Heine, Snoek, & Pouwer (2006)	541 Dutch aged 55-75 years	CES-D	HOMA-IR	Glucose tolerance status, gender	A weak positive correlation between CES-D scores and HOMA-IR scores, which did not differ for women and men.
Lawlor, Smith, & Ebrahim (2003)	4,286 British women aged 60 -79 years	Use of antidepressant medication, self-reported of depression diagnosis, and the EQ-5D[a] mood question of the EuroQOL	HOMA-IR IR: categorized according to quartiles	BMI, WHR, smoking, alcohol consumption, physical activity, and social class	A negative association between IR and depression.

Table 1 continued

Authors (Year)	Subjects	Measures on depression	Measure on IR	Covariates	Findings
Lawlor, Ben-Shlomo, Ebrahim, Smith, Stansfeld, Yarnell, & Gallacher (2005)	2,512 Welsh men aged 45-59 years old	GHQ	HOMA-IR IR: categorized according to quartiles	Smoking, alcohol consumption, physical activity, social class	No association between depressive symptoms and IR.
Roos, Lidfeldt, Agardh, Nyberg, Nerbrand, Samsioe, & Westrin (2007)	1,047 Swedish women with risk factors for diabetes aged 50-64 years	Gothenburg Quality of Life	HOMA-IR IR: categorized according quartiles	BMI, WHR, physical exercise, smoking, alcohol consumption	No significant association between depressive symptoms and IR

Notes. Studies are presented in order of findings (positive, negative, and no association). IR = insulin resistance; HSCL-25 = Hopkins' Symptom Checklist-25; QUICKI = Qualitative Insulin Sensitivity Check Index; BMI = body mass index; CRP = C-reactive protein; HOMA-IR = Homeostasis model assessment for insulin resistance; CIDI = Composite International Diagnostic Interview; PCOS = polycystic ovary syndrome; CES-D = Center for Epidemiological Studies of Depression scale; OR = odds ratio; CI = confidence interval; EuroQOL = European Quality of Life scale; WHR = waist-hip-ratio; GHQ = General Household Questionnaire.
[a]EQ-5D is a standardized instrument for use as a measure of health outcome.

by Hopkins' Symptom Checklist-25 (HSCL-25). Furthermore, they reported that insulin resistance was positively associated with severe depressive symptoms (adjusted *OR* = 2.18, 95% *CI* = [1.19, 4.00]) in logistic regression analysis, when insulin resistance was defined as the lowest quartile (25%) of QUICKI values. The OR increased to 3.15 with a 95% CI of 1.48-6.68 when a tighter definition of insulin resistance was used (i.e., the lowest decile [10%] of QUICKI values). Participants in this study lived in northern Finland and other factors such as low exposure to sunlight must be considered when interpreting the study results.

In a second study, Timonen et al. (2007) investigated the association between insulin resistance and depressive symptoms among 1,054 healthy Finnish male military conscripts aged 18-28 years. In this study, insulin resistance was measured by the HOMA-IR and defined as the highest decile (10%) of the HOMA-IR values. Depressive symptoms were assessed using the modified 13-item Beck Depression Inventory (R-BDI). Moderate-to-severe depressive symptoms were defined as a R-BDI score ≥ 8 and mild depressive symptoms were defined as a R-BDI score between 5 to 7. The researchers found that moderate-to-severe but not mild depressive symptoms was significantly associated with insulin resistance (*OR* = 2.8, 95% *CI* = [1.2, 6.5]). However, stress associated with being newly recruited into military service might have contributed to depression among these young adults.

In a more recent study, the relationship between depression and insulin resistance was examined among 1,732 Australian adults aged 26 to 36 years (Pearson, et al.,

2010). Gender differences in the relationship also were investigated. The study sample was derived from a nationally representative sample of 8,498 children surveyed in 1985. This study used the CIDI to evaluate depression over the previous 12 months. Depression was defined as those participants who had mild, moderate, or severe depressive disorder. Insulin resistance was measured by the HOMA-IR. The HOMA-IR scores were logarithmically transformed and used as a continuous variable in the analyses. Ratio of means, defined as the mean HOMA-IR score of participants with depression relative to that of those without depression, were reported in linear regression analysis. The authors found that the mean of insulin resistance was significantly higher among men (17.2%, $p = .04$) and women (11.4%, $p = .02$) with depressive disorder than those without in the unadjusted model. However, the positive relationship between depression and insulin resistance became insignificant, after adjusting for age, education, physical activity, smoking, alcohol, and use of antidepressants in men ($p = .12$) and after adjusting for age, education, polycystic ovary syndrome, fish consumption, and use of antidepressants among women ($p = .25$). Study findings also suggested that waist circumference was a mediator in the relationship between depression and insulin resistance. Clinical significance of the log-transformed HOMA-IR score is difficult to interpret. In this study, a significantly higher ratio of mean log-transformed HOMA-IR did not necessarily indicate the presence of insulin resistance. Moreover, the low response rate (1,732 of 8,498 or 20%) of the study sample may impose non-response bias to the results of this study. In addition, the authors did not clearly specify if the two-stage unequal probability

sampling design was accounted for in the statistical analyses to produce reliable estimates.

Studies that found a positive relationship between depression and insulin resistance in middle- or older-age adults included the study by Timonen et al. (2005) who examined 491 Finnish adults aged 61-63 years. In this study, insulin resistance was measured by the QUICKI and depressive symptoms were evaluated by Beck's depression inventory 21. Pan et al. (2008) examined the association among 3,285 Chinese aged 50-70 years, using data from the Nutrition and Health of Aging Population in China Study. Depressive symptoms were assessed by the Center for Epidemiological Studies of Depression scale (CES-D) with a cut point of 16. Insulin resistance was calculated using the updated HOMA-IR (HOMA2-IR) and defined as the highest quartile of HOMA2-IR. The findings showed that participants with depressive symptoms had significantly higher HOMA2-IR than those without depressive symptoms and were 50% more likely to be insulin resistant (*OR* = 1.54, 95% *CI* = [1.17-2.04]. Addriaanse et al. (2006) examined the relationship between depression and insulin resistance in 541 Dutch men and women aged 55-75 years with various glucose tolerance states (260 had normal glucose tolerance [NGT], 164 had impaired glucose tolerance [IGT], and 117 had established type 2 diabetes). Depression was assessed by CES-D and insulin resistance was measured by HOMA-IR. Both CES-D and HOMA-IR scores were analyzed as continuous variables. A significant but weak overall correlation between depression and insulin resistance was found ($r = .156$, $p < .001$); however, the correlations were attenuated

and even became insignificant when subjects were stratified by glucose tolerance status (NGT: r = .041, p = .509, IGT: r = .112, p = .160, and type 2 diabetes: r = .007, p = .942). The relationship between depression and insulin resistance did not differ between men and women (men - NGT: r = .033, p = .712, IGT: r = .072, p = .517, and type 2 diabetes: r = -.019, p = .891; women - NGT: r = .063, p = .478, IGT: r = .101, p = .389, and type 2 diabetes: r = -.016, p = .901).

A Negative Association

Contradictory to the previous discussed studies, depression was found to be negatively associated with insulin resistance in one cross-sectional study conducted among a randomly selected sample of 4,286 British women aged 60-79 years (Lawlor, et al., 2003). In this study, depression was assessed via three methods: use of antidepressant medications, self-report of having a clinical diagnosis of depression, and the EQ5D mood question of the EuroQOL. Insulin resistance was calculated by HOMA-IR. Participants without diabetes were categorized into four groups by HOMA-IR quartiles (lowest 25%, 25-50%, 50-75%, and highest 25% of HOMA-IR). Participants with diabetes composed the fifth group. Logistic regression analysis of the relationship between insulin resistance categories as the independent variable and depression as the dependent variable showed that the prevalence of depression decreased linearly as insulin resistance increased among nondiabetic women, but increased in women with diabetes. For every increase in the HOMA-IR categories among nondiabetic women, the risk of being depression decreased (current

antidepressant use: *OR* = 0.86, 95% *CI* = [0.76 - 0.96]; ever being diagnosed with depression: *OR* = 0.84, 95% *CI* = [0.74 - 0.97]; reporting feeling depressed: *OR* = 0.89, 95% *CI* = [0.79 - 0.99]). The findings of this study indicated a potential protective effect of insulin resistance on depression, but as the authors noted that the results were novel and need further investigation.

No Association

Two studies have reported no significant association between depression and insulin resistance. In a prospective 4-phase cohort study (phase I: 1979-1983; phase II: 1984-1988; phase III: 1989-1993; Phase IV: 1993-1997), Lawlor et al. (2005) found no significant association between depression and insulin resistance among Wales men aged 45-59 years. Insulin resistance was measured by HOMA-IR and depression was evaluated by General Health Questionnaire (GHQ) in this study.

Similarly, Roos et al. (2007) found no association between insulin resistance and depressive symptoms in a retrospective study among 1,047 Swedish women with risk factors for diabetes aged 50- 64 years old. Insulin resistance was measured by HOMA-IR. Depressive symptoms were examined by items retrieved from the Gothenburg Quality of Life instrument which posed a threat to the internal validity of the study because the validity and reliability of the measure for depressive symptom had not been appropriately evaluated.

Summary of Previous Studies

All of the above studies were correlational studies; therefore, no causation between depression and insulin resistance was established. Of the nine previous studies, six were limited to middle and older-aged adults, and often failed to examine the effect of gender on the relationship between depression and insulin resistance. Moreover, all were conducted in Europe, Australia, or Asia. None of these previous studies have investigated the role of race/ethnicity in the relationship. Few examined the role of gender in this relationship in young adults. In addition, measures of depression and insulin resistance varied across the studies. Depression was primarily measured by self-report depression questionnaires or inventory, such as use of antidepressant medicine, self-report of being diagnosed with depression, and response to EuroQOL mood questions (Lawlor, et al., 2003), with the Beck's depression inventory (Timonen, et al., 2005; Timonen, et al., 2007), with the CES-D (Adriaanse, et al., 2006; Pan, et al., 2008), with the 30-item GHQ (Lawlor, et al., 2005), with Hopkins Symptom Checklist (Timonen, et al., 2006), or with self-rated symptoms of depression from the Gothenburg Quality of Life Instrument (Roos, et al., 2007). There was only one study that used the CIDI to make a clinical diagnosis of depression (Pearson, et al., 2010).

Compared to the wide range use of depression measures, methods used to estimate insulin resistance in these previous studies were limited to two. Insulin resistance was most often measured by the HOMA-IR (Adriaanse, et al., 2006;

Lawlor, et al., 2003; Pan, et al., 2008; Pearson, et al., 2010; Roos, et al., 2007; Timonen, et al., 2007), on occasion, QUICKI was used (Adriaanse, et al., 2006; Timonen, et al., 2005; Timonen, et al., 2006). However, two of the studies included subjects with type 2 diabetes in their analyses (Adriaanse, et al., 2006; Pan, et al., 2008) confounding the generalizability of study results to the non-diabetic population.

Pathophysiological Link between Depression and Insulin Resistance

Although the underlying mechanism is still unclear, several pathophysiological pathways have been proposed to explain the relationship between depression and insulin resistance, including hypothalamus-pituitary-adrenal (HPA) hyperactivity, increased immunoinflammatory cytokines and lifestyle risk behaviors.

Hypothalamus-pituitary-adrenal Hyperactivity

Evidence suggests that 40-60 % of patients with major depression had HPA hyperactivity that is followed by increased release of corticotrophin-releasing hormone, adrenocorticotropic hormone and cortisol. Excess cortisol and its disruption of glucoregulatory mechanisms can lead to insulin resistance, impaired glucose tolerance, and promote visceral fat deposition (Brown, Varghese, & McEwen, 2004; Musselman, et al., 2003; Ramasubbu, 2002). This was supported by Weber-Hamann, Gilles, Lederbogen, Heuser, and Deuschle (2005) in a study that examined 70 patients with moderate depression. They found significant differences in oral glucose tolerance test (OGTT) values across morning saliva cortisol levels (low: cortisol < 15

mmol/l; moderate: cortisol < 25 mmol/l; high: < 35 mmol/l; and very high: > 35 mmol/l) and a significant negative association between the insulin sensitivity index (ISI, a measure of insulin receptor sensitivity) and HPA system activity. The HPA activity was measured by the mean of morning saliva cortisol concentrations collected for 6 days under drug-free conditions.

Lending further support to this hypothesis, research has found that antidepressant medications can alter the activity of the HPA and improve insulin sensitivity. Amitriptyline, a tricyclic antidepressant (TCA), was found to decrease the HPA activity; while paroxetine, a selective serotonin reuptake inhibitor (SSRI), does not have the effect on the HPA activity (Deuschle et al., 2003). The effect of amitriptyline and paroxetine on the HPA activity and insulin sensitivity was further examined among 80 nondiabetic participants with an episode of MDD in a double-blinded randomized trial (Weber-Hamann, Gilles, Lederbogen, Heuser, & Deuschle, 2006). Depression was measured by Hamilton Rating Scale for Depression (HAM-D) and all 80 participants in the study had a HAM-D score ≥ 18. The effectiveness of antidepressant treatment (amitriptyline vs paroxetine) was assessed by the change in HAM-D scores. *Response to antidepressant treatment* was defined as a decrease in HAM-D score of at least 50% during the active treatment phase. *Remission* was defined as a final HAM-D score of < 7. The study found a significant increase of insulin sensitivity among participants who were treated with either amitriptyline or paraxetine and had the HAM-D score of < 7. In contrast, there was no significant change in insulin sensitivity for participants who were treated with amitriptyline and

responded to the antidepressant treatment (a drop of 50% HMA-D score), even though saliva cortisol concentrations had reduced. Interestingly, insulin sensitivity improved among participants who were treated and remitted with paraxetine, although no changes were observed in HPA activity. The authors commented that the results of the study do not exclude the HPA system as a major contributor to insulin resistance in depressed patients, but underscore the assumption of additional factors.

Increased in Immunoinflammatory Cytokines

Depression is associated with increased release of immunoinflammatory cytokines (CRP**,** interleukin [IL-1], IL-6, and tumor necrosis factor-α [TNF-α]). Central obesity probably is the link between depression and increased inflammatory cytokines. A recent meta-analysis by Howren et al. (2009) confirmed that CRP, IL-6, and IL-1 were positively associated with depression, although the strength of the relationships varied between populations (clinical-based v.s. community-based samples) and methods for depression assessment (clinical interview v.s. self-report measure of depressive symptoms). TNF-α is a cytokine that is primarily secreted by macrophages and regulates many biological processes such as cell proliferation, differentiation, apoptosis, lipid metabolism, and coagulation. A review by Borst (2004) found accumulating evidence to support TNF-α's role in the development of insulin resistance by impairing insulin signaling pathways. IL-6 is a protein that is mainly produced when there is acute or chronic inflammation. It exerts its functions in various inflammation associated disease states, such as insulin resistance, diabetes,

and systemic juvenile rheumatoid arthritis. Depression was found to be a significant predictor for IL-6 in a 6-year prospective cohort study (Stewart, Rand, Muldoon, & Kamarck, 2009). Elevated CRP was positively associated with depression among men. In contrast, the relationship between CRP and depression among women was not as strong as that in men (Danner, Kasl, Abramson, & Vaccarino, 2003; Elovainio et al., 2009; Liukkonen et al., 2006). Inflammation is one of the possible mechanisms through which depression exerts its effect on insulin resistance.

The relationship between depression and insulin resistance may not be unidirectional. Insulin resistance also could play a role in the pathogenesis of depression, especially in combination with central obesity. The elevation of immunoinflammatory cytokines associated with insulin resistance can stimulate the noradrenergic stress system. Consequently, the dysregulation of HPA axis and diminished serotonergic activity in the central nervous system could lead to depression (Dunbar et al., 2008; Koponen, Jokelainen, Keinanen-Kiukaanniemi, Kumpusalo, & Vanhala, 2008).

Depression in turn can lead to loss of interest in their usual activities or changes in appetite that is usually associated with overeating. Excessive consumption of food rich in carbohydrate and fat among depressed patients can promote development of obesity and release of various adipokines secreted from adipose tissue. Reduced

energy utilization associated with physical inactivity can in turn decrease insulin sensitivity of skeletal muscle.

Conclusion

The relationship between depression and insulin resistance is not clear as studies that have examined their association reported conflicting results. Moreover, the pathophysiological pathway to explain this relationship is not well established. Nevertheless, depression has been implicated as a risk factor for insulin resistance. Therefore, the relationship between depression and insulin resistance warrants further investigation, especially among young adults in the U.S. by gender and racial/ethnic distribution.

CHAPTER III METHODOLOGY

The purpose of the study was to examine the relationship between major depression and insulin resistance among U.S. nondiabetic adults aged 20-39 years old. Review of the literature revealed the gap in knowledge regarding the relationship between major depression and insulin resistance among young adults and by gender and race/ethnicity in the U.S. population. The information is important as early intervention to ameliorate this risk factor for insulin resistance may help prevent or delay the progression of insulin resistance to type 2 diabetes. In Chapter III, the research design is presented followed by an overview of the National Health and Nutrition Examination Survey (NHANES), including its history, content, design, operations, and quality control methods. The sampling frame, study population and sample were discussed. Procedures for dataset derivation and the data collection methods for the main variables are delineated. Protection of human subject is addressed. Finally, pilot work for the study and proposed statistical analyses are described.

Research Design

The study used a cross-sectional, correlational study design to examine the relationship between major depression and insulin resistance. A cross-sectional, correlational design is appropriate for this study because the purpose of the study is to describe the relationship between major depression and insulin resistance at a fixed

point in time (Polit & Beck, 2004). A correlational design provides a cost-effective way to observe the relationship between major depression and insulin resistance in a natural setting. The design also is suitable for this study as manipulation of some variables, for example, age, gender, or race/ethnicity, was impossible. A limitation to the design is lack of control over study variables. Therefore, this study does not identify a causal relationship between major depression and insulin resistance.

Secondary analyses of existing data were performed for the study. Secondary analysis is a research method in which data collected in a previous study are used to test new hypotheses or are reanalyzed to answer new research questions. To perform a secondary analysis, the researcher must identify and gain access to the appropriate database, and thoroughly evaluate the quality of available dataset and its suitability to address the research questions (i.e., if variables of interest are included). Use of existing data is time- and cost- efficient and also provides opportunities to maximize use of the data (Polit & Beck, 2004). Data from the NHANES were determined to be appropriate to address the research questions because the NHANES includes variables of interest for this study.

Overview of the NHANES

History. The NHANES is a major program of the National Center for Health Statistics (NCHS), which is part of Centers for Disease Control and Prevention (CDC). The NHANES program was designed to evaluate the health and nutritional

status of civilian, non-institutionalized adults and children in the U.S. Starting in the early 1960s, the NHANES program conducted a series of surveys focusing on different population groups or health topics, including the National Health Examination Survey, Cycle I (NHES I) 1959-1962, NHES II 1963-1965, NHES III 1966-1970, the Hispanic Health and Nutrition Examination Survey (HHANES), the First National Health and Nutrition Examination Survey (NHANES I), the Second National Health and Nutrition Examination Survey (NHANES II), and the Third National Health and Nutrition Examination Survey (NHANES III). Beginning in 1999, the NHANES changed from a periodic survey to an ongoing annual cross-sectional survey. These NHANES focus on a variety of health and nutrition measurements among a nationally representative sample of the U.S. population. NHANES data are released on public use data files in two-year increments (i.e., NHANES 1999-2000, NHANES 2001-2002, or NHANES 2003-2004 etc.) and publicly available through the CDC website (CDC/NCHS, 2009b).

Survey content. Specific purposes of NHANES have been to: 1) estimate the prevalence of diagnosed and undiagnosed chronic conditions in the U.S. population; 2) examine the risk factors or behaviors that may increase the chances of developing a certain disease; and 3) collect information on certain aspects of reproductive health, such as use of oral contraceptives and breastfeeding practice. The full list of the diseases, medical conditions, and health indicators collected in NHANES include: anemia, cardiovascular disease, diabetes, environmental exposure, eye diseases, hearing loss, infectious disease, kidney disease, nutrition, obesity, oral health,

osteoporosis, physical fitness and physical functioning, reproductive history and sexual behavior, respiratory disease (asthma, chronic bronchitis, emphysema), sexually transmitted diseases, vision, and mental diseases (i.e., depression, generalized anxiety disorder, and panic disorder).

Survey design. The NHANES uses a complex, stratified, multistage probability-based design to obtain a nationally representative sample of the non-institutionalized civilian U.S. population. Persons living in nursing homes, institutionalized persons, members of the armed forces, and U.S. nationals living abroad are not included in the sample. The NHANES sampling procedure is accomplished in four stages, which is illustrated in Figure 2 (CDC/NCHS, 1999d). The *first* stage of sampling involves the selection of primary sampling units (PSUs) that are usually single counties. In some special cases, small contiguous counties are combined to meet a minimum population size. The selection of PSUs is based on probability proportional to population size; in other words, the larger the population within a PSU, the higher probability of selection for the PSU than other PSUs. PSUs are selected from strata, which are defined by geography and proportions of minority populations. The second stage of sampling is selection of segments within PSUs that are usually a block or group of blocks containing a cluster of households. Same as each PSU, sample segments are selected with probability proportional to a measure of size. The third stage of sampling is to randomly select households within each selected segment. However, in some geographic areas where the proportion of age, ethnic, or income groups selected for oversampling (discussed in detail in the

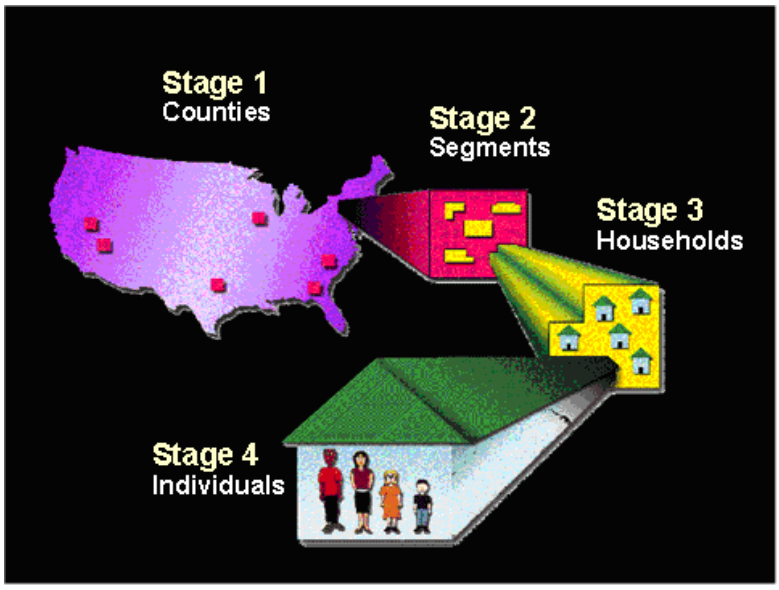


Figure 2. Four Stages of NHANES Sampling Procedure.

(Source: CDC (1999). Four stage of NHANES sampling procedure. Retrieved from: http://www.cdc.gov/nchs/tutorials/Nhanes/SurveyDesign/SampleDesign/Info1.htm)

following paragraph) is high, then the probability of selection for those groups is greater than in other areas. The fourth stage of sampling includes the selection of one or more persons within a selected household to participate in the NHANES home interview and health examination. Selected households are first contacted by an advance letter followed by an NHANES interviewer. Each person in a selected household is screened for demographic characteristics (age, gender, and race/ethnicity) using a Household Screener Questionnaire to determine if they are eligible to participate in the NHANES home interview and health examination. In some cases, a fifth stage of sampling occurs. In the fifth stage of sampling, additional data such as mental health examination in NHANES 1999-2004 or morning fasting blood lab

work at the MEC are collected on a subsample of those that participated in the NHANES health examination. Participants in the subsample are selected randomly from those that were examined with a specified sampling fraction (i.e., 1/2 or 1/3 of the total examined participants). Because of the complex sampling procedure, it is highly unlikely that the same individual is selected to participate in more than one NHANES survey.

Variations to the survey design. In NHANES 1999-2006, persons aged 60 years and older, adolescents aged 12-19 years, low-income persons, African Americans, and Mexican Americans were over-sampled to enhance the reliability and precision of estimates of health status indicator for these groups. The selection of subgroups for oversampling depended on public health trends and concerns. Beginning in 2007, there were several changes in the oversampling methods. These changes included: 1) the oversampling of Mexican Americans was extended to the entire Hispanic population; 2) the 12-15 and 16-19 year old age groups were combined to one; 3) the 40-59 year old age group in minority was sub-divided into 40-49 year old and 50-59 year old age groups; and 4) oversampling of pregnant women was discontinued to allow oversampling of the Hispanic population (CDC/NCHS, 2009c). The NHANES produced sample weights based on the stratification and clustering of the survey design that must be used in all analyses to obtain unbiased population estimates and the standard errors of estimates (CDC/NCHS, 2006a). Sample weights are discussed in detail in the section of Statistical Analyses.

During the years 1999-2001, the sampling frame in the *first* stage of selection was based on a design linked to the 1995 National Health Interview Survey (NHIS). The PSUs of NHANES 1999-2001 were a subset of the PSUs previously selected for the NHIS. An independent set of PSU's was selected for NHANES 2002-2008 and the sampling frame for this design included all counties in the U.S. In NHANES 1999, 12 PSUs were visited. Beginning with NHANES 2000, 15 PSUs were visited each year.

Survey operations. The NHANES survey includes a home interview and a health examination that involves a physical examination and laboratory tests. Eligible persons in the screened sample are contacted and invited to participate in the health interview which is conducted in the respondents' homes. Data on demographic, socioeconomic, dietary, and health-related questions are collected by highly trained interviewers. At the conclusion of the interview, all interviewed persons are asked to participate in the health examination. When persons agree to participate in the health examination, the interviewers call the NHANES field office from participants' home to establish an appointment for the examination.

The health examinations are performed in specially-designed and equipped mobile examination centers (MEC, see Appendix A). The MEC is divided into rooms to assure the privacy of participants during the examination. The study team at the MEC consisted of a physician, a phlebotomist, medical and health technicians, as well as highly trained interviewers. There are two examination sessions a day,

including morning and afternoon or morning and evening sessions. Persons are randomly selected to participate in either the morning or afternoon or evening sessions, which is pre-determined by their household ID labels. Components of health examinations are determined by participants' age, gender, and current medical conditions. Various biological and environmental specimens are collected in the MEC. Specifically, blood is drawn on participants aged 1 year and above and urine is collected from individuals who are 6 years and older. Additional survey questionnaires are conducted in the MEC, including a dietary questionnaire, and questionnaires on selected special topics.

All of the NHANES data are collected and processed by an advanced computer system using high-end servers, desktop PCs, and wide-area networking. This system allows interviewers to use notebook computers with electronic pens. Data collected at the MEC are automatically transmitted into databases through devices as digital scales and stadiometers. Touch-sensitive computer screens are used for certain sensitive questions entered by respondents themselves, insuring complete privacy. Specimens of blood, urine, oral rinse and vaginal swabs collected in the MEC are processed, stored, and shipped to different laboratories (federal, private, or university-based) under contract to NCHS for various laboratory analyses.

Quality control. The NHANES program uses multiple measures to ensure the high quality of data and minimize non-sampling and measurement errors. For example, extensive protocols are developed and reviewed by the public health and

scientific community prior to data collection. All NHANES field staffs participate in comprehensive training and annual refresher training for interviewers and MEC staff prior to and during data collection. In addition, a variety of quality control techniques are used during the field period to assure the quality of the interviews such as field observations, field editing, field office review of cases for errors and discrepancies, and validation. Extensive quality control procedures are applied when processing data. The detailed information on the NHANES can be found elsewhere (CDC/NCHS, 2009a).

Population and Sample

For this study, data obtained during NHANES 1999-2000, NHANES 2001-2002, NHANES 2003-2004, NHANES 2005-2006, and NHANES 2007-2008 (CDC, 1999-2008) were combined to achieve a sample size sufficient for the planned statistical analyses based on the author's preliminary work (Shen, Bergquist-Beringer, & Sousa, 2011) that is discussed later.

Population

The target population for the current study was nondiabetic U.S. adults aged 20-39 years. The accessible population was nondiabetic U.S. adults aged 20-39 years who participated in NHANES 1999-2008. The choice of U.S. adults aged 20-39 years was made because few studies were found that investigated the relationship between depression and insulin resistance among this age group as identified in Chapter II of

this dissertation. In addition, studies have shown that persons aged 20-39 years have high likelihood of having depression (Jorm, 2000). Moreover, depression, one of the main variables for the current study, was measured on NHANES participants aged 20-39 years from 1999-2008.

The NCHS reported the total number of subjects who were screened and selected to participate in NHANES and the number of subjects who were actually interviewed and examined in the MEC by age for each two-year survey cycle (CDC/NCHS, 1999-2008). As shown in Table 2, for NHANES 1999-2000, there were 12,160 persons selected for the sample. Of these, 9,965 were interviewed (unadjusted response rate: 81.9%) and 9,282 (76.3%) were examined in the MEC. For NHANES 2001-2002, there were 13,156 persons selected for the sample. Of these, 11,039 were interviewed (83.9%) and 10,477 (79.6%) were examined in the MEC. For NHANES 2003-2004, there were 12,761 persons selected for the sample. Of these, 10,122 were interviewed (79.3%) and 9,643 (75.6%) were examined in the MEC. For NHANES 2005-2006, there were 12,862 persons selected for the sample. Of these, 10,348 were interviewed (80.5 %) and 9,950 (77.4 %) were examined in the MEC. For NHANES 2007-2008, there were 12,943 persons selected for the sample. Of these, 10,149 were interviewed (78.4 %) and 9,762 (75.4 %) were examined in the MEC. In total, 63,882 persons were selected to participate in NHANES during 1999-2008. Of these, 51,623 were interviewed (80.8%) and 49,130 were examined in the MEC (76.9%). Among adults aged 20-39 years, a total of 11,617 adults were selected to participate in

Table 2
Unweighted Response Rate for National Health and Nutrition Examination Survey (NHANES) 1999-2008

Year period	Screened sample [a]		Interviewed sample [b]		Examined sample [c]	
	Control total [d]	Sample size	Unweighted sample size	Unweighted response rate (%) [e]	Unweighted sample size	Unweighted response rate (%) [f]
1999-2000						
All ages	272,156,833	12,160	9965	81.9	9298	76.3
20-39 years	82,799,779	2127	1695	79.7	1569	73.8
2001-2002						
All ages	279,972,786	13,156	11,039	83.9	10,477	79.6
20-39 years	80,787,839	2353	1925	81.8	1843	78.3
2003-2004						
All ages	286,222,757	12,761	10,122	79.3	9643	75.6
20-39 years	79,392,841	2250	1742	77.4	1656	73.6
2005-2006						
All ages	291,616,892	12,862	10,348	80.5	9950	77.4
20-39 years	79,857,212	2436	1923	78.9	1839	75.5
2007-2008						
All ages	297,136,095	12,943	10,149	78.4	9,762	75.4
20-39 years	80,737,526	2451	1910	77.9	1844	75.2
Total						
All ages		63,882	51,623	80.8	49,130	76.9
20-39 years		11,617	9195	79.2	8751	75.3

Note. Source: CDC (1999-2008). National Health and Nutrition Examination Survey response rates and CPS totals. Retrieved September 15, 2010, from http://www.cdc.gov/nchs/nhanes/response_rates_CPS.htm.
[a]The screened sample consists of participants who were screened and selected to participate in NHANES. [b]The interviewed sample consists of participants who were actually interviewed. [c]The examined sample consists of participants who were actually examined in the mobile examination center after home interview. [d]Control total is the estimated total civilian noninstitutionalized U.S. population for the midpoint of each 2-year NHANES cycle. [e]Unweighted response rate for interviewed sample is the percentage of participants in the total screened sample who were actually interviewed. [f]Unweighted response rate for examined sample is the percentage of participants in the total screened sample who were actually examined.

NHANES during 1999-2008. Of these, 9,195 were interviewed (79.2 %) and 8,751 (75.3%) were examined in the MEC.

Sample

Subjects for this study were drawn from the 8,751 adults aged 20-39 years who participated in both the home interview and health examination during NHANES 1999-2008. Subjects were included in the study if they had documented measures on depression, fasting glucose, and fasting insulin. Subjects were excluded from the study if they: 1) had known diabetes; 2) had fasting glucose level ≥ 126 mg/dl; and 3) had fasted less than 8 hours or more than 24 hours before the fasting blood sample was drawn. No other co-morbid conditions were used to exclude participants. Study variables also included age, gender, race/ethnicity, waist circumference, BMI, systolic blood pressure, triglyceride level, high sensitivity C-reactive protein (hs-CRP), smoking status, alcohol consumption and leisure time physical activity.

Data Collection

The process of data collection was discussed under the overview of the NHANES in the Research Design section. NHANES data are made available to the public and can be downloaded from the CDC/NCHS website. The NHANES web tutorial (CDC/NCHS, 2008a) provided at the CDC/NCHS website was used as a guide to prepare the analytic dataset for the current study. The variables of interest to the study (demographic: age, gender, and race/ethnicity; examination: blood pressure, BMI,

waist circumference; laboratory: hs-CRP, fasting glucose and insulin, triglycerides; questionnaire: diabetes status, depression screener, smoking and tobacco use, alcohol use, leisure time physical activity) were first located within each survey cycle (NHANES 1999-2000, NHANES 2001-2002, NHANES 2003-2004, NHANES 2005-2006, and NHANES 2007-2008). Data files containing these variables for each 2-year survey cycle were then downloaded to a local laptop. Each variable within the different survey cycles was appended. These data files were then merged by the sequence number (SEQN), a unique identifier for each sample person, to obtain a combined dataset. Study inclusion and exclusion criteria were applied to determine the final dataset for the current study.

Diabetes Status

Diabetes status in NHANES was determined by the question “Have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?” and the responses included: “1 = Yes”, “2 = No”, “3 = borderline or prediabetes”, “7 = refused”, or “9 = Don’t know”. Borderline or prediabetes was considered as having no diabetes in this study. This variable was used to exclude participants who answered “Yes” to this question and had known diabetes.

Insulin Resistance

The estimate of insulin resistance was calculated using the homeostasis model assessment for insulin resistance (HOMA-IR), which is expressed as: HOMA-IR =

[fasting glucose (mmol/L) × fasting insulin (μU/mL)]/22.5 (Matthews et al., 1985; Wallace, Levy, & Matthews, 2004). The formula required fasting glucose and insulin levels for calculation.

Blood specimens were processed, stored, and shipped to the University of Missouri-Columbia for analysis of fasting plasma glucose and insulin in NHANES 1999-2004. For NHANES 2005-2008, glucose and insulin were analyzed by the Fairview Medical Center Laboratory at the University of Minnesota. Participants with fasting plasma glucose and insulin values were a subsample of the health examination sample that were randomly selected to provide morning fasting blood sample in the fifth stage of sampling.

Fasting plasma glucose. Fasting plasma glucose concentration was measured using the enzyme Hexokinase method with a series enzymatic reaction on Roche Cobas Mira system (Cobas Mira Chemistry System; Roche Diagnostic Systems, Inc., Montclair, NJ) in NHANES 1999-2004. Collection and assay methodologies for glucose were identical in NHANES 1999-2004. There was change in the equipment and laboratory in NHANES 2005-2006. Plasma glucose was measured using the method of Hexokinase on Roche/Hitachi 911 (Roche Diagnostics, Indianapolis, IN). A linear regression analysis was done in a crossover study to compare the Roche/Hitachi 911 method used in NHANES 2005-2006 to the Roche Cobas Mira method in NHANES 2003-2004. The glucose (mg/dl) in NHANES 2005-2006 was converted using this regression equation to make it comparable to those in NHANES

1999-2004: Y (Cobas Mira) = 0.9835 * (Hitachi 911) (Equation 1) (CDC/NCHS, 2008b). In NHANES 2007-2008, glucose analysis was conducted on the Roche Modular P chemistry analyzer (Roche ModP) (Roche Diagnostic, Indianapolis, IN). A crossover study was conducted to compare glucose data in 2007-2008 to those in 2005-2006. A Deming regression analysis was completed and a regression equation was suggested for the conversion of glucose data in 2007-2008 to be comparable to those in 2005-2006: Y (Hitachi 911) = X (Roche ModP) - 1.139 (Equation 2) (CDC/NCHS, 2010a). The glucose values in NHANES 2007-2008 were first converted to be comparable with those in NHANES 2005-2006 using Equation 2 and then to be comparable with those in NHANES 1999-2004 using Equation 1. The instruments, lab methods, and conversion equations for glucose in NHANES 1999-2008 are listed in Table 3**.**

The fasting glucose value in mg/dl was converted to mmol/L by multiplying by 0.05551 (rounded to 3 decimals). The coefficient of variation (CV) for glucose assay ranged from 1.3 to 3.0% in NHANES 1999-2004, 1.3 to 2.2% in NHANES 2005-2006, and 0.8 to 2.6% in NHANES 2007-2008.

Fasting insulin. Concentrations of fasting insulin in NHANES 1999-2000 and 2001-2002 were measured by the Pharmacia method using insulin radioimmunoassay (RIA) (Pharmacia Diagnostics AB, Uppsala, Sweden). There were changes to the equipment and lab method in NHANES 2003-2004. A Tosoh method using a two-site immunoenzymometric assay was used for NHANES 2003-2004. The mean value for

Table 3
Instruments, Lab Methods, and Conversion Equations used for Glucose for NHANES 1999-2008

Year	Instrument	Method	Conversion Equation
1999-2000	Roche Cobas	Hexokinase	
2001-2002	Roche Cobas	Hexokinase	
2003-2004	Roche Cobas Mira	Hexokinase	
2005-2006	Roche/Hitachi 911	Hexokinase	Y (Cobas Mira) = 0.9835 * (Hitachi 911)
2007-2008	Roche Modular P chemistry analyzer	Hexokinase	1. Y (Hitachi 911) = X (Roche ModP)- 1.139 2. Y (Cobas Mira) = 0.9835 * (Hitachi 911)

Note. NHANES = National Health and Nutrition Examination Survey.

the Tosoh method was about 11% lower than the Pharmacia method mean value. Two crossover studies were performed to compare the Pharmacia to the Tosoh values on split specimens. The value of insulin (μU/mL) in NHANES 2003-2004 was converted using the recommended regression equation based on the results of the crossover studies to make it comparable to those in NHANES 1999-2002: Y (Pharmacia) = (Tosoh + 2.2934)/1.0027 (Equation 3) (CDC/NCHS, 2006b). Additional changes were made to the equipment and laboratory in NHANES 2005-2008. Insulin was measured by ELISA on Merocodia insulin in NHANES 2005-2008. The values of insulin (μU/mL) in NHANES 2005-2008 were adjusted using the recommended regression equation based on a crossover study to make it comparable to those in NHANES 2003-2004: Y (Tosoh) = 1.0526 * (Mercodia) - 1.5674 (Equation 4) (CDC/NCHS, 2008b). Then they were converted to be comparable to NHANES 1999-2002, using equation 3. The instruments, lab methods, and conversion equations for insulin in NHANES 1999-2008 are listed in Table 4**.**

The coefficient of variation (CV) for insulin assay ranged from 3.3 to 5.4% in NHANES 1999-2002, 2.0 to 4.6% in NHANES 2003-2004, 3.4 to 4.9% in NHANES 2005-2006, and 5.5 to 8.8% in NHANES 2007-2008.

HOMA-IR. HOMA-IR is a simple surrogate index for insulin resistance derived from fasting steady-state condition where blood glucose concentration is homeostatically maintained in the normal range and there is no significant change in insulin level and hepatic glucose production. The method was developed by

Table 4
Instruments, Lab Methods and Conversion Equations used for Insulin for NHANES 1999-2008

Year	Instrument	Method	Conversion equation
1999-2000	Pharmacia	radioimmunoassay	
2001-2002	Pharmacia	radioimmunoassay	
2003-2004	Tosoh AIA®-PACK IRI	Immune-enzymometric	Y (Pharmacia) = (Tosoh + 2.2934) / 1.0027
2005-2006	Merocodia Insulin	ELISA	1. Y (Pharmacia) = 1.0526 * (Mercodia) - 1.5674 2. Y (Pharmacia) = (Tosoh + 2.2934) / 1.0027
2007-2008	Merocodia Insulin	ELISA	1. Y (Pharmacia) = 1.0526 * (Mercodia) - 1.5674 2. Y (Pharmacia) = (Tosoh + 2.2934) / 1.0027

Note. NHANES = National Health and Nutrition Examination Survey; Tosoh AIA®-PACK IRI is a two-site immunoenzymometric assay; IRI = immunoreactive insulin; ELISA = enzyme linked immunosorbent assay.

Matthews et al. (1985) and is a model of interactions between glucose and insulin dynamics which is used to predict levels of glucose and insulin for a wide range of possible combinations of insulin resistance and β-cell function under fasting steady state. HOMA-IR is widely used in large epidemiological or clinical studies. HOMA-IR was found to be highly and negatively correlated with the hyperinsulinemic euglycemic glucose clamp (r = -.820, p < .001), the gold standard for assessing insulin sensitivity (Bonora et al., 2000). Lansang, Williams and Carroll (2001) also found a significant negative association between insulin sensitivity derived from hyperinsulinemic euglycemic clamp and HOMA-IR scores in both hypertensive (p < .0001) and normotensive subjects (p = .002). The sensitivity of HOMA-IR for detecting individuals who were insulin resistant was comparable to the hyperinsulinemic euglycemic clamp (κ = .63). The CV of HOMA-IR scores range from 9.4% to 15%.

For an individual with normal insulin sensitivity, HOMA-IR = 1. The top 25% with highest HOMA-IR values among normal healthy population were defined as insulin resistant individuals (Balkau & Charles, 1999), which is the most commonly used definition of insulin resistance in research studies. More strictly defined insulin resistance (i.e., use the lowest quintile [20%] (Bonora et al., 1998) or decile [10%] of the HOMA-IR values) was sometimes used by other researchers. Because no standardized insulin assay has been established, it was not possible to define a universal cutoff point of HOMA-IR for insulin resistance (Muniyappa, Lee, Chen, & Quon, 2008). Nevertheless, several researchers have suggested threshold values of

HOMA-IR for insulin resistance, which ranged from 1.7 (Nakai et al., 2002) to 3.8 (Ascaso et al., 2001), depending on the studied racial/ethnic populations. The current study defined insulin resistance using the 75% percentile of HOMA-IR value among nondiabetic adults aged ≥ 20 years in NHANES 1999-2008 as the cut-point, according to Balkau and Charles (1999). Participants with a HOMA-IR score ≥ 75% percentile were defined as insulin resistant and were coded as "1 - yes". Those with a HOMA-IR score < 75% percentile were defined as non-insulin resistant and were coded as "0 - no".

Major Depression

Depression was measured by the WHO CIDI on a half-sample of examination participants aged 20-39 years in NHANES 1999-2004. In NHANES 2005-2008, depression was measured by the PHQ-9, a screener for depression, on all participants aged 12 years and above. For this study, depression was defined as a positive diagnosis of major depression by the CIDI for participants in NHANES 1999-2004 or a positive diagnosis of major depression by the PHQ-9 for those who participated in NHANES 2005-2008. In the following section, these two measurements are described and their psychometric properties are discussed, followed by a comparison between the CIDI and the PHQ-9.

The composite international diagnostic interview. The CIDI is a standardized interview developed by the WHO that is used to make clinical diagnoses of mental disorders, according to the fourth edition of the American Psychiatric Association's

Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 1994) and the International Classification of Diseases (ICD-10) diagnostic criteria (WHO, 1994). The CIDI is available in lifetime and 12-month versions and in both paper-and-pencil and computer-administered forms. The NHANES CIDI was developed as a computer-administered version and consisted of three diagnostic modules, including panic disorder, generalized anxiety disorder, and major depression (see Appendix B). These modules assessed symptoms present in the past 12 months. The NHANES CIDI was administered by trained interviewers in the MEC following guidelines instituted by CIDI. The self-report responses from participants obtained during the interview were entered into a computer program and compared to the diagnostic algorithm (CDC/NCHS, 2006c). In brief, major depression was diagnosed when either a depressed mood or markedly diminished interest in nearly all activities was present for at least 2 weeks plus four of seven additional symptoms: significant appetite/weight change, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, excessive guilt or feelings of worthlessness, diminished ability to think or concentrate or indecisiveness, and suicidal thoughts. A negative diagnosis of major depression was made if the symptoms did not meet the diagnostic criteria. The variable of major depression diagnostic score of the CIDI was used in the study. A positive diagnosis of major depression was coded as “1” and a negative diagnosis of major depression was coded as “5” in the NHANES data. The coding for negative diagnosis was recoded to “0” for this study.

The CIDI has been shown to be reliable in WHO CIDI Field Trails and other numerous studies conducted throughout the world. Two systemic reviews by Wittchen (1994) and by Andrews and Peters (1998) have been conducted on the psychometric properties of the CIDI. Kappas for inter-rater reliability of the CIDI were greater than .90 in 17 diagnoses modules except for somatization (.67), bulimia nervosa (.78), and anorexia nervosa (.80) (Wittchen, 1994). The kappas of inter-rater reliability for major depression were .97 for single episode and .93 for recurrent episodes. The diagnostic sensitivity of the CIDI for major depression ranges from .84 to .98; diagnostic specificity ranges from .46 to .74. Overall kappa agreement between the CIDI and other diagnostic interview methods (i.e., Present State Examination [PSE], Schedules for Clinical Assessment in Neuropsychiatry [SCAN]) ranges from .55 to .77.

The patient health questionnaire 9. The PHQ is a self-administered version of the Primary Care Evaluation of Mental Disorders (PRIME-MD) diagnostic instrument for common mental disorders. It is a relatively new instrument developed to make criteria-based diagnoses of depressive and other mental disorders commonly encountered in primary care and non-psychiatric settings (Spitzer, Kroenke, & Williams, 1999). The PHQ-9 is the depression module, which consists of nine items of depressive symptoms derived from the DSM-IV criteria for the diagnosis of depressive disorders (See Appendix C). It is half the length of many other depression instruments. The nine items are: 1) loss interest in activity; 2) depressed mood; 3) trouble in sleeping; 4) feeling tired; 5) change in appetite; 6) feeling guilty or

worthlessness; 7) trouble in concentrating; 8) feeling slowed down or restless; 9) suicidal thoughts. The PHQ-9 aims to measure the presence of these nine symptoms in the previous 2 weeks. There are four responses to each symptom question with "0" (not at all), "1" (several days), 2 "more than half the days", and "3" (nearly every day). Participants' responses to each symptom item were recorded in NHANES 2005-2008.

The PHQ-9 can work as a dual-purpose instrument: 1) it can establish the diagnoses of depressive disorder; 2) it can help estimate the severity of depressive symptom (Kroenke, Spitzer, & Williams, 2001). Major depression is diagnosed if 5 or more of the 9 depressive symptom criteria have been present at least "more than half the days" in the past 2 weeks, and 1 of the symptoms is depressed mood or loss interest in activity. Minor depression is diagnosed if 2, 3, or 4 depressive symptoms have been present at least "more than half the days" in the past 2 weeks, and 1 of the symptoms is depressed mood or loss interest in activity. One of the 9 symptom criteria ("thoughts that you would be better off dead or of hurting yourself in some way") counts if present at all, regardless of duration. No depression is diagnosed if 1 or less depressive symptoms were present "more than half of the days" in the past 2 weeks (Kroenke, et al., 2001). When used as a severity measure, PHQ-9 scores of 5, 10, 15, 20 represented mild, moderate, moderately severe, and severe depression respectively (Kroenke, et al., 2001).

In this study, the PHQ-9 was used as a diagnostic tool. Syntax was written in the statistical program to establish a diagnosis of major depression, according to the diagnostic criteria described above. A variable named diagnosis score was created with 1 representing a positive diagnosis of major depression and 0 representing a negative diagnosis of major depression (including minor depression and no depression).

Studies have shown that the PHQ-9 is a reliable and valid measure of depression for the purpose of diagnosis. The meta-analysis by Gilbody, Richards, Brealey, and Hewitt (2007) showed that the pooled sensitivity of PHQ-9 as a diagnostic tool for major depression was .80 (95% confidence interval [CI]: .71-.87) and specificity was .92 (95% CI: .88-.95).

Comparison of the PHQ-9 to the CIDI. The CIDI is well recognized as the gold standard for diagnosis of major depression, but it requires a trained interviewer and a complex diagnostic algorithm to make a clinical diagnosis. It may take up to 10 minutes to complete the CIDI. The PHQ-9 also consists of the 9 DSM-IV diagnostic criteria for depression, but is much easier to administer and can be used as a screening tool in clinical practice to identify patients with depression. Accumulated evidence shows that the PHQ-9 is a valid and reliable instrument in diagnosing depression, when comparing it to the CIDI (Gilbody, et al., 2007; Kroenke, Spitzer, Williams, & Lowe, 2010). Diagnostic criteria of the CIDI for major depression exclude conditions that might cause depressive symptoms, such as substance abuse, general medical

condition, or bereavement; while the PHQ-9 does not exclude these conditions that cause depressive symptoms.

Demographic Data and Other Covariates

Age, gender, race/ethnicity. Age, gender, race/ethnicity were self-reported during the NHANES home interview. Based on the self-reported information, race/ethnicity was differentiated into four categories: non-Hispanic White, non-Hispanic Black, Mexican American, and other race/ethnicity. Other race/ethnicity included those with single racial/ethnic identity other than non-Hispanic White, non-Hispanic Black or Mexican American; those who reported being multi-racial and missing values on race/ethnicity. As mentioned previously, covariates important to the study were selected according to the review of literature and the clinical guidelines of NCEP APT III and WHO on metabolic syndrome. These covariates included systolic blood pressure, triglyceride level, hs-CRP, BMI or waist circumference, leisure time physical activity, smoking status, and alcohol consumption.

Systolic blood pressure. Blood pressure was measured by physicians who were trained and certified for blood pressure measurement in the training program from Shared Care Research and Education Consulting. All blood pressures were taken in the MEC. Each participant was instructed to rest quietly in a sitting position for 5 minutes prior to the measurement. Appropriate cuffs were selected for participant's arm circumference. After determining the maximum inflation level, three consecutive blood pressure readings were obtained with a mercury sphygmomanometer. A fourth

attempt was made, if a blood pressure measurement was interrupted or incomplete. An average systolic blood pressure was then calculated as follows: if only one blood pressure reading was obtained, the systolic pressure identified was recorded as the average; if two blood pressure readings were obtained, the second of the two systolic readings was recorded as the average; if more than two blood pressure readings were obtained, the first reading was excluded from the calculation of the average. The average systolic blood pressure was recorded in the NHANES and was used as the measure of systolic blood pressure for the current study.

Triglyceride level. Blood specimens were processed, stored, and shipped to the Lipoprotein Analytical Laboratory at Johns Hopkins University School of Medicine for analysis of triglycerides in NHANES 1999-2006. Triglyceride level was measured enzymatically in serum using a series of coupled reactions (Hitachi 704 Analyzer, Roche Diagnostics, Indianapolis, IN) in NHANES 1999-2004. No changes were made to the lab method or lab site in NHANES 2005-2006; however, the lab equipment was changed from Hitachi 704 to Hitachi 717 and Hitachi 912 (CDC/NCHS, 2008c). In NHANES 2007-2008, serum triglycerides were analyzed by the Fairview Medical Center Laboratory at the University of Minnesota on Roche Modular P chemistry analyzer. However, no adjustment or conversion of values was necessary to account for the change in instrumentation for triglycerides between NHANES 1999-2004, NHANES 2005-2006 and NHANES 2007-2008 (CDC/NCHS, 2010b). The ranges of CV were 1.5 to 3.1% in NHANES 1999-2004, 1.8 to 2.1 % in NHANES 2005-2006 (CDC/NCHS, 2008d), 1.3 to 2.4% in NHANES 2007-2008

(CDC/NCHS, 2010c). The sensitivity for triglycerides glycerophosphate oxidase (GPO) determination was 10mg/dl. The variable of LBXTR in the unit of mg/dl from NHANES data was used for the current study.

High sensitivity C-reactive protein. Blood specimens were processed, stored and shipped to Department of Laboratory Medicine in University of Washington for analysis. Hs-CRP was quantified by latex-enhanced nephelometry on Dade Behring Nephelometer II Analyzer System (Dade Behring Diagnostic Inc, Somerville, New Jersey). The equipment, lab methods, and lab site was consistent in NHANES 1999-2008. The CV ranges from 3.1 to 9.9%. The lowest detectable hs-CRP is 0.02 mg/dL and results were reported to the nearest hundredth (0.01). For this study, hs-CRP values were categorized as low (< 1.0 mg/L), moderate (1.0 to 3.0 mg/L), and high levels (> 3.0 mg/L). The three concentration categories were used in the data analyses.

BMI and waist circumference. BMI, an indicator for overall obesity, and waist circumference, an index for central obesity, were used in the study to evaluate the strength of their association with insulin resistance. Because these variables are likely highly correlated, they were tested during data analyses to determine which is more highly associated with insulin resistance. BMI was calculated by weight (kg)/height $(m)^2$ and was provided in the NHANES data.

Measurement of weight and height were included in the health examination and were performed in the body measurement room at the MEC by a trained health

technician and a recorder. For these anthropometry measurements, participants wore the standard MEC examination gown and underwear beneath the gown. Weight was measured on a Toledo digital weight scale in pounds and converted to kilograms in the automated system in NHANES 1999-2006 (CDC/NCHS, 2000, 2002, 2004, 2005) and weight was measured in kilogram in NHANES 2007-2008 (CDC/NCHS, 2007). Participants were instructed to stand still in the center of weight scale platform, put their hands at side, and look straight ahead. The displayed weight would be recorded when the reading became stable and the recorder clicked the "Get Weight" button on the screen. The maximum capacity of the digital scale is 440 pound. Two portable weight scales were available to use when participants' weight exceeded 440 pounds, the digital weight scale malfunctioned or there was a power outage.

Standing height was measured with a fixed standiometer with a vertical backboard and a moveable headboard. Participants were instructed to stand on the floor, positioning the heels of both feet together with the toes pointing outward at approximately a 60 degree angle. Body parts of the heels, the buttocks, shoulder blades, and the back of the head were positioned to contact with the vertical backboard. The head was aligned in a way that the horizontal line from the ear canal to the lower border of the orbit of the eyes was parallel to the floor and perpendicular to the vertical backboard. Participants were instructed to take a deep breath and stand as tall as possible. The health technicians lowered the headboard to firmly position on the top of the head and the height was recorded automatically.

Toledo digital weight scale was calibrated formally at the beginning of each stand and in the mid-term. Six of the 50 pounds calibration weights were placed on the scale and technicians would check for displayed weight. If the displayed weight was outside the acceptable range (299.75 to 300.25 pounds), the weight scale would be recalibrated by a service representative. Informal calibration was performed daily. The technicians checked the weight scale by weighing themselves first on the weight scale and then adding one or two 10-pound calibrated weights on the weight scale and checking if the displayed weight increased correspondingly. There have been changes in calibration procedures for digital weight scale since 2007 (CDC/NCHS, 2007). Full calibration of the digital scale was done at the start, middle, and end of a stand and 15 of the 10 kilogram calibration weights were used. The acceptable weight ranges were 149.85 - 150.15 kg. The daily calibration procedures included placing five of the 10 kilogram calibration weights on the scale and the acceptable weight ranges were 49.70 - 50.30 kg. If the results fell outside the acceptable range, the full calibration procedures would be performed. If the result fell within the acceptable range of the full calibration, then the daily calibration procedure would be repeated. If the results still were outside the acceptable range, then the scale would be recalibrated by a service representative.

The standiometer was calibrated at the start of each stand and weekly. One 80 cm - long calibration rod was placed on the floor of the standiometer and the horizontal bar of the standiometer was then put firmly against the top of the calibration rod. If

the displayed reading was not 80 cm, the standiometer would be recalibrated by technicians.

Waist circumference was measured by a highly trained health technician in the MEC and validated by a data recorder who accompanied the health technician for the waist circumference measurement. Participants were instructed to stand and hold the examination gown above the waist, lower the pants and underclothing slightly. The health technicians stood behind and to the right of the participants to palpate the hip area to locate the right ilium. A horizontal line was drawn above the uppermost lateral border of the right ilium and then a vertical line was drawn cross the line to indicate the midaxillary line of the body. The measuring tape was placed around the trunk in a horizontal plane at the level marked on the right side of the trunk and the zero end of the measuring tape was placed below the measurement value. The mirror on the wall was used to ensure correct horizontal alignment of the measuring tape. The recorder validated that the tape was parallel to the floor and that the tape was snug, but did not compress the skin. The measurement was made at the end of a normal expiration to the nearest millimeter.

Leisure-time physical activity. In NHANES, physical activity was assessed by a physical activity questionnaire that was completed during the home interview. This physical activity questionnaire included questions on daily activities, leisure time activities, and sedentary activities. These questions have been used in previous NHANES questionnaires or in other federal surveys. Participants' responses to the

questions on leisure-time physical activities (LTPA) were used as the measure of physical activity for the current study because research has shown that LTPA can produce long-term health benefits (U.S. Department of Health and Human Services, 2008). In NHANES 1999-2008, participants were asked if they did any moderate or vigorous LTPA for at least 10 minutes in the past 30 days. If the answer was "yes", they were asked to report the frequency and duration of LTPA they performed. In NHANES 1999-2006, participants also were asked to specify the types of moderate or vigorous LTPA.

To quantify the absolute intensity of the physical activity, a metabolic equivalent (MET) score was assigned by NHANES to each type of LTPA. A MET is a measure of energy expenditure of a physical activity relative to the rate of energy expenditure at rest. In general, 1 MET is the rate of energy expenditure during rest and equals 3.5 mL oxygen uptake per kilogram of body weight per minute. The METs for moderate activities range from 3.0 to 5.9 and vigorous activities have METs of 6.0 or above. According to the 2008 *Physical Activity Guidelines for Americans* by U.S. Department of Health and Human Services, adults should do at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity physical activity per week. This equals 500-1000 MET-minutes per week (U.S. Department of Health and Human Services, 2008).

For this study, the total MET-minutes per week were calculated for participants who reported participating in either moderate or vigorous LTPA in the past 30 days.

In NHANES 1999-2006, total MET-minute per week = [(MET score for activity 1 * Frequency of activity 1 (in number of times/30 days) * Duration of activity 1 (in minutes/time) + MET score for activity 2 * Frequency of activity 2 * Duration of activity 2…)/30]*7. In NHANES 2007-2008, total MET-minute per week = [MET score for moderate LTPA* Frequency of moderate LTPA (in days/week) * Duration of moderate LTPA (in minutes/day) + MET score for vigorous LTPA * Frequency of vigorous LTPA (in days/week) * Duration of vigorous LTPA (in minutes/day)]. For participants who reported they did not engage in any moderate or vigorous LTPA, a value of zero was assigned. Total MET-minute per week indicated level of LTPA. Using criteria established in the *2008 Physical Activity Guidelines for Americans*, participants were categorized into four groups: no LTPA (total MET-minute per week = 0), low LTPA (total MET-minute per week < 500), moderate LTPA (500 ≤ total MET-minute per week ≤ 1000), and high LTPA (total MET-minute per week > 1000) (US Department of Health and Human Services, 2008).

Smoking status. Smoking and tobacco use were assessed by two questions during the home interview. The wording and responses to these two questions were consistent in NHANES 1999-2008. The first question is "Have you smoked at least 100 cigarettes in your entire life?" and the responses were coded as 1 = "yes" and 2 = "no". The second question is "Do you now smoke cigarettes?". The responses were coded as 1 = "every day", 2 = "some days", and 3 = "not at all". The responses to these two questions were used to determine smoking status. Current smoker was defined as report of having smoked ≥ 100 cigarettes during a person's lifetime and

currently smoking every day or some days. Former smoker was defined as having smoked ≥ 100 cigarettes during a person's lifetime, but not currently smoking. Nonsmoker was defined as report of having smoked < 100 cigarettes during a person's lifetime.

Alcohol consumption. Alcohol consumption was assessed by a set of questions related to lifetime and past 12 months use of alcohol in the questionnaire administered to participants during the physical examination at the MEC using a computer-assisted personal interview (CAPI) system. For the current study, alcohol consumption status was determined by the following questions: 1) "In any one year, have you had at least 12 drinks of any type of alcoholic beverage?"; 2) "In your entire life, have you had at least 12 drinks of any type of alcoholic beverage?"; 3) "In the past 12 months, how often did you drink any type of alcoholic beverage (i.e., days per week, per month, or per year)?"; 4) "In the past 12 months, on those days that you drank alcoholic beverages, on the average, how many drinks did you have?". The wording of these questions was identical in NHANES 1999-2008.

Current drinker was defined as report of having at least 12 drinks in one's lifetime and 1 or more drinks in the past 12 months. Former drinkers were defined as report of having at least 12 drinks in one's lifetime but had no drinks in the past 12 months. Nondrinker was defined as report of having less than 12 drinks in one's lifetime. Current drinkers were further differentiated into light, moderate, and heavy drinkers based on weekly drinking amount. It was calculated by the product of

self-reported drinking frequency (in number of days per week) and number of drinks per day. If drinking frequency was reported in days per month or per year, it was calculated as the following: [(number of days per month) * (number of drinks per day)/30]*7, or [(number of days per year) * (number of drinks per day)/365]*7 respectively. Light drinkers were defined as report of having an average of ≤ 3 drinks per week. Moderate drinkers were defined as report of having an average of more than 3 drinks, but up to 14 drinks per week for men or more than 3 drinks to 7 drinks per week for women (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2005). Heavy drinkers were defined as report of having an average of >14 drinks per week for men and > 7 drinks per week for women (CDC, 2010a).

Human Subject Review

The NHANES 1999-2008 were approved by CDC/NCHS institutional review board/ ethnics review board. Participation in NHANES was fully voluntary. Informed consent was obtained from all subjects prior to home interview, physical examination and laboratory testing. All identifying information was kept confidential to protect participants.

Approval for this study was obtained from the University of Kansas Medical Center (KUMC) Human Subject Committee and was deemed to not involve human subjects. The study was a secondary analysis of NHANES data that were available to

the public through the CDC/NCHS website (CDC, 1999-2008). All public use NHANES data had been de-identified and subject sequence number assigned to each participant. This investigator has not had direct contact with the participants in NHANES nor has this investigator had access to information that links participants with their survey responses. Findings are reported in the aggregate.

Preliminary Study

A preliminary study was done in Fall 2007 to fulfill the requirement of NRSG 959 Research Project and to explore the possibility for a dissertation topic. The study was a secondary analysis of NHANES data 1999-2002, looking at the relationship between major depressive disorder (MDD) and insulin resistance among non-diabetic young adults aged 20-39 years old in the United States. The study also examined the role of gender in the association between MDD and insulin resistance. The sample consisted of 279 men and 358 women aged 20-39 years (N = 637) who were nondiabetic and had complete data on depression, fasting glucose and insulin. This sample was derived from 3,620 young adults aged 20-39 years who participated in NHANES 1999-2002. Logistic regression analyses found no statistically significant association between MDD and insulin resistance, but gender had a moderating effect on the relationship. For men, MDD was negatively associated with insulin resistance after adjusting for age, race/ethnicity, waist circumference, smoking status, systolic blood pressure and triglyceride level (B = -2.12, p = .01, OR = 0.12, 95% CI [0.02, 0.62]). No significant association between MDD and insulin resistance among women

was found (B = 0.61, p = .38, OR = 1.84, 95% CI [0.47,7.14]) (Shen, et al., 2011). Findings from this preliminary study suggested the need for increasing sample size. Due to the small sample size in the preliminary study, the analysis of the effect of race/ethnicity on the relationship between depression and insulin resistance could not be performed. Moreover, previous studies failed to examine the effect of race/ethnicity on the relationship between depression and insulin resistance. Therefore, the current study was expanded to add adults of the same age range that participated in NHANES 2003-2008 for a total NHANES sample of 20-39 years old spanning 1999-2008 to examine this relationship.

Data Analysis

Data analyses for this study incorporated the complex design information of the NHANES. According to the September 2006 update of the NHANES Analytic Guidelines (CDC/NCHS, 2006a), SUDAAN, SAS and STATA are appropriate statistical software to use for analyses of NHANES data, although SUDAAN was specifically designated for NHANES data analyses. The CDC/NCHS released NHANES data sets as SAS transport files. The survey procedures provided in SAS can adequately estimate appropriate sampling errors by using the Taylor series method. Because of previous experience of using SAS in the preliminary study and its appropriateness in analyzing NHANES data as recommended by CDC/NCHS, data analyses for this study were conducted using survey procedures in SAS version 9.2 (SAS Institute, Inc., Cary, NC).

Survey Procedures in SAS

The survey procedures in SAS are different from traditional SAS procedures in that they can make statistically valid estimates by accounting for the probability-based complex sample designs (i.e., stratification, clustering and unequal weighting), while the traditional SAS procedures compute statistics under the assumption that the sample is drawn from an infinite population by simple random sampling. The CDC/NCHS recommends the following survey procedures for analyses of NHANES data: SURVEYMEANS, SURVEYFREQ, SURVEYREG, and SURVEYLOGISTIC. These procedures can produce variance of estimates (or sampling error) through the method of Taylor Series Linearization, a variance approximation procedure that accounts for the complex survey design and computes design effects. Specifically, the SURVEYMEANS procedure calculates descriptive statistics for sample survey data, including means, totals, proportions, ratios, and their standard errors. The SURVEYFREQ procedure produces one-way to n-way frequency and cross tabulation tables from sample survey data, including estimates of population totals, population proportions, and their standard errors. It also can compute confidence limits, coefficients of variation, and design effects. The SURVEYREG procedure fits linear regression models, performs hypothesis tests and provides estimates for survey data (An & Watts, 2000). The SURVEYLOGISTIC fits linear logistic regression models for categorical response survey data by the method of maximum likelihood (An, 2002). To produce valid statistical estimates of

population, the complex survey design information, including stratification, clustering, and unequal weighting were incorporated into all the analyses (CDC/NCHS, 2006a).

Survey Design Variables

Because the NHANES was a complex, stratified, multistage probability-based clustered design, survey design information such as strata and PSUs was applied in the data analyses to obtain valid estimates of statistics as recommended by CDC/NCHS. Strata and PSUs represented the variance units, which were defined as sampling units used to estimate sampling error. In NHANES data, the design variables for the stratum and the PSU were *sdmvstra* and *sdmvpsu* respectively. These two variables were incorporated in all data analyses discussed later.

Sample Weights

A sample weight was assigned to each sample person in the NHANES. It is a measure of the number of people in the population represented by a sample person in NHANES. The sample weight accounted for unequal selection probability, nonresponse adjustment, and adjustment to match 2000 U.S. Census population totals (CDC/NCHS, 1999b). Each sample person was a member of the interview sample. Some sample persons also were members of the health examination sample. As previously mentioned, the subsample was defined as a subset of individuals that were randomly selected from the examined sample during the fifth stage of selection.

However, each of these samples (interview, examination, or subsample) in the NHANES survey was a nationally representative sample (CDC/NCHS, 1999f). Each sample was assigned a weight. Consequently, there were three types of sample weights in NHANES: interview weights, examination weights, and subsample weights. Subsample weights accounted for this additional sampling stage and nonresponse and were different from the full examination weights (CDC/NCHS, 1999f). Selection of the correct sample weight to use in the analyses is important to produce unbiased national estimates and depends on the variables of interest included for the data analyses. The rule of thumb is to use the weight associated with the variable on which data were collected from the smallest sample subpopulation (CDC/NCHS, 1999a). For example, if only variables from the interviewed sample are used, then the interview weights should be used. If one or some of variables of interest were collected during the MEC examination is used, the appropriate sample weight to use is the examination weight. If data analyses include variables collected from a subsample of the examination sample, the proper weight to be applied the analyses is the subsample weight specific to that variable. For the current study, variables such as fasting glucose and insulin were collected from a subsample of the examined sample; therefore, fasting sample weights were used in the analyses in order to produce unbiased statistical estimates.

The NHSC provided sample weights for each 2-year cycle of NHANES. Therefore, it was necessary to calculate new sample weights when combining two or more 2-year cycles of NHANES data except for NHANES 1999-2002 which had

special 4-year sample weights. This special 4-year sample weight was calculated by the NCHS, because there were differences in Census population estimates used in NHANES 1999-2000 and NHANES 2001-2002. In particular, the sample weights for NHANES 1999-2000 were based on population estimates developed by the Bureau of the Census before the Year 2000 Decennial Census Count became available; while the two-year sample weights for NHANES 2001-2002 were based on population estimates of the year 2000 Census counts. The population estimates in NHANES 2003-2008 also were based on the year 2000 Census counts (CDC/NCHS, 2006a).

Sampling weights for subjects in the study were applied according to the NHANES web tutorial and the analytic guideline provided by the NCHS on how to construct 10-year sample weights when combining NHANES 1999-2008 for data analyses. Using this guideline, a 10-year fasting sample weight variable was created by: 1) assigning 2/5 of the 4 year fasting sample weight for 1999-2002 if the person was sampled in 1999-2002, or 2) assigning 1/5 of the 2 year fasting sample weight for 2003-2004 if the person was sampled in 2003-2004, or 3) assigning 1/5 of the 2 year fasting sample weight for 2005-2006 if the person was sampled in 2005-2006, or 4) assigning 1/5 of the 2 year fasting sample weight for 2007-2008 if the person was sampled in 2007-2008 (CDC/NCHS, 1999e). According to CDC/NCHS, the fractions used to calculate the new 10-year fasting sample weight were derived from averaging the sample weights from each survey cycle. For example, in NHANES 1999-2002, the averaged sample weight for the 4-year weight in a 10-year dataset was 4/10

(which equals to 2/5) and the average sample weight for a 2-year weight was 2/10 (which equals to 1/5).

Statistical Analyses

The NHANES web tutorial provided by CDC/NCHS includes an NHANES analyses course that demonstrates how to select appropriate statistical techniques when analyzing NHANES data. These statistical techniques include descriptive statistics, hypothesis testing, age standardization and population estimates, linear regression and logistic regression. This NHANES analyses course was used as a guide for the data analyses conducted in SAS in this study (CDC/NCHS, 1999c).

Descriptive analyses were performed to describe the sample and the population represented. For continuous variables (age, waist circumference, BMI, systolic blood pressure, triglycerides), results were reported as mean and standard deviation (*SD*) for the sample and weighted mean and standard error (SE) for the population. For categorical variables (gender, race/ethnicity, smoking status, alcohol consumption status, leisure time physical activity, insulin resistance, major depression diagnosis, and hs-CRP status), frequency and percentage were reported for the sample and weighted percent and SE were reported for the population. Statistical significance was set at $p \leq .05$. The analyses were outlined by research questions as follows:

Question #1: What is the overall prevalence of major depression among nondiabetic U.S. adults aged 20-39 years?

This was reported as weighted percent and standard error using PROC SURVEYFREQ.

Question #2: What is the overall prevalence of insulin resistance among nondiabetic U.S. adults aged 20-39 years?

This was reported as weighted percent and standard error using PROC SURVEYFREQ.

Question #3: What is the relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years?

a) What is the unadjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years?

   Logistic regression analysis was performed with major depression as independent variable and insulin resistance as the dependent variable, using PROC SURVEYLOGISTIC.

b) What is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by gender, adjusting for age, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), leisure time physical activity (LTPA), smoking status, and alcohol consumption?

b1) Is there an interaction between gender and major depression in the relationship with insulin resistance among nondiabetic U.S. adults aged 20-39 years?

An interaction term of major depression and gender (major depression * gender) was introduced into logistic regression analysis with major depression, major depression * gender and gender as independent variables and insulin resistance as the dependent variable. The interaction term was significant with $p \leq .05$.

b2) If the interaction between gender and major depression is significant, what is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by gender, adjusting for age, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption?

Logistic regression analysis with major depression, age, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption as independent variables and insulin resistance as the dependent variable was conducted separately for men and women, using PROC SURVEYLOGISTIC. The correlations among independent variables were performed to detect any collinearity. The two indexes for obesity: BMI and waist circumference were

tested in separate models to investigate the strength of their relationships to insulin resistance and determine which variable best fits the model. Odds ratios and 95% confidence intervals (CI) generated from the two models were compared. The goodness of fit of the two models was determined by model fit statistics such as -2 log likelihood and Akaike information criterion (AIC). The best model is the one with the minimum -2 log likelihood and AIC value.

b3) If the interaction between gender and major depression is not significant, what is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years, adjusting for age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption?

Logistic regression analysis with major depression, age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption as independent variables and insulin resistance as the dependent variable were conducted using PROC SURVEYLOGISTIC. The two indexes for obesity: BMI and waist circumference were tested in separate models to investigate the strength of their relationships to insulin resistance and determine which variable best fits the model. Odds ratios and 95% CI generated from the two models were compared. The goodness of fit of the two models was determined by model fit

statistics such as -2 log likelihood and AIC. The best model is the one with the minimum -2 log likelihood and AIC value.

c) What is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by race/ethnicity, adjusting for age, gender, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption?

c1) Is there an interaction between race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, and other) and major depression in the association with insulin resistance among nondiabetic U.S. adults aged 20-39 years?

An interaction term of depression and race/ethnicity (major depression * race/ethnicity) were introduced into logistic regression analysis with major depression, major depression * race/ethnicity and race/ethnicity as independent variables and insulin resistance as the dependent variable. The interaction term was significant with $p \leq .05$.

c2) If the interaction between race/ethnicity and depression is significant, what is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by race/ethnicity, adjusting for age, gender, systolic blood pressure,

triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption?

Logistic regression analysis with depression, age, gender, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption as independent variables and insulin resistance as the dependent variable were conducted separately for each race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, and other), using PROC SURVEYLOGISTIC. The two indexes for obesity: BMI and waist circumference were tested in separate models to investigate the strength of their relationships to insulin resistance and determine which variable best fits the model. Odds ratios and 95% CI generated from the two models were compared. The goodness of fit of the two models was determined by model fit statistics such as -2 log likelihood and AIC. The best model is the one with the minimum -2 log likelihood and AIC value.

c3) If the interaction between race/ethnicity and depression is not significant, what is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years, adjusting for age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption?

Logistic regression analysis with depression, age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption as independent variables and insulin resistance as the dependent variable were conducted using PROC SURVEYLOGISTIC. The two indexes for obesity: BMI and waist circumference were tested in separate models to investigate the strength of their relationships to insulin resistance and determine which variable best fits the model. Odds ratios and 95% CI generated from the two models were compared. The goodness of fit of the two models was determined by model fit statistics such as -2 log likelihood and AIC. The best model is the one with the minimum -2 log likelihood and AIC value.

Question #4: What is the relationship between major depression and insulin resistance by type of depression measure among nondiabetic U.S. adults aged 20-39 years?

a) What is the unadjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by type of depression measure?

Separate logistic regression analyses were performed for participants in NHANES 1999-2004 using the CIDI as depression measure and for participants in NHANES 2005-2008 using the PHQ-9 as depression measure. PROC SURVEYLOGISTIC was used with depression as independent variable and

insulin resistance as the dependent variable. Odds ratios and 95% CI generated from the two models were then compared.

b) What is the adjusted relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years by type of depression measure, adjusting for age, gender, race/ethnicity, xsystolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption?

Separate logistic regression analyses were performed for participants in NHANES 1999-2004 using the CIDI as the depression measure and for participants in NHANES 2005-2008 using the PHQ-9 as the depression measure. PROC SURVEYLOGISTIC was used with depression, age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, obesity (BMI or waist circumference), LTPA, smoking status, and alcohol consumption as independent variables and insulin resistance as the dependent variable. The two indexes for obesity: BMI and waist circumference were tested in separate models to investigate the strength of their relationships to insulin resistance and determine which variable best fits the model. Odds ratios and 95% CI generated from the two models were compared. The goodness of fit of the two models was determined by model fit statistics such as -2 log likelihood and AIC. The best model is the one with the minimum -2 log likelihood and AIC value. Research

questions, measurements of variables, level of measurements, and data analyses are summarized in Table 5.

Table 5
Research Questions, Measurements of Variables, Level of Measurements, and Data Analyses

Research questions	Measurement	Level of measurement	Data analysis
1. What is the overall prevalence of MD among nondiabetic U.S. adults aged 20-39 years?	NHANES 1999-2004: The WHO CIDI NHANES 2005-2008: The PHQ-9	Nominal (yes/no)	**Analysis:** descriptive **Statistics:** weighted percent, standard error **Procedure:** SURVEYFREQ.
2. What is the overall prevalence IR among nondiabetic U.S. adults aged 20-39 years?	HOMA-IR = [fasting glucose (mmol/L) × fasting insulin (μU/mL)]/22.5 IR: if HOMA-IR score ≥ 75 percentile of HOMA-IR. Non-IR: if HOMA-IR score < 75 percentile of HOMA-IR.	Nominal (yes/no)	**Analysis:** descriptive **Statistics:** weighted percent, standard error **Procedure:** SURVEYFREQ.
3. What is the relationship between MD and IR among nondiabetic U.S. adults aged 20-39 years?			
a) What is the unadjusted relationship between MD and IR among nondiabetic U.S. adults aged 20-39 years?	MD: see above IR: see above	MD: nominal (yes/no) IR: nominal (yes/no)	**Analysis:** logistic regression **Statistics:** *b*, *p*, *OR*, 95% *CI* **Procedure:** SURVEYLOGISTIC **Independent variable:** MD **Dependent variable:** IR
b) What is the adjusted relationship between MD and IR among nondiabetic U.S. adults aged 20-39 years ***by gender***, adjusting for age, race/ethnicity, SBP, TG, hs-CRP, obesity (BMI or WC), LTPA, smoking status, and alcohol consumption?			

Table 5 continued

Research questions	Measurement	Level of measurement	Data analysis
b1) Is there an interaction between gender and MD in the relationship with IR among nondiabetic U.S. adults aged 20-39 years?	MD: see above IR: see above Gender: self-reported	MD: nominal (yes/no) IR: nominal (yes/no) Gender: nominal	**Analysis:** logistic regression **Statistics:** *b*, *p*, *OR*, 95% *CI* **Procedure:** SURVEYLOGISTIC **Independent variable:** MD, gender, MD*gender **Dependent variable:** IR
b2) If the interaction between gender and MD is significant, what is the adjusted relationship between MD and IR among nondiabetic U.S. adults aged 20-39 years by gender, adjusting for age, race/ethnicity, SBP, TG, hs-CRP, obesity (BMI or WC), LTPA, smoking status, and alcohol consumption?	MD: see above IR: see above Age: self-reported Gender: self-reported Race/ ethnicity: self-reported SBP: measured by trained physician using mercury sphygmomanometer. TG: enzymatic reaction on Hitachi 704, Hitachi 717, Hitachi 912. Hs-CRP: latex-enhanced nephelometry on Dad Behring Nephelometer II Analyzer system Obesity: BMI and WC LTPA: categorized by total MET-minutes/week Smoking status: self-reported Alcohol consumption: self-reported	MD: nominal (yes/no) IR: nominal (yes/no) Age: interval Gender: nominal Race / ethnicity: nominal SBP: interval TG: interval Hs-CRP status: ordinal BMI: interval WC: interval LTPA: ordinal Smoking status: ordinal Alcohol consumption: ordinal	**Analysis:** logistic regression **Statistics:** *b*, *p*, *OR*, 95% *CI* **Procedure:** SURVEYLOGISTIC **Independent variable:** MD, age, race/ethnicity, SBP, TG, hs-CRP, obesity, LTPA, smoking status, and alcohol consumption **Dependent variable:** IR ● BMI and WC were tested in separate models. ● Separate models were conducted for men and women.

Table 5 continued

Research questions	Measurement	Level of measurement	Data analysis
b3) If the interaction between gender and MD is not significant, what is the adjusted relationship between MD and IR among nondiabetic U.S. adults aged 20-39 years, adjusting for age, gender, race/ethnicity, SBP, TG, hs-CRP, obesity (BMI or WC), LTPA,smoking status, and alcohol consumption?	See above	See above	**Analysis:** logistic regression **Statistics:** *b, p, OR,* 95% *CI* **Procedure:** SURVEYLOGISTIC **Independent variable:** MD, age, gender, race/ethnicity, SBP, TG, hs-CRP, obesity, LTPA,smoking status, and alcohol consumption **Dependent variable:** IR ● BMI and WC were tested in separate models.
c) What is the adjusted relationship between MD and IR among nondiabetic U.S. adults aged 20 - 39 years ***by race/ethnicity***, adjusting for age, gender, SBP, TG, hs-CRP, obesity (BMI or WC), LTPA,smoking status, and alcohol consumption?			
c1) Is there an interaction between race/ethnicity (non-Hispanic White, non-Hispanic Black, Mexican American, and other) and MD in the association with IR among nondiabetic U.S. adults aged 20-39 years?	See above	See above	**Analysis:** logistic regression **Statistics:** *b, p, OR,* 95% *CI* **Procedure:** SURVEYLOGISTIC **Independent variable:** MD, race/ethnicity, MD*race/ethnicity; **Dependent variable:** IR

Table 5 continued

Research questions	Measurement	Level of measurement	Data analysis
c2) If the interaction between race/ethnicity and MD is significant, what is the adjusted relationship between MD and IR among nondiabetic U.S. adults aged 20-39 years by race/ethnicity, adjusting for age, gender, SBP, TG, hs-CRP, obesity (BMI or WC), LTPA, smoking status, and alcohol consumption?	See above	See above	**Analysis:** logistic regression **Statistics:** *b, p, OR,* 95% *CI* **Procedure:** SURVEYLOGISTIC **Independent variable:** MD, age, gender, SBP, TG, hs-CRP, obesity, LTPA, smoking status, and alcohol consumption **Dependent variable:** IR ● BMI and WC were tested in separate models. ● Separate models were conducted for each racial/ethnic group
c3) If the interaction between race/ethnicity MD is not significant, what is the adjusted relationship between MD and IR among nondiabetic U.S. adults aged 20-39 years, adjusting for age, gender, race/ethnicity, SBP, TG, hs-CRP, obesity (BMI or WC), LTPA, smoking status, and alcohol consumption?	See above	See above	**Analysis:** logistic regression **Statistics:** *b, p, OR,* 95% *CI* **Procedure:** SURVEYLOGISTIC **Independent variable:** MD, age, gender, race/ethnicity, SBP, WC, hs-CRP, obesity, LTPA, smoking status, and alcohol consumption **Dependent variable:** IR ● BMI and WC were tested in separate models.

Table 5 continued

4. What is the relationship between MD and IR ***by types of depression measure*** among nondiabetic U.S. adults aged 20-39 years?

Research questions	Measurement	Level of measurement	Data analysis
a) What is the unadjusted relationship between MD and IR among nondiabetic U.S. adults aged 20-39 years by types of depression measure?	See above	See above	**Analysis:** logistic regression **Statistics:** *b, p, OR,* 95% *CI* **Procedure:** SURVEYLOGISTIC **Independent variable:** MD **Dependent variable:** IR ● BMI and WC were tested in separate models. ● Separate models were conducted for participants in NHANES 1999-2004 and participants in NHANES 2005-2008.
b) What is the adjusted relationship between MD and IR among nondiabetic U.S. adults aged 20-39 years by types of depression measure, adjusting for age, gender, race/ethnicity, SBP, TG, hs-CRP, obesity (BMI or WC), LTPA,smoking status, and alcohol consumption?	See above	See above	**Analysis:** logistic regression **Statistics:** *b, p, OR,* 95% *CI* **Procedure:** SURVEYLOGISTIC **Independent variable:** MD, age, gender, race/ethnicity, SBP, TG, hs-CRP, obesity, LTPA,smoking status, and alcohol consumption **Dependent variable:** IR ● BMI and WC were tested in separate models. ● Separate models were conducted for participants in NHANES 1999-2004 and participants in NHANES 2005-2008.

Note. MD = major depression; U.S. = United States; NHANES = National Health and Nutrition Examination Survey; WHO = World Health Organization; CIDI = composite international diagnostic interview; PHQ-9 = patient health questionnaire -9; IR = insulin resistance; HOMA-IR = homeostasis model assessment for insulin resistance; OR = odds ratio; CI = confidence interval; BMI = body index mass; WC = waist circumference; SBP = systolic blood pressure; TG = triglyceride; hs-CRP = high sensitivity C-reactive protein; LTPA =leisure time physical activity.

CHAPTER IV RESULTS

This chapter presents the findings from analyses of cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) 1999-2008 on: 1) the prevalence of major depression and insulin resistance among nondiabetic adults aged 20-39 years in the United States; 2) the relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years; and 3) the role of gender, race/ethnicity, and measure of depression on the relationship between major depression and insulin resistance. The findings reported include information about derivation of the study sample, demographic characteristics of the study sample and the represented population, prevalence of major depression and insulin resistance, risk factors associated with insulin resistance, and the relationship between major depression and insulin resistance.

Derivation of the Study Sample

Initial stratified multistage sampling procedures identified a total of 63,882 persons at all ages (from birth to 85 years and above) that were eligible to participate in NHANES 1999-2008. Of these, 51,623 were interviewed (80.8%) in the home and 49,130 (76.9%) completed both the home interview and health examination at the mobile examination center. Among adults aged 20-39 years, a total of 11,617 adults were selected to participate in NHANES 1999-2008. Of these, 9,195 were interviewed (79.2%) in the home and 8,751 (75.3%) completed both the home

interview and health examination. Of the 8,751 adults aged 20-39 years who participated in the home interview and health examination, 2,548 had participated in the fifth stage of sampling, and had complete data on measures of major depression, fasting glucose and insulin levels. Among these 2,548 subjects, 60 had known diabetes, 27 had fasting glucose ≥ 126 mg/dl, and 196 had fasted less than 8 hours or more than 24 hours before the fasting blood sample was drawn. These participants were excluded from the study, leaving 2,265 participants for inclusion in the current study sample. No other co-morbid conditions were used to exclude participants. See Figure 3 for the flow chart of the steps for including and excluding subjects for this study.

Description of the Study Sample

The study sample was comprised of 2,265 U.S. adults aged 20-39 years who participated in NHANES 1999-2008 and did not have known diabetes or fasting glucose level ≥ 126 mg/dl at the time of participation. These subjects had complete data on measures of major depression, fasting glucose and insulin level. The weighted mean age of the population was 29.5 years (*SE* = 0.18). The demographic characteristics of the study sample and the weighted percent for the population that the study sample represented are shown in Table 6. In the study sample, 1,054 subjects (46.5%) were male and 1,211 (53.5%) were female. The weighted percent of males and females in the population that the study sample represented was 50.2% (*SE* = 1.15) and 49.8% (*SE* = 1.15) respectively. Most participants were non-Hispanic

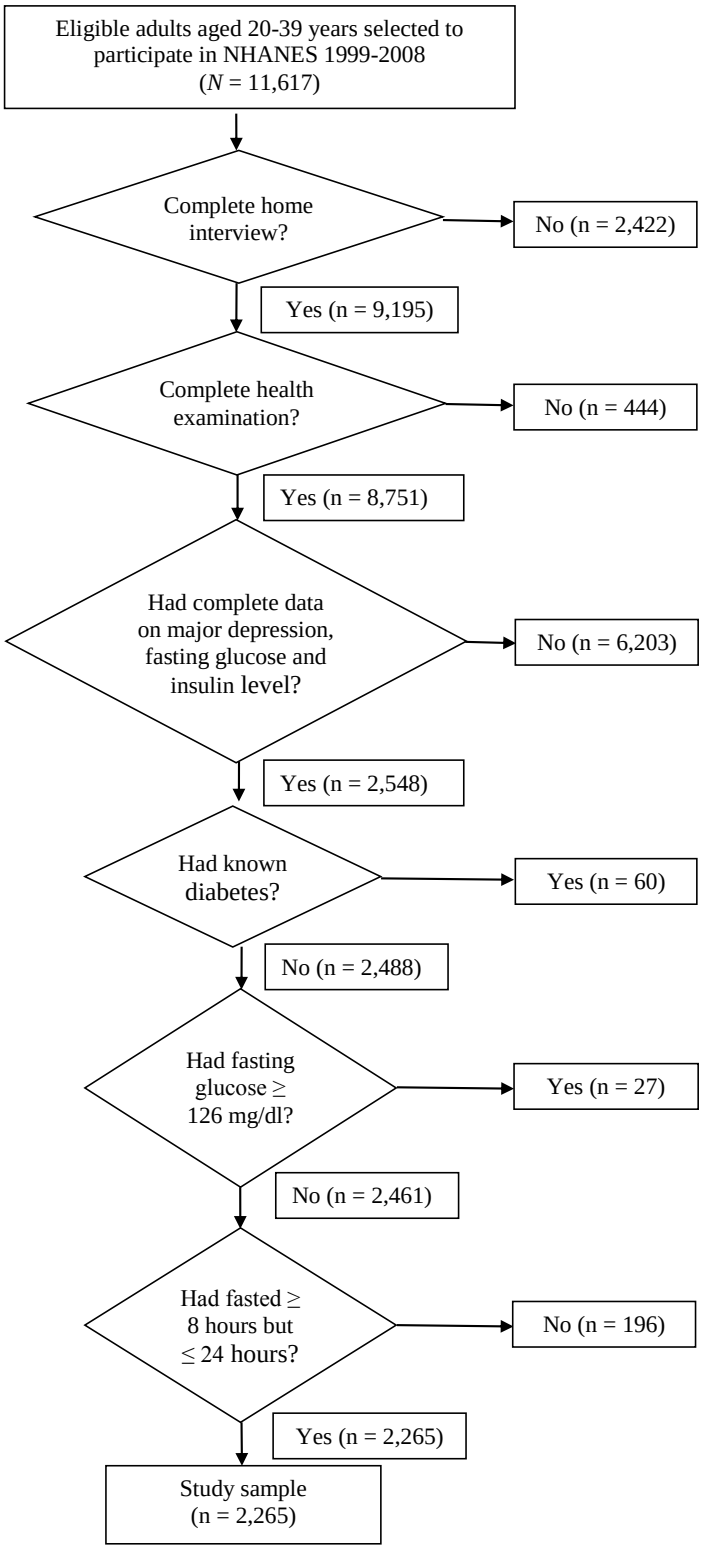


Figure 3. Flow Chart of Study Subjects' Inclusion and Exclusion

Table 6

Demographic Characteristics of the Study Sample and the Population of Nondiabetic U.S. Adults Aged 20-39 Years in NHANES 1999-2008 (N = 2,265)

	Study Sample		Population Represented	
	n	%	weighted %	*SE*
Gender				
Male	1,054	46.5	50.2	1.2
Female	1,211	53.5	49.8	1.2
Race/Ethnicity				
Non-Hispanic White	978	43.2	64.4	1.6
Non-Hispanic Black	462	20.4	11.8	1.0
Mexican American	568	25.1	12.0	0.9
Other	257	11.3	11.8	1.1
Education Levels				
Less than 9^{th} grade	161	7.0	4.5	0.5
9^{th} -11^{th} grade	384	17.0	13.2	1.1
High school graduate or GED	575	25.4	25.0	1.3
Some college or Associate's degree	685	30.3	32.2	1.2
College graduate or above	458	20.2	25.1	1.5
Marital Status				
Married	1046	46.8	45.2	1.5
Widowed	2	0.1	0.1	0.1
Divorced	98	4.4	5.1	0.5
Separated	59	2.6	2.2	0.4
Never married	721	32.3	33.9	1.5
Living with partner	309	13.8	13.5	1.3

Note. SE = standard error; GED = general education development.

Whites (*n* = 978, 43.2%), followed by Mexican Americans (*n* = 568, 25.1%), non-Hispanic Blacks (*n* = 462, 20.4%), and other race/ethnicity (*n* = 257, 11.3%). The weighted percent for each race/ethnicity in the population that the study sample represented was 64.4% (*SE* = 1.6), 12.0% (*SE* = 0.9), 11.8% (*SE* = 1.0), and 11.8% (*SE* = 1.1) for non-Hispanic Whites, Mexican Americans, non-Hispanic Blacks, and other race/ethnicity respectively.

Two subjects had missing values for education status. Among the remaining 2,263 subjects, more (*n* = 685; 30.3%) had some college education or an Associate's degree, 575 (25.4%) had graduated from high school or had passed a general education development (GED) test, 458 (20.2%) were college graduates, 384 (17.0%) had finished the 9th to 11th grade, and 161 (7.0%) had less than the 9th grade education. The weighted percentages for education levels in the population represented by the study sample were 32.2% (*SE* = 1.2), 25.1% (*SE* = 1.5), 25.0% (*SE* = 1.3), 13.2% (*SE* = 1.1), and 4.5% (*SE* = 0.5) for some college education or an Associate's degree, college graduates, high school graduate or GED, the 9th to 11th grade, and less than the 9th grade, correspondingly.

Data on marital status were available for 2,235 of the 2,265 (98.7%) subjects. Approximately half (*n* = 1,046, 46.8%) were married, about one third (*n* = 721, 32.3%) were never married, more than 10% (*n* = 309, 13.8%) were living with partner, less than 5% (*n* = 98, 4.4%) were divorced, 2.6% (*n* = 59) were separated, and 0.1% (*n* = 2) were widowed. The weighted percentages of marital status in the

population that the study sample represented were 45.2% (*SE* = 1.5), 33.9% (*SE* = 1.5), 13.5% (*SE* = 1.3), 5.1% (*SE* = 0.5), 2.2% (*SE* = 0.4), and 0.1% (*SE* = 0.1) accordingly for married, never married, living with partner, divorced, separated, and widowed.

Prevalence of Major Depression

Prevalence of Major Depression among Nondiabetic U.S. Adults Aged 20-39 Years for NHANES 1999-2008

The prevalence of major depression among nondiabetic adults aged 20-39 years was estimated from data on subjects aged 20-39 years who were nondiabetic and had data on the measures of major depression but may not have had data on fasting glucose and insulin levels (*N* = 2,287). The number of subjects who had major depression, regardless of depression measures, was 84 or 3.8 % (84/2287, *SE* = 0.4). The prevalence rates of major depression among nondiabetic adults aged 20-39 years are presented in Table 7 by gender, race/ethnicity, and measures of depression. Females (48 out of 1223, weighted % = 4.3, *SE* = 0.7) had a higher prevalence of major depression than males (36 out of 1064, weighted % = 3.3, *SE* = 0.7), but the differences were not statistically significant (Rao-Scott modified χ^2 = 1.09, *df* = 1, *p* =.30). Major depression was the most prevalent among non-Hispanic Whites (45 out of 989, weighted % = 4.4, *SE* = 0.6), followed by non-Hispanic Blacks (18 out of 468, weighted % = 4.0, *SE* = 1.0), Mexican Americans (16 out of 572, weighted % = 2.5,

Table 7

Prevalence of Major Depression among Nondiabetic Adults Aged 20-39 Years in NHANES 1999-2008 by Gender, Race/Ethnicity, and Measures of Depression (N = 2,287)

	Unweighted prevalence of major depression		Weighted prevalence of major depression	
	Number of subjects with major depression	Unweighted %	Weighted %	*SE*
Gender				
Male (*n* = 1,064)	36	3.4	3.3	0.7
Female (*n* = 1,223)	48	3.9	4.3	0.7
Race/Ethnicity				
Non-Hispanic White (*n* = 989)	45	4.6	4.4	0.6
Non-Hispanic Black (*n* = 468)	18	3.8	4.0	1.0
Mexican American (*n* = 572)	16	2.8	2.5	0.7
Other (*n* = 258)	5	1.9	1.4	0.8
Measures of Depression				
CIDI (*n* = 941)	54	5.7	6.6	0.9
PHQ-9 (*n* = 1,346)	30	2.2	1.8	0.4
Total (*N* = 2,287)	84	3.7	3.8	0.4

Note. Prevalence of major depression among nondiabetic adults aged 20-39 years in NHANES 1999-2008 was estimated from data on subjects aged 20-39 years who were nondiabetic and had data on the measures of major depression in NHANES 1999-2008. NHANES = National Health and Nutrition Examination Survey; SE = standard error; CIDI = composite international diagnostic interview; PHQ-9 = patient health questionnaire-9.

SE = 0.7), and other race/ethnicity (5 out of 258, weighted % = 1.4, *SE* = 0.8) (Rao-Scott modified χ^2 = 12.12, *df* = 3, *p* = .007). When stratified by the measures of depression, 54 out of 941 subjects (weighted % = 6.6, *SE* = 0.9) in NHANES 1999-2004 had major depression measured by the Composite International Diagnostic Interview (CIDI). In contrast, only 1.8 % of subjects (30 out of 1346, *SE* = 0.4) in NHANES 2005-2008 had major depression that was assessed by the Patient Health Questionnaire 9 (PHQ-9). The differences by measures of depression were statistically significant (Rao-Scott modified χ^2 = 24.50, *df* = 1, *p* <.0001)

Prevalence of Major Depression in the Study Sample

The overall prevalence rate of major depression among nondiabetic adults aged 20-39 years in the study sample who had data on the measure of major depression, fasting glucose and insulin levels was comparable to the weighted rate (84 out of 2,265 = 3.7%; weighted % = 3.8, *SE* = 0.4). The prevalence of major depression in the study sample by gender, race/ethnicity, and measures of depression are reported in Table 8. The number of female (*n* = 48) and male subjects (*n* = 36) who had major depression in the study sample was the same as that in the population. The prevalence of major depression for females (weighted % = 4.4, *SE* = 0.7) and males (weighted % = 3.3, *SE* = 0.7) in the study sample was relatively similar to the population proportion. Although the prevalence of major depression was higher among females in the study relative to males, the differences were not statistically significant (Rao-Scott modified χ^2 = 1.13, *df* = 1, *p* = .29).

Table 8

Prevalence of Major Depression in the Study Sample by Gender, Race/Ethnicity, and Measures of Depression (N = 2,265)

	Unweighted prevalence of major depression		Weighted prevalence of major depression	
	Number of subjects with major depression	Unweighted %	Weighted %	*SE*
Gender				
Male (*n* = 1,054)	36	3.4	3.3	0.7
Female (*n* = 1,211)	48	4.0	4.4	0.7
Race/Ethnicity				
Non-Hispanic White (*n* = 978)	45	4.6	4.5	0.6
Non-Hispanic Black (*n* = 462)	18	3.9	4.1	1.0
Mexican American (*n* = 568)	16	2.8	2.5	0.7
Other (*n* = 257)	5	1.9	1.4	0.8
Measures of Depression				
CIDI (*n* = 931)	54	5.8	6.6	0.9
PHQ-9 (*n* = 1,334)	30	2.2	1.8	0.4
Total (*N* = 2,265)	84	3.7	3.8	0.4

Note. SE = standard error; CIDI = composite international diagnostic interview; PHQ-9 = patient health questionnaire-9.

The prevalence of major depression by race/ethnicity found in the study sample also was significantly different (Rao-Scott modified $\chi^2 = 12.23$, $df = 3$, $p = .007$), and was similar to the population proportion. Non-Hispanic Whites had the higher prevalence of major depression (weighted % = 4.6, *SE* = 0.6), relative to non-Hispanic Blacks (weighted % = 4.1, *SE* = 1.0), Mexican Americans (weighted % = 2.5, *SE* = 0.7), or other race/ethnicity (weighted % = 1.4, *SE* = 0.8). As before, the prevalence of major depression in the study sample diagnosed by the CIDI in NHANES 1999-2004 (54 out of 931; weighted % = 6.6, *SE* = 0.9) was significantly higher than that evaluated by the PHQ-9 (30 out of 1,334; weighted % = 1.8, *SE* = 0.4) in NHANES 2005-2008 (Rao-Scott modified $\chi^2 = 24.21$, $df = 1$, $p < .0001$).

Prevalence of Insulin Resistance

A homeostasis model assessment for insulin resistance (HOMA-IR) score was calculated for all subjects in NHANES 1999-2008 who were aged ≥ 20 years, nondiabetic, and had complete data on fasting glucose and insulin levels (n = 8,894). According to Balkau and Charles (1999), it is important that the 75 percentile of HOMA-IR scores used to define insulin resistance be established from the general population without previously diagnosed diabetes. The formula used for the calculation was: HOMA-IR = [fasting glucose (mmol/L) × fasting insulin (μU/mL)]/22.5. The 75 percentile of the HOMA-IR scores among nondiabetic adults aged ≥ 20 years in NHANES 1999-2008 was 3.4351, which was used as the cutoff value to define insulin resistance for this study.

Prevalence of Insulin Resistance among Nondiabetic U.S. Adults Aged 20-39 Years for NHANES 1999-2008

The prevalence of insulin resistance among nondiabetic adults aged 20-39 years was estimated from data on subjects aged 20-39 years who were nondiabetic and had data on fasting glucose and insulin levels but may not have data on the measure of major depression (N = 3,474). Of these, 874 subjects (25.2%) had a HOMA-IR score $\geq$ 3.4351 and were defined as having insulin resistance (weighted % = 22.5, SE = 1.0). Table 9 presents the prevalence of insulin resistance in the population of nondiabetic adults aged 20-39 years by gender and race/ethnicity. As shown in Table 9, males (415 out of 1586, weighted % = 24.5, SE = 1.2) had a significantly higher prevalence of insulin resistance than females (459 out of 1888, weighted % = 20.5, SE = 1.3) (Rao-Scott modified χ^2 = 6.97, df = 1, p = .008).

Insulin resistance was the most prevalent among Mexican Americans (266 out of 876, weighted % = 31.0, SE = 2.0), followed by non-Hispanic Blacks (214 out of 713, weighted % = 30.1, SE = 2.2), non-Hispanic Whites (307 out of 1499, weighted % = 20.0, SE = 1.2), and other race/ethnicity (87 out of 386, weighted % = 20.0, SE = 2.7) (Rao-Scott modified χ^2 = 29.9, df = 3, $p < .0001$). When stratified by gender, insulin resistance was most prevalent among non-Hispanic Black females (weighted % = 36.2, SE = 2.8), followed by Mexican American females (weighted % = 29.4, SE = 2.7), non-Hispanic White females (weighted % = 17.0, SE = 1.8), other race/ethnicity

Table 9

Prevalence of Insulin Resistance among Nondiabetic Adults Aged 20-39 Years in NHANES 1999-2008 by Gender and Race/Ethnicity (N = 3,474)

	Unweighted prevalence of IR		Weighted prevalence of IR	
	Number of subjects with IR	Unweighted %	Weighted %	*SE*
Gender				
Male (*n* = 1,586)	415	26.2	24.5	1.2
Female (*n* = 1,888)	459	24.3	20.5	1.3
Race/Ethnicity				
Non-Hispanic White (*n* = 1,499)	307	20.5	20.0	1.2
Non-Hispanic Black (*n* = 713)	214	30.0	30.1	2.2
Mexican American (*n* = 876)	266	30.4	31.0	2.0
Other (*n* = 386)	87	22.5	20.0	2.7
Total (*N* = 3,474)	874	25.2	22.5	1.0

Note. Prevalence of insulin resistance among nondiabetic adults aged 20-39 years in NHANES 1999-2008 was estimated from data on subjects aged 20-39 years who were nondiabetic and had data on fasting glucose and insulin levels in NHANES 1999-2008. NHANES = National Health and Nutrition Examination Survey; IR = insulin resistance; SE = standard error.

(weighed % = 14.8, *SE* = 3.1) (Rao-Scott modified χ^2 = 45.38, *df* = 3, *p* < .0001). In contrast, Mexican American males had the highest prevalence of insulin resistance (32.3%, *SE* = 2.61), in comparison to non-Hispanic White males (weighted % = 23.1, *SE* = 1.5), non-Hispanic Black males (weighted % = 22.8, *SE* = 2.6), and other racial/ethnic males (weighted % = 24.9, *SE* = 3.6) (Rao-Scott modified χ^2 = 8.48, *df* = 3, *p* = .037).

Prevalence of Insulin Resistance in the Study Sample

HOMA-IR scores among nondiabetic adults aged 20-39 years who had data on the measure of major depression, fasting glucose and insulin levels in the study sample ranged from 0.30 to 48.6 with a weighted mean of 2.7 (*SE* = 0.06). Of the 2265, 582 (25.7%) subjects had a HOMA-IR score ≥ 3.4351 and were defined as insulin resistant. The weighted prevalence of insulin resistance in the study sample was 22.7% (*SE* = 1.1). Subjects with a HOMA-IR < 3.4351 (*n* = 1,683; 74.3%) were defined as non-insulin resistant. The prevalence of insulin resistance in the study sample by gender and race/ethnicity are summarized in Table 10.

Males had a significantly higher prevalence of insulin resistance (weighted % =25.5, *SE* = 1.4) than females (weighted % =19.8, *SE* = 1.5) (Rao-Scott modified χ^2 = 9.15, *df* = 1, *p* = .0025). In the study sample, insulin resistance was most prevalent among non-Hispanic Blacks (Rao-Scott modified χ^2 = 26.9, *df* = 3, *p* < .0001). Non-Hispanic Blacks had slightly higher prevalence of insulin resistance (weighted % = 31.3, *SE* = 3.1) than Mexican Americans (weighted % = 31.2, *SE* = 2.0).

Table 10
Prevalence of Insulin Resistance in the Study Sample by Gender and Race/Ethnicity (N = 2,265)

	Unweighted prevalence of IR		Weighted prevalence of IR	
	Number of subjects with IR	Unweighted %	Weighted %	*SE*
Gender				
Male (*n* = 1,054)	285	27.0	25.5	1.4
Female (*n* = 1,211)	297	24.5	19.8	1.5
Race/Ethnicity				
Non-Hispanic White (*n* = 978)	206	21.6	20.1	1.4
Non-Hispanic Black (*n* = 462)	145	31.4	31.3	3.1
Mexican American (*n* = 568)	174	30.6	31.2	2.0
Other (*n* = 257)	57	22.2	19.1	2.7
Total (*N* = 2,265)	582	25.7	22.7	1.1

Note. IR = insulin resistance; SE = standard error.

Non-Hispanic Whites had about 10% lower prevalence of insulin resistance (weighted % = 20.1, *SE* = 1.4), compared to non-Hispanic Blacks or Mexican Americans. Non-Hispanic Black females (weighted % = 37.3, *SE* = 4.3) and Mexican American males (weighted % = 33.1, *SE* = 2.8) had the highest prevalence of insulin resistance, when stratified by gender.

Risk Factors for Insulin Resistance among the Study Sample

Systolic Blood Pressure

Systolic blood pressure was available for 2,222 of 2,265 subjects (98.1%). Systolic blood pressure readings ranged from 84 mmHg to 174 mmHg and averaged 113.9 mmHg (*SE* = 0.3). Seventy five of the 2,222 subjects had a systolic blood pressure ≥ 140 mmHg (weighted % = 3.3, *SE* = 0.5), which indicated hypertension according to the *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure* (JNC-7) (Chobanian et al., 2003). Males had a higher systolic blood pressure on average (weighted mean = 118.4 mmHg, *SE* = 0.5) than females (weighted mean = 109.3 mmHg, *SE* = 0.4). The proportion of males with a systolic blood pressure ≥ 140 mmHg was 5.4% (*SE* = 0.9), whereas only 1.1% of females had systolic blood pressure equal or larger than 140 mmHg (*SE* = 0.3) (Rao-Scott modified $\chi^2 = 20.9$, $df = 1$, $p < .0001$). Non-Hispanic Blacks (weighted mean = 117.3 mmHg, *SE* = 0.6) had the highest systolic blood pressure on average relative to Mexican Americans (weighted mean = 113.2 mmHg,

SE = 0.6), non-Hispanic Whites (weighted mean = 113.5 mmHg, *SE* = 0.4), and other race/ethnicity (weighted mean = 113.0 mmHg, *SE* = 0.7). The highest percentage of subjects with a systolic blood pressure ≥ 140 mmHg was found in non-Hispanic Blacks (weighted % = 5.4, *SE* = 1.0); the lowest proportion of subjects with a systolic blood pressure ≥ 140 mmHg was observed among Mexican Americans (weighted % = 2.7, *SE* = 0.6) (Rao-Scott modified χ^2 = 5.02, *df* = 3, *p* = .17). Table 11 presents the means of systolic blood pressure and the proportions of subjects whose systolic blood pressure ≥ 140 mmHg by gender, race/ethnicity, and insulin resistance status.

The average systolic blood pressure was 119.1 mmHg (*SE* = 0.7) for insulin resistant subjects. Although this average was within normal limits (< 120 mmHg) (Chobanian, et al., 2003), it was about 7 mmHg higher than the average of 112.3 mmHg (*SE* = 0.4) for non-insulin resistant individuals. As shown in Table 11, 38 out of 570 insulin resistant subjects had systolic blood pressure equal or larger than 140 mmHg (weighted % = 7.3, *SE* = 1.4). In comparison, the weighted percentage of non-insulin resistant subjects with a systolic blood pressure ≥ 140 mmHg was 2.0% (37 out of 1,652; *SE* = 0.4). The proportions of subjects with a systolic blood pressure ≥ 140 mmHg between insulin resistant and non-insulin resistant subjects were statistically significant (Rao-Scott modified χ^2 = 15.8, *df* = 1, *p* < .0001).

Table 11

Means of Systolic Blood Pressure and Proportions of Subjects Whose Systolic Blood Pressure ≥140 mmHg among Nondiabetic Adults aged 20-39 Years in NHANES 1999-2008 by Gender, Race/Ethnicity, and Insulin Resistance (N = 2,222)

	Mean of SBP (*SE*) (in mmHg)	Number of subjects with SBP ≥ 140 mmHg	Proportion of subjects with SBP ≥ 140 mmHg weighted % (*SE*)
Gender			
Male (*n* = 1,042)	118.4 (0.5)	59	5.4 (0.9)
Female (*n* = 1,180)	109.3 (0.4)	16	1.1 (0.3)
Race/Ethnicity			
Non-Hispanic White (*n* = 966)	113.5 (0.4)	29	2.9 (0.6)
Non-Hispanic Black (*n* = 451)	117.3 (0.6)	24	5.4 (1.0)
Mexican American (*n* = 555)	113.2 (0.6)	13	2.7 (0.6)
Other (*n* = 250)	113.0 (0.7)	9	3.5 (1.2)
Insulin Resistance			
Yes (*n* = 570)	119.1 (0.7)	38	7.3 (1.4)
No (*n* = 1,652)	112.3 (0.4)	37	2.0 (0.4)
Total (*N* = 2,222)	113.9 (0.3)	75	3.3 (0.5)

Note. NHANES = National Health and Nutrition Examination Survey; SBP = systolic blood pressure; SE = standard error.

Triglyceride Level

Values of fasting triglyceride level were missing for nine subjects (0.4%). Fasting triglyceride level among the 2,256 subjects with data on these levels ranged from 14.0mg/dl to 1,779 mg/dl with a mean of 122.5 mg/dl (*SE* = 2.5). Six hundred and five subjects of the 2,256 had a triglyceride level ≥ 150 mg/dl (weighted % = 23.1, *SE* = 1.2), indicating borderline high triglycerides according to the clinical guideline on high blood cholesterol in adults from the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) (NCEP ATP III, 2002). Because of the highly skewed distribution, triglyceride values were log-transformed to approximate a normal distribution for logistic regression analyses. After log-transformation, the average log-transformed triglycerides was 4.62 mg/dl (*SE* = 0.02) with a range of 2.64 mg/dl to 7.48 mg/dl. Table 12 provides the means of triglyceride level and the proportions of subjects with triglyceride level ≥ 150 mg/dl by gender, race/ethnicity, and insulin resistance status.

Males had an average triglyceride level of 136.9 mg/dl (*SE* = 3.9) with a range of 14.0 to 1,779 mg/dl. Of the 1,047 males, 290 had a triglyceride level ≥ 150 mg/dl (weighted % = 27.8, *SE* = 1.6). In contrast, the average triglyceride level among females was 108.0 mg/dl (*SE* = 2.3) with a range of 19.0 to 857 mg/dl. The number of females with a triglyceride level ≥ 150 mg/dl was 315 (weighted % = 18.5, *SE* = 1.5). The proportions of male and female subjects with a triglyceride level ≥ 150 mg/dl were significantly different (Rao-Scott modified $\chi^2 = 18.5$, $df = 1$, $p < .0001$). The

Table 12

Means of Triglyceride Level and Proportions of Subjects with Triglyceride Level ≥ 150 mg/dl among Nondiabetic Adults aged 20-39 Years in NHANES 1999-2008 by Gender, Race/Ethnicity, and Insulin Resistance (N = 2,256)

	Mean of TG (*SE*) (in mg/dl)	Mean of log-transformed TG (*SE*) (in mg/dl)	Number of subjects with TG ≥ 150 mg/dl	Proportion of subjects with TG ≥ 150 mg/dl weighted % (*SE*)
Gender				
Male (*n* = 1,047)	136.9 (3.9)	4.7 (0.02)	290	27.8 (1.6)
Female (*n* = 1,209)	108.0 (2.3)	4.5 (0.02)	315	18.5 (1.5)
Race/Ethnicity				
Non-Hispanic White (*n* = 976)	124.4 (3.5)	4.6 (0.02)	282	24.0 (1.6)
Non-Hispanic Black (*n* = 457)	100.7 (5.4)	4.4 (0.03)	62	13.3 (1.8)
Mexican American (*n* = 566)	138.9 (5.2)	4.7 (0.02)	194	30.1 (2.0)
Other (*n* = 257)	116.9 (4.3)	4.6 (0.03)	67	21.3 (2.9)
Insulin Resistance				
Yes (*n* = 580)	172.9 (6.5)	5.0 (0.02)	261	44.2 (2.9)
No (*n* = 1,676)	107.7 (2.5)	4.5 (0.01)	344	17.0 (1.0)
Total (*N* =2,256)	122.5 (2.5)	4.6 (0.02)	605	23.1 (1.2)

Note. NHANES = National Health and Nutrition Examination Survey; TG = triglyceride; SE = standard error.

means of the log-transformed triglyceride level for males (weighted mean = 4.7, *SE* = 0.02) and females (weighted mean = 4.5, *SE* = 0.02) were relatively similar.

Mexican Americans had the highest average triglyceride level (weighted mean = 138.9 mg/dl, *SE* = 5.2), followed by non-Hispanic Whites (weighted mean = 124.4 mg/dl, *SE* = 3.5), and non-Hispanic Blacks (weighted mean = 100.7, *SE* = 5.4). About 30.1% of Mexican Americans had a triglyceride level ≥ 150 mg/dl (194 out of 566, *SE* = 2.0), which was significantly higher than the 24.0% of non-Hispanic Whites (*SE* = 1.6), or the 13.3% of non-Hispanic Blacks (*SE* = 1.8) (Rao-Scott modified $\chi^2 = 25.3$, $df = 3$, $p < .0001$). After log-transformation, the means of triglyceride level across race/ethnicity were similar as shown in Table 12.

Insulin resistant subjects had higher levels of triglycerides (weighted mean = 172.9 mg/dl, *SE* = 6.5) than non-insulin resistant subjects (weighted mean = 107.7 mg/dl, *SE* = 2.5). Of the 580 subjects who were insulin resistant, 261 had triglyceride level equal or larger than 150 mg/dl (weighted % = 44.2, *SE* = 2.9). In contrast, 344 of 1,676 subjects who were non-insulin resistant (weighted % = 17.0, *SE* = 1.0) had triglyceride level ≥ 150 mg/dl. There was a significant difference in the percentages of subjects whose triglyceride level ≥ 150 mg/dl between subjects who had and did not have insulin resistance (Rao-Scott modified $\chi^2 = 80.5$, $df = 1$, $p < .0001$).

High Sensitivity C-Reactive Protein

Data on high sensitivity C-reactive protein (hs-CRP) were available for 2,264 of 2,265 subjects (99.9%). The majority of subjects (*n* = 2,018, weighted % = 92.0, *SE* = 0.6) were classified as having low hs-CRP (hs-CRP < 1.0 mg/L). The number of subjects with moderate hs-CRP (1.0 mg/L ≤ hs-CRP ≤ 3.0mg/L) was 216 (weighted % = 6.9, *SE* = 0.6). Only 30 subjects had hs-CRP larger than 3.0 mg/L (high hs-CRP) (weighted % = 1.1, *SE* = 0.3).

The proportion of subjects with low, moderate, and high hs-CRP differed significantly by gender (Rao-Scott $\chi^2 = 19.2$, $df = 2$, $p < .0001$). The majority of males had hs-CRP values less than 1mg/L (weighted % = 95.1, *SE* = 0.8), 4% males had a moderate level of hs-CRP, and less than 1% males had hs-CRP > 3mg/L. In contrast, nearly 10% females had moderate levels of hs-CRP (174 out of 1,210; weighted % = 9.8, *SE* = 1.0). The weighted percentage of females with hs-CRP less than 1 mg/L was 88.9% (1,016 out of 1,210; *SE* = 0.8) and 1.3% had high hs-CRP (20/1210; *SE* = 0.5). The descriptive analyses of hs-CRP categories by gender, race/ethnicity, and insulin resistance status can be found in Table 13.

Race/ethnicity and hs-CRP status also were significantly associated (Rao-Scott $\chi^2 = 20.7$, $df = 6$, $p = .002$). Non-Hispanic Blacks had the highest prevalence of moderate hs-CRP (weighted % = 11.4, *SE* = 1.3), followed by Mexican Americans (weighted % = 9.7, *SE* = 1.0) and non-Hispanic Whites (weighted % = 5.9, *SE* = 0.8). The percentage of non-Hispanic Black subjects who had hs-CRP level > 3mg/L was

Table 13

Descriptive Analyses of High Sensitivity C - reactive protein among Nondiabetic Adults aged 20-39 Years in NHANES 1999-2008 by Gender, Race/Ethnicity, and Insulin Resistance (N = 2,264)

	hs-CRP					
	Low [a]		Moderate [b]		High [c]	
	n	Weighted % (*SE*)	*n*	Weighted % (*SE*)	*n*	Weighted % (*SE*)
Gender						
Male (*n* = 1,054)	1002	95.1 (0.8)	42	4.0 (0.8)	10	0.9 (0.3)
Female (*n* = 1,210)	1016	88.9 (0.8)	174	9.8 (1.0)	20	1.3 (0.5)
Race/Ethnicity						
Non-Hispanic White (*n* = 977)	888	93.1 (0.8)	78	5.9 (0.8)	11	0.9 (0.4)
Non-Hispanic Black (*n* = 462)	397	86.6 (1.2)	56	11.4 (1.3)	9	2.0 (0.7)
Mexican American (*n* = 568)	497	89.6 (1.1)	66	9.7 (1.0)	5	0.6 (0.3)
Other (*n* = 257)	236	93.7 (1.6)	16	4.4 (1.3)	5	1.9 (1.0)
Insulin Resistance						
Yes (*n* = 582)	459	82.4 (1.8)	115	16.0 (1.8)	8	1.7 (0.7)
No (*n* = 1,682)	1559	94.8 (0.6)	101	4.2 (0.6)	22	1.0 (0.3)
Total (*N* = 2,264)	2018	92.0 (0.6)	216	6.9 (0.6)	30	1.1 (0.3)

Note. NHANES = National Health and Nutrition Examination Survey; hs-CRP = high sensitivity C-reactive protein; SE = standard error.

[a]Low hs-CRP is defined as hs -CRP < 1.0 mg/L; [b]Moderate hs-CRP is defined as 1.0 mg/L ≤ hs -CRP ≤ 3.0 mg/L; [c]High hs-CRP is defined as hs-CRP > 3.0 mg/L.

2.0% (*SE* = 0.7), which was higher than that of non-Hispanic Whites (weighted % = 0.9, *SE* = 0.4) and Mexican Americans (weighted % = 0.6, *SE* = 0.3) (Table 13).

The proportion of subjects in each hs-CRP category were independent of race/ethnicity among males (Rao-Scott modified $\chi^2 = 8.12$, $df = 6$, $p = .23$). For females, there was a significant association between hs-CRP status and race/ethnicity (Rao-Scott modified $\chi^2 = 31.39$, $df = 6$, $p < .0001$). More non-Hispanic Black females had moderate levels of hs-CRP (*n* = 48, weighted % = 18.0, *SE* = 2.3) or high levels of hs-CRP (*n* = 5, weighted % = 2.0, *SE* = 0.9) than females in the other racial/ethnic group. In contrast, more non-Hispanic White females had low levels of hs-CRP (*n* = 458, weighted % = 90.4, *SE* = 1.1), relative to Mexican American females (*n* = 242, weighted % = 83.3, *SE* = 2.2), and non-Hispanic Black females (*n* = 186, weighted percent = 80.0, *SE* = 2.3).

Hs-CRP status was significantly associated with insulin resistance (Rao-Scott modified $\chi^2 = 47.3$, $df = 2$, $p < .0001$). The 582 insulin resistant subjects had a higher prevalence of moderate (weighted % = 16.0, *SE* = 1.8) and high levels of hs-CRP (weighted % = 1.7, *SE* = 0.7), relative to non-insulin resistant individuals and a lower prevalence of low hs-CRP (weighted % = 82.4, *SE* = 1.8) relative to non-insulin resistant subjects (weighted % = 94.8, *SE* = 0.6) (Table 13).

Body Mass Index

Data on body mass index (BMI) was complete for 2,254 of 2,265 subjects in the study sample (99.5%). Overall, the average BMI was 27.4 kg/m^2 (*SE* = 0.16) with a range of 15.5 kg/m^2 to 72.6 kg/m^2. Mean BMI and BMI distribution by gender, race/ethnicity, and insulin resistance status are reported in Table 14.

Approximately 2.9% of subjects (51 of 2,254; *SE* = 0.5) had a BMI < 18.5 kg/m^2 indicating they were underweight, 40.4% of subjects (809 out of 2,254; *SE* = 1.3) had normal weight, 28.9% of subjects (694 of 2,254; *SE* = 1.2) had a BMI of 25-29.9 kg/m^2 indicating they were overweight, and 27.8% of subjects (700 of 2,254; *SE* = 1.2) had a BMI ≥ 30 kg/m^2 indicating they were obese. By gender, the mean BMI for males was 27.3 kg/m^2 (*SE* = 0.2) and the mean BMI for females was 27.4 kg/m^2 (*SE* = 0.3). However, more females were underweight (weighted % = 4.1, *SE* = 0.7) or obese (weighted % = 30.8, *SE* = 1.7) relative to males and more males were overweight (weighted % = 35.3, *SE* = 1.9) than females (weighted % = 22.5, *SE* = 1.5) (Rao-Scott modified $\chi^2 = 32.66$, $df = 3$, $p < .0001$).

Non-Hispanic Blacks had the highest average BMI (weighted mean = 29.6 kg/m^2, *SE* = 0.4), followed by Mexican Americans (weighted mean = 27.9 kg/m^2, *SE* = 0.3), non-Hispanic Whites (weighted mean = 27.0 kg/m^2, *SE* = 0.2), and other race/ethnicity (weighted mean = 26.7 kg/m^2, *SE* = 0.5). Obesity (BMI ≥ 30 kg/m^2) was most prevalent among non-Hispanic Blacks (weighted % = 43.3, *SE* = 2.1), followed by Mexican Americans (weighted % = 29.9, *SE* = 2.6), and non-Hispanic

Table 14

Descriptive Analyses of Body Mass Index and Proportions of Weight Categories among Nondiabetic Adults aged 20-39 Years in NHANES 1999-2008 by Gender, Race/Ethnicity, and Insulin Resistance (N = 2,254)

		Weight categories							
	Mean BMI (*SE*) (in kg/m^2)	Underweight [a]		Normal weight [b]		Overweight [c]		Obese [d]	
		n	% (*SE*)	*n*	% (*SE*)	*n*	% (*SE*)	*n*	% (*SE*)
Gender									
Male (*n* = 1,047)	27.3 (0.2)	14	1.7 (0.6)	388	38.2 (1.9)	373	35.3 (1.9)	272	24.8 (1.6)
Female (*n* = 1,207)	27.4 (0.3)	37	4.1 (0.7)	421	42.6 (1.9)	321	22.5 (1.5)	428	30.8 (1.7)
Race/Ethnicity									
NHW (*n* = 976)	27.0 (0.2)	33	3.6 (0.6)	400	43.4 (1.8)	277	27.8 (1.7)	266	25.2 (1.7)
NHB (*n* = 458)	29.6 (0.4)	7	1.5 (0.6)	145	32.4 (2.2)	112	22.8 (1.9)	194	43.3 (2.1)
MA (*n* = 565)	27.9 (0.3)	6	1.1 (0.5)	164	30.5 (2.6)	221	38.5 (2.4)	174	29.9 (2.6)
Other (*n* = 255)	26.7 (0.5)	5	2.4 (1.1)	100	42.3 (4.0)	84	31.0 (3.8)	66	24.2 (3.2)
Insulin Resistance									
Yes (*n* = 579)	33.8 (0.3)	1	0.1 (0.1)	46	9.3 (1.8)	137	23.5 (2.2)	395	67.1 (2.4)
No (*n* = 1,675)	25.5 (0.2)	50	3.7 (0.6)	763	49.6 (1.5)	557	30.5 (1.4)	305	16.2 (1.2)
Total (*N* = 2,254)	27.4 (0.2)	51	2.9 (0.5)	809	40.4 (1.3)	696	28.9 (1.2)	698	27.8 (1.2)

Note. Percentages are presented as weighted %. NHANES = National Health and Nutrition Examination Survey; BMI = body mass index; SE = standard error; NHW = non-Hispanic White; NHB = non-Hispanic Black; MA = Mexican American.

[a]Underweight is defined as a BMI < 18.5 kg/m^2. [b]Normal weight is defined as 18.5 kg/m^2 ≤ BMI <25 kg/m^2. [c] Overweight is defined as 25 kg/m^2 ≤ BMI < 30 kg/m^2. [d] Obese is defined as a BMI ≥ 30 kg/m^2.

Whites (weighted % = 25.2, *SE* = 1.7) (Rao-Scott modified $\chi^2 = 60.57$, *df* = 9, $p < .0001$). In contrast, more Mexican Americans (weighted % = 38.5, *SE* =2.4) were overweight than non-Hispanic Whites (weighted % = 27.8, *SE* = 1.7) or non-Hispanic Blacks (weighted % = 22.8, *SE* = 1.9). Normal BMI was highest among non-Hispanic Whites (weighted % = 43.4, *SE* = 1.8), relative to other races/ethnicities. When stratified by gender, non-Hispanic Black females had the highest BMI (weighted mean = 31.1 kg/m^2, *SE* = 0.51), followed by Mexican American females (weighted mean = 28.4 kg/m^2, *SE* = 0.51) and non-Hispanic White females (weighted mean = 26.7 kg/m^2, *SE* = 0.4). Among males, the average BMI was similar across race/ethnicity.

Compared to non-insulin resistant subjects (weighted mean = 25.5 kg/m^2, *SE* = 0.2), insulin resistant subjects had a higher BMI (weighted mean = 33.8 kg/m^2, *SE* = 0.3). T-test showed that the average BMI differed significantly between insulin resistant and non-insulin resistant subjects [t (75) = 21.28, $p < .0001$]. Weight categories were significantly associated with insulin resistance status (Rao-Scott modified $\chi^2 = 432.84$, *df* = 3, $p < .0001$). More than 90% of insulin resistant subjects had a BMI $\geq$ 25 kg/m^2. Of these, 67.1% were obese (*SE* = 2.4) and 23.5% were overweight (*SE* = 2.2). In comparison, most non-insulin resistant subjects had a BMI < 25 kg/m^2 and were either underweight (weighted % = 3.7, *SE* = 0.6) or of normal weight (weighted % = 49.6, *SE* = 1.5) (Table 14).

Waist Circumference

Data on waist circumference were available for 2,236 of 2,265 subjects (98.7%). Mean waist circumference and the prevalence of central obesity by gender, race/ethnicity, and insulin resistance status are summarized in Table 15. The average waist circumference was 92.7 cm (*SE* = 0.39) with a range of 59.1 cm to 169.7 cm. Overall, males (weighted mean = 94.9 cm, *SE* = 0.5) had a larger waist circumference than females (weighted mean = 90.5 cm, *SE* = 0.6). Of the 2,236 subjects, 973 (weighted % = 37.7, *SE* = 1.2) had central obesity, which is defined as a waist circumference > 88 cm (35 inches) for women and > 102 cm (40 inches) for men (NCEP ATP III, 2002). Females had a significant higher prevalence of central obesity than males (Rao-Scott modified $\chi^2 = 67.71$, $df = 10$, $p < .0001$).

As shown in Table 15, waist circumference was largest among non-Hispanic Blacks (weighted mean = 95.1 cm, *SE* = 0.9), followed by Mexican Americans (weighted mean = 94.3 cm, *SE* = 0.7), non-Hispanic Whites (weighted mean = 92.5 cm, *SE* = 0.6), and other race/ethnicity (weighted mean = 90.1 cm, *SE* = 1.2). Central obesity also was the most prevalent in non-Hispanic Blacks (weighted % = 45.8, *SE* = 1.9) (Rao-Scott modified $\chi^2 = 14.62$, $df = 3$, $p = .0022$). When stratified by race/ethnicity, males generally had a larger waist circumference than females with the exception of non-Hispanic Blacks. Non-Hispanic Black females had larger waist circumference (weighted mean = 97.2 cm, *SE* = 1.17) than non-Hispanic Black males (weighted mean = 92.6 cm, *SE* = 1.19).

Table 15

Descriptive Analyses of Waist Circumference and Prevalence of Central Obesity among Nondiabetic Adults aged 20-39 Years in NHANES 1999-2008 by Gender, Race/Ethnicity, and Insulin Resistance (N = 2,236)

	Mean WC (*SE*) (in cm)	Number of subjects with central obese [a]	Prevalence of central obesity weighted % (*SE*)
Gender			
Male (*n* = 1,040)	94.9 (0.5)	272	26.6 (1.7)
Female (*n* = 1,196)	90.5 (0.6)	701	48.9 (1.9)
Race/Ethnicity			
Non-Hispanic White (*n* = 970)	92.5 (0.6)	407	36.6 (1.7)
Non-Hispanic Black (*n* = 454)	95.1 (0.9)	207	45.8 (1.9)
Mexican American (*n* = 559)	94.3 (0.7)	261	41.3 (2.6)
Other (*n* = 253)	90.1 (1.2)	98	31.6 (3.3)
Insulin Resistance			
Yes (*n* = 571)	108.8 (0.8)	428	73.0 (2.3)
No (*n* = 1,665)	88.1 (0.4)	545	27.4 (1.3)
Total (*N* = 2,236)	92.7 (0.4)	973	37.7 (1.2)

Note. NHANES = National Health and Nutrition Examination Survey; WC = waist circumference; SE = standard error.

[a]Central obesity is defined as a waist circumference > 88 cm (35 inches) for females and > 102 cm (40 inches) for males.

Insulin resistant subjects (weighted mean = 108.8 cm, *SE* = 0.8) had a significantly larger waist circumference than those without insulin resistance (weighted mean = 88.1 cm, *SE* = 0.4). T-test showed that the average waist circumference differed significantly between insulin resistant and non-insulin resistant subjects [t (75) = 21.01, $p < .0001$]. Over 70% of insulin resistant subjects had central obesity (*SE* = 2.3), in contrast to the 27.4% of non-insulin resistant subjects (*SE* = 1.3) (Rao-Scott modified $\chi^2 = 172.88$, $df = 1$, $p < .0001$).

Leisure Time Physical Activity

Data on leisure time physical activity (LTPA) were available for 2,264 of 2,265 subjects (99.9%). Among these 2,264 subjects, 817 subjects (weighted % = 30.1, *SE* = 1.2) self-reported having no LTPA. The number of subjects who reported that they participated in less than 500 MET minutes/week LTPA was 442 (weighted % = 20.9, *SE* = 1.0). Approximately 13.7 % of subjects (n = 292, *SE* = 1.1) reported participating in moderate LTPA (500 MET minutes/week ≤ LTPA ≤ 1000 MET minutes/week). Seven hundred and thirteen subjects (weighted % = 35.3, *SE* = 1.2) engaged in high levels of LTPA with a MET minutes/week larger than 1000. Table 16 presents the prevalence of leisure time physical activity by gender, race/ethnicity, and insulin resistance status.

LTPA varied significantly between males and females (Rao-Scott modified $\chi^2 = 20.44$, $df = 3$, $p = .0001$). Among the 1,053 males, 422 subjects (weighted % = 41.0, *SE* = 1.7) reported high levels of LTPA with MET min/week larger than 1000, 127

Table 16

Descriptive Analyses of Leisure Time Physical Activity among Nondiabetic Adults aged 20-39 Years in NHANES 1999-2008 by Gender, Race/Ethnicity, and Insulin Resistance (N = 2,264)

	Leisure time physical activity level							
	No		Low[a]		Moderate[b]		High[c]	
	n	% (*SE*)	*n*	% (*SE*)	*n*	% (*SE*)	*n*	% (*SE*)
Gender								
Male (*n* = 1,053)	319	27.8 (1.8)	185	18.5 (1.5)	127	12.6 (1.3)	422	41.0 (1.7)
Female (*n* = 1,211)	498	32.4 (1.6)	257	23.4 (1.3)	165	14.8 (1.6)	291	29.5 (2.0)
Race/Ethnicity								
NHW (*n* = 977)	270	25.5 (1.9)	220	22.4 (1.3)	143	14.4 (1.4)	344	37.8 (1.6)
NHB (*n* = 462)	169	35.2 (2.0)	85	19.4 (2.0)	48	10.9 (1.5)	160	34.6 (2.3)
MA (*n* = 568)	279	45.6 (2.2)	87	16.5 (2.3)	70	13.8 (1.6)	132	24.2 (1.8)
Other (*n* = 257)	99	34.3 (3.8)	50	19.3 (2.7)	31	12.8 (2.5)	77	33.6 (3.5)
Insulin Resistance								
Yes (*n* = 582)	240	35.1 (2.2)	113	21.3 (1.7)	73	14.4 (1.7)	156	29.1 (2.3)
No (*n* = 1,682)	577	28.6 (1.3)	329	20.8 (1.2)	219	13.5 (1.2)	557	37.1 (1.4)
Total (*N* = 2,264)	817	30.1 (1.2)	442	20.9 (1.0)	292	13.7 (1.1)	713	35.3 (1.2)

Note. Percentages are presented as weighted %. NHANES = National Health and Nutrition Examination Survey; SE = standard error; NHW = non-Hispanic White; NHB = non-Hispanic Black; MA = Mexican American.

[a]Low LTPA is defined as metabolic equivalent (MET) minutes/week < 500. [b]Moderate LTPA is defined as 500 ≤ MET minutes/week ≤ 1000. [c]High LTPA is defined as MET minutes/week > 1000.

subjects (weighted % = 12.6, *SE* = 1.3) reported engaging in moderate LTPA, 185 subjects (weighted % = 18.5, *SE* = 1.5) reported participating in less than 500 MET minutes/week (low level of LTPA), and 319 males (weighted % = 27.8, *SE* = 1.8) reported having no LTPA. In total, more than half of males (549/1053, weighted % = 53.7) were physically active with a total MET minutes/week larger than 500, according to *2008 Physical Activity Guidelines for Americans* by U.S. Department of Health and Human Services (2008). Among the females, less than one third (291/1,211; weighted % = 29.5, *SE* = 2.0) reported participating in high levels of LTPA, fewer than 15% of females (165/1,211; weighted % = 14.7, *SE* = 1.6) reported engaging in moderate levels of LTPA, approximately 20% of female subjects (257/1,211; weighted % = 23.4, *SE* = 1.3) reported participating in less than 500 MET minutes/week LTPA, and an alarming 30% females (498/1,211; weighted % = 32.4, *SE* = 1.6) reported having no LTPA. In sum, only 44.3% of females (456 out of 1,211) were physically active with a total MET minutes/week > 500.

Rao-Scott modified Chi-Square test showed that LTPA differed by race/ethnicity (Rao-Scott modified $\chi^2 = 54.4$, $df = 9$, $p < .0001$). More than half of non-Hispanic Whites reported engaging in moderate or high levels of LTPA (weighted % = 14.4, *SE* = 1.4 for moderate level of LTPA; weighted % = 37.8, *SE* = 1.6 for high level of LTPA). In contrast, the majority of Mexican Americans were physically inactive with 45.6% reporting no LTPA (279/568, *SE* = 2.2) and 16.5% reporting low levels of LTPA (87/598, *SE* = 2.3). About 35.2% of non-Hispanic Blacks also reported not

engaging in LTPA (169/462, *SE* = 2.0), but a similar number of non-Hispanic Blacks reported participating in high LTPA (160/462, weighted % = 34.6, *SE* = 2.3).

Among males, Mexican Americans had the highest percentage of no LTPA (*n* = 110, weighted % = 40.3, *SE* = 3.2), compared to non-Hispanic Whites (*n* = 118, weighted % = 25.0, *SE* = 2.5), non-Hispanic Blacks (*n* = 54, weighted % = 24.3, *SE* = 3.1), or other race/ethnicity (*n* = 37, weighted % = 31.6, *SE* = 4.9). Similarly, Mexican American females (169 out of 300, weighted % = 52.6, *SE* = 3.6) had the highest percentage of no LTPA, compared to any other racial/ethnic group. In contrast, non-Hispanic White females were the most physically active with 49.2 % of subjects engaging in moderate (85/528; weighted % = 15.9, *SE* = 2.3) to high LTPA (158/528; weighted % = 33.3, *SE* = 2.4), followed by other race/ethnicity (47 out of 144, weighted % = 38.1), non-Hispanic Blacks (79 out of 239, weighted % = 36.1), and Mexican Americans (85 out of 300, weighted % = 29.9).

LTPA was significantly associated with insulin resistance (Rao-Scott modified χ^2 = 11.8, *df* = 3, *p* = .008). As shown in Table 16, a higher percentage of non-insulin resistant individuals reported participating in moderate to high level of LTPA (weighted % = 50.6) relative to insulin resistant subjects (weighted % = 43.6). More than one third of insulin resistant subjects reported no LTPA (240/582, weighted % = 35.1, *SE* = 2.2), compared to 28.6% of non-insulin resistant individuals (*SE* = 1.3).

Smoking Status

Two thousand and two hundred and sixty three of the 2,265 subjects had adequate data on their smoking status (99.9%). As discussed in Chapter III, current smoker was defined as self-report having smoked ≥ 100 cigarettes during a person's lifetime and current smoking every day or some days in the current study. Former smoker was defined as having smoked ≥ 100 cigarettes during a person's lifetime, but not currently smoking. Nonsmoker was defined as report of having smoked < 100 cigarettes during a person's lifetime. Smoking status by gender, race/ethnicity, and insulin resistance are presented in Table 17. The majority of subjects (n = 1,380; weighted % = 57.1, SE = 1.2) were nonsmokers. About 15.3 % of subjects (n = 330, SE = 1.0) were former smokers. The number of current smokers was 553 (weighted % = 27.6, SE = 1.2). Smoking status was significantly associated with gender (Rao-Scott modified $\chi^2 = 24.9$, $df = 2$, $p < .0001$). About one third of males were current smokers (weighted % = 33.0, SE = 1.5), compared to the 22.5% of females who were current smokers (SE = 1.7). More females were nonsmokers (weighted % = 63.3, SE = 2.0) than males (weighted % = 51.0, SE = 1.5).

Smoking status differed significantly by race/ethnicity (Rao-Scott modified $\chi^2 = 86.5$, $df = 6$, $p < .0001$). More non-Hispanic Whites were current smokers (weighted % = 32.1, SE = 1.7), relative to non-Hispanic Blacks (weighted % = 25.8, SE = 2.4), other race/ethnicity (weighted % = 17.3, SE = 2.6), and Mexican Americans (weighted % =15.8, SE = 1.7). However, when stratified by gender, the

Table 17

Descriptive Analyses of Smoking Status among Nondiabetic Adults aged 20-39 Years in NHANES 1999-2008 by Gender, Race/Ethnicity, and Insulin Resistance (N = 2,263)

	Smoking Status					
	Nonsmoker[a]		Former Smoker[b]		Current Smoker[c]	
	n	Weighted % (*SE*)	*n*	Weighted % (*SE*)	*n*	Weighted % (*SE*)
Gender						
Male (*n* = 1,052)	551	51.0 (1.5)	163	16.0 (1.5)	338	33.0 (1.5)
Female (*n* = 1,211)	829	63.3 (2.0)	167	14.5 (1.4)	215	22.3 (1.7)
Race/Ethnicity						
Non-Hispanic White (*n* = 977)	493	50.8 (1.9)	176	17.1 (1.3)	308	32.1 (1.7)
Non-Hispanic Black (*n* = 462)	312	68.4 (2.1)	30	5.8 (1.0)	120	25.8 (2.4)
Mexican American (*n* = 567)	407	69.0 (2.5)	83	15.2 (1.4)	77	15.8 (1.7)
Other (*n* = 257)	168	67.8 (3.4)	41	14.9 (2.9)	48	17.3 (2.6)
Insulin Resistance						
Yes (*n* = 582)	367	57.7 (2.3)	92	20.0 (1.9)	123	22.3 (1.7)
No (*n* = 1,681)	1013	56.9 (1.4)	238	13.9 (1.2)	430	29.2 (1.6)
Total (*N* = 2,263)	1380	57.1 (1.2)	330	15.3 (1.0)	553	27.6 (1.2)

Note. NHANES = National Health and Nutrition Examination Survey; SE = standard error.

[a] Nonsmoker is defined as having smoked less than 100 cigarettes in lifetime. [b] Former smoker is defined as having smoked more than 100 cigarettes in lifetime, but currently did not smoke. [c] Current smoker is defined as having smoked more than 100 cigarettes in lifetime and currently smoked.

proportion of non-Hispanic White males (171/449, weighted % = 37.2, *SE* = 2.1) that were current smokers was similar to the proportion of non-Hispanic Black males (82 out of 223, weighted % = 37.4, *SE* = 3.0) that were current smokers. In contrast, fewer Mexican American males (weighted % = 22.2, *SE* = 2.4) and females (weighted % = 7.3, *SE* = 1.8) were current smokers relative to the other races/ethnicities.

There were significant differences in smoking status among insulin resistant subjects and non-insulin resistant subjects (Rao-Scott modified $\chi^2 = 11.7$, $df = 2$, $p = .0028$). More insulin resistant subjects (weighted % = 20.0, *SE* = 1.9) were former smokers than the non-insulin resistant individuals (weighted % = 13.9, *SE* = 1.2). Smoking was more prevalent among non-insulin resistant subjects (weighted % = 29.2, *SE* = 1.6) than insulin resistant subjects (weighted % = 22.3, *SE* = 1.7). A similar percentage of nonsmokers was found among insulin resistant (weighted % = 57.7, *SE* = 2.3) and non-insulin resistant subjects (weighted % = 57.0, *SE* = 1.4).

Alcohol Consumption Status

Out of 2,265 subjects, 2,261 (99.8%) had complete data on alcohol consumption. As discussed in Chapter III, nondrinker was defined as report of having less than 12 drinks in one's lifetime in the current study. Former drinker was defined as report of having at least 12 drinks in one's lifetime but had no drinks in the past 12 months. Light drinker was defined as report of having an average of ≤ 3 drinks per week. Moderate drinker was defined as report of having an average of 4 to 14 drinks per

week for men or 4 to 7 drinks per week for women (U.S. Department of Agriculture and U.S. Department of Health and Human Services, 2005). Heavy drinker was defined as report of having an average of > 14 drinks per week for men and > 7 drinks per week for women (CDC, 2010a).

Nearly 90% of subjects (1,960/2,261) reported having had at least 12 drinks in their lifetime. Among these 1,960 subjects, 264 were former drinkers (weighted % = 9.9, *SE* = 0.9) and 1,696 were current drinkers (weighted % = 79.2). Approximately 48% of the 1,696 current drinkers were light drinkers (*n* = 1,088, weighted % = 47.9, *SE* = 1.3), 23.2% were moderate drinkers (*n* = 454, *SE* = 1.3), and 8.1% were heavy drinkers (*n* = 154, *SE* = 0.9). Alcohol consumption status by gender, race/ethnicity, and insulin resistance status are summarized in Table 18.

Alcohol consumption status was significantly associated with gender (Rao-Scott modified $\chi^2 = 164.00$, $df = 4$, $p < .0001$). About 75% of the 1,052 males were either light (459/1,052; weighted % = 41.7, *SE* = 1.7) or moderate drinkers (339/1,052; weighted % = 33.6, *SE* = 1.8). Approximately 11% of males (107 out of 1,052; weighted % = 10.9, *SE* = 1.2) were heavy drinkers. In contrast, 66.9% females were either light drinkers (629 of 1,209; weighted % = 54.2, *SE* = 1.9) or moderate drinkers (115 out of 1,209; weighted % = 12.7, *SE* = 1.4). Less than 6% of females were heavy drinkers (47 out of 1,209; weighted % = 5.2, *SE* = 0.9).

Alcohol consumption status differed by race/ethnicity (Rao-Scott modified $\chi^2 = 43.6$, $df = 12$, $p < .0001$). Heavy drinkers were the most prevalent among

Table 18

Descriptive Analyses of Alcohol Consumption Status among Nondiabetic Adults aged 20-39 Years in NHANES 1999-2008 by Gender, Race/Ethnicity, and Insulin Resistance (N = 2,261)

	Alcohol consumption status									
	Nondrinker[a]		Former[b]		Light[c]		Moderate[d]		Heavy[e]	
	n	% (*SE*)	*n*	% (*SE*)	*n*	% (*SE*)	*n*	% (*SE*)	*n*	% (*SE*)
Gender										
Male (*n* = 1,052)	63	6.1 (1.1)	84	7.6 (1.1)	459	41.7 (1.7)	339	33.6 (1.8)	107	10.9 (1.2)
Female (*n* = 1,209)	238	15.8 (1.9)	180	12.2 (1.1)	629	54.2 (1.9)	115	12.7 (1.4)	47	5.2 (0.9)
Race/Ethnicity										
NHW (*n* = 978)	97	9.3 (1.9)	105	8.6 (1.1)	459	46.3 (2.1)	230	26.0 (1.8)	87	9.8 (1.4)
NHB (*n* = 460)	73	25.3 (1.9)	61	13.8 (1.7)	215	47.4 (2.5)	85	17.8 (1.7)	26	5.4 (1.1)
MA (*n* = 566)	92	12.1 (1.1)	72	11.6 (1.9)	275	49.6 (2.1)	92	19.8 (2.0)	35	6.9 (1.2)
Other (*n* = 257)	39	14.5 (2.9)	26	11.4 (2.9)	139	55.3 (4.3)	47	16.5 (2.6)	6	2.4 (1.0)
Insulin Resistance										
Yes (*n* = 580)	77	11.3 (1.7)	81	13.6 (1.7)	296	50.7 (2.2)	100	20.1 (1.8)	26	4.4 (1.0)
No (*n* = 1,681)	224	10.8 (1.3)	183	8.8 (1.0)	792	47.1 (1.5)	354	24.1 (1.6)	128	9.1 (1.0)
Total (*N* = 2,261)	301	10.9 (1.3)	264	9.9 (0.9)	1088	47.9 (1.3)	454	23.2 (1.3)	154	8.1 (0.9)

Note. Percentages are presented as weighted %. NHANES = National Health and Nutrition Examination Survey; SE = standard error; NHW = non-Hispanic White; NHB = non-Hispanic Black; MA = Mexican American.

[a]Had less than 12 drinks in lifetime. [b]Had at least 12 drinks in lifetime, but had no drinks in the past 12 months. [c]Had at least 12 drinks in lifetime and had an average of ≤ 3 drinks per week. [d]Had at least 12 drinks in lifetime and had an average of > 3 but ≤14 drinks per week (men) or of > 3 but ≤ 7 drinks per week (women). [e]Had at least 12 drinks in lifetime and had an average of > 14 drinks per week (men) or > 7 drinks per week (women).

non-Hispanic Whites (weighted % = 9.8, *SE* = 1.4), followed by Mexican Americans (weighted % = 6.9, *SE* = 1.2), non-Hispanic Blacks (weighted % = 5.4, *SE* = 1.1), and other race/ethnicity (weighted % = 2.4, *SE* = 1.0). Conversely, other race/ethnicity had the highest percentage of light drinkers (weighted % = 55.3, *SE* = 4.3) while non-Hispanic Whites had the lowest percentage (weighted % = 46.2, *SE* = 2.1).

By gender, non-Hispanic White males had the highest percentage of moderate (159 of 450, weighted % = 36.5, *SE* = 2.6) to heavy drinkers (60 of 450, weighted % = 13.5, *SE* = 1.9). Light drinkers were most prevalent among Mexican American males (130 of 268, weighted % = 47.6, *SE* = 3.2). Among females, non-Hispanic Whites had the highest prevalence of light (weighted % = 55.0, *SE* = 2.7), moderate (weighted % = 15.7, *SE* = 2.2) or heavy drinkers (weighted % = 6.2, *SE* = 1.4), compared to the other racial/ethnic groups.

Alcohol consumption was significantly different between insulin resistant and non-insulin resistant subjects (Rao-Scott modified $\chi^2 = 21.6$, $df = 4$, $p = .0002$). As demonstrated in Table 18, more non-insulin resistant subjects were moderate (weighted % = 24.1, *SE* = 1.6) or heavy drinkers (weighed % = 9.1, *SE* = 1.0) relative to insulin resistant subjects. Conversely, more insulin resistant individuals were either nondrinkers (weighted % = 11.3, *SE* = 1.7), former drinkers (weighted % = 13.6, *SE* = 1.7) or light drinkers (weighted % = 50.7, *SE* = 2.2).

Correlations among Independent Variables

Correlations between Continuous Independent Variables

Pearson correlations were conducted to examine the correlations among the continuous independent variables. According to Cohen (1988), a correlation coefficient of .1 is small, .3-.5 is moderate, and > .5 is large. In this study, most of the correlation coefficients ranged from .08 to .36, indicating low to moderate correlations (Cohen, 1988). Body mass index (BMI) and waist circumference were highly correlated with each other ($r = .92$, $p < .0001$). The highly correlated BMI and waist circumference were entered into multivariate logistic regression analyses separately to avoid their multicollinearity. The inter-correlation coefficients among continuous independent variables are presented in Table 19.

Correlations between Categorical Independent Variables

Pearson correlations also were conducted to examine the correlations among categorical independent variables. The correlation coefficients ranged from -.11 to .29, indicating small correlations (Cohen, 1988). Table 20 provides the inter-correlation coefficients among categorical independent variables.

Table 19
Pearson Correlation Coefficients for Continuous Independent Variables

	Age (n = 2,265)	Systolic blood pressure (n = 2,222)	Body mass index (n = 2,254)	Waist circumference (n =2,236)	Triglycerides (n = 2,256)
Age	1.0	-	-	-	-
Systolic blood pressure	.02	1.0	-	-	-
Body mass index	.12	.26	1.0	-	-
Waist circumference	.14	.30	.92*	1.0	-
Triglycerides	.08	.22	.28	.36	1.0

Note. *Highly correlated.

Table 20
Pearson Correlation Coefficients for Categorical Independent Variables

	MD (*n* = 2,265)	hs-CRP (*n* = 2,264)	LTPA (*n* = 2,264)	Smoking (*n* = 2,263)	Alcohol consumption (*n* = 2,261)
MD	1.0	-	-	-	-
Hs-CRP	.01	1.0	-	-	-
LTPA	-.05	-.07	1.0	-	-
Smoking	.08	-.03	-.04	1.0	-
Alcohol consumption	.02	-.11	.17	.29	1.0

Notes. MD = major depression; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

Logistic Regression Analyses

Univariate Logistic Regression

Univariate logistic regression analyses revealed that major depression was not associated with insulin resistance (B = 0.1442, p = .5545). The odds ratio for subjects with major depression to develop insulin resistance was 1.155 with 95% confidence interval (CI) ranging from 0.716 to 1.863.

Interaction between Gender and Major Depression

Major depression was negatively associated with insulin resistance (B = -0.6715, p = .0324) in the model when major depression, gender and the interaction term for major depression and gender were entered. A significant interaction between gender and major depression (B = 1.3942, p = .0031) was found. Therefore, separate multivariate logistic regression models were conducted for men and women. Covariates entered into each model included age, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, BMI or waist circumference, leisure time physical activity (LTPA), smoking, and alcohol consumption. BMI and waist circumference were tested in separate models.

Adjusted Logistic Regression among Men in the Model with BMI

Among men, major depression was negatively associated with insulin resistance (B = -1.2128, p = .0035, OR = 0.297, 95% CI = [0.132, 0.671]), when adjusting for

age, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, BMI, LTPA, smoking, and alcohol consumption. Age was not associated with insulin resistance in this model (*B* = -0.0206, *p* = .2929, *OR* = 0.980, 95% *CI* = [0.943, 1.018]). The model fit statistics of -2 log likelihood and AIC were 18738539 and 18738579 respectively. Results of the adjusted logistic regression among men in the model with BMI as one of the covariates are presented in Table 21.

Compared to non-Hispanic White men, Mexican American men were more likely to be insulin resistant (*B* = 0.4975, *p* = .0330, *OR* = 1.645, 95% *CI* = [1.041, 2.599]). However, no significant association between non-Hispanic Black men and insulin resistance was found (*B* = 0.2301, *p* = .3975, *OR* = 1.259, 95% *CI* = [0.739, 2.145]). Similarly, being of other race/ethnicity was not associated with insulin resistance (*B* = 0.1212, *p* = .7008, *OR* = 1.129, 95% *CI* = [0.608, 2.094]).

BMI was significantly and positively associated with insulin resistance (*B* = 0.2268, *p* < .0001, *OR* = 1.255, 95% *CI* = [1.195, 1.318]) among men. For every 1 unit change in BMI, the likelihood of having insulin resistance increases by 25.5%, after controlling for other variables including age, race/ethnicity, major depression, systolic blood pressure, triglyceride level, hs-CRP, smoking, LTPA and alcohol consumption.

A significant positive relationship between systolic blood pressure and insulin resistance also was observed (*B* = 0.0213, *p* = .0358, *OR* = 1.022, 95% *CI* = [1.001, 1.042]) among men, after adjusting for age, race/ethnicity, major depression,

Table 21
Adjusted Logistic Regression of Major Depression and Insulin Resistance among Men in the Model with Body Mass Index

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	-1.2128	0.4155	8.5199	.0035	0.297	[0.132, 0.671]
Age	-0.0206	0.0196	1.1063	.2929	0.980	[0.943, 1.018]
Race/ethnicity						
NH-White					0.000	
NH-Black	0.2301	0.2719	0.7158	.3975	1.259	[0.739, 2.145]
Mexican American	0.4975	0.2334	4.5446	.0330	1.645	[1.041, 2.599]
Other	0.1212	0.3153	0.1477	.7008	1.129	[0.608, 2.094]
BMI	0.2268	0.0250	82.2578	<.0001	1.255	[1.195, 1.318]
SBP	0.0213	0.0102	4.4054	.0358	1.022	[1.001, 1.042]
Triglyceride	1.1460	0.1860	37.9520	<.0001	3.146	[2.185, 4.530]
hs-CRP						
Low					0.000	
High	-0.3714	0.7930	0.2194	.6395	0.690	[0.146, 3.264]
Moderate	0.5582	0.4483	1.5507	.2130	1.748	[0.726, 4.207]
Smoking						
Nonsmoker					0.000	
Current	-0.0830	0.2344	0.1254	.7232	0.920	[0.581, 1.457]
Former	1.0073	0.2260	19.8648	<.0001	2.738	[1.758, 4.264]
LTPA						
Moderate					0.000	
High	-0.3493	0.3275	1.1375	.2862	0.705	[0.371, 1.340]
Low	0.0395	0.3290	0.0144	.9044	1.040	[0.546, 1.982]
No	-0.1887	0.3087	0.3735	.5411	0.828	[0.452, 1.516]
Alcohol consumption						
Nondrinker					0.000	
Former	0.1284	0.5841	0.0483	.8260	1.137	[0.362, 3.572]
Light	-0.0210	0.5864	0.0013	.9714	0.979	[0.310, 3.090]
Moderate	-0.5140	0.5992	0.7357	.3911	0.598	[0.185, 1.936]
Heavy	-0.7423	0.6910	1.1540	.2827	0.476	[0.123, 1.844]

Note. *n* = 1026; -2 log likelihood = 18738539; AIC = 18738579. SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; BMI = body mass index; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

triglyceride level, hs-CRP, BMI, smoking, LTPA and alcohol consumption. There also was a strong positive association between triglyceride level and insulin resistance (*B* = 1.1460, *p* < .0001, *OR* = 3.146, 95% *CI* = [2.185, 4.530]). However, hs-CRP was not significantly associated with insulin resistance, regardless of hs-CRP levels.

Compared to nonsmokers, males who were former smokers were more likely to have insulin resistance (*B* = 1.0073, *p* < .0001, *OR* = 2.738, 95% *CI* = [1.758, 4.264]). There was no significant relationship between current smokers and insulin resistance (*B* = -0.0830, *p* = .7232, *OR* = 0.920, 95% *CI* = [0.581, 1.457]). The association between LTPA and insulin resistance was not statistically significant. Also, no significant relationship between alcohol consumption and insulin resistance was found among men.

Adjusted Logistic Regression among Men in the Model with Waist Circumference

Waist circumference was entered into the adjusted logistic regression model to replace BMI to examine the strength of the association with insulin resistance among men. Compared to the adjusted logistic regression model with BMI as one of the covariates, the significance of the model with waist circumference were: 1) the negative association between major depression and insulin resistance remained significant (*B* = -1.2219, *p* = .0033, *OR* = 0.295, 95% *CI* = [0.130, 0.666]); 2) age became a significant predictor for insulin resistance (*B* = -0.0394, *p* = .0465, *OR* = 0.961, 95% *CI* = [0.925, 0.999]); 3) the association between Mexican Americans and

insulin resistance remained significant, but was stronger (*B* = 0.7116, *p* = .0033, *OR* = 2.037, 95% *CI* = [1.267, 3.275]); 4) the association between non-Hispanic Blacks and insulin resistance became significant (*B* = 0.6368, *p* = .0238, *OR* = 1.890, 95% *CI* = [1.088, 3.283]); 5) waist circumference was significantly associated with insulin resistance (*B* = 0.0909, *p* < .0001, *OR* = 1.095, 95% *CI* = [1.076, 1.115]), but the strength of this relationship was less than BMI to insulin resistance; 6) triglyceride level continued to be a significant predictor of insulin resistance, but the association between systolic blood pressure and insulin resistance was attenuated to nonsignificance; 7) former smoker remained a significant predictor of insulin resistance. The model fit statistics of -2 log likelihood and AIC were 18446247 and 18446287 respectively. The complete results of the adjusted logistic regression model with waist circumference among men are presented in Table 22.

Adjusted Logistic Regression among Women in the Model with BMI

No significant association between major depression and insulin resistance was found among women (*B* = 0.5733, *p* = .2685, *OR* = 1.774, 95% *CI* = [0.643, 4.898]), when adjusting for age, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, BMI, smoking, LTPA, and alcohol consumption. Age was not associated with insulin resistance (*B* = -0.0306, *p* = .1774, *OR* = 0.970, 95% *CI* = [0.928, 1.014]). The model fit statistics of -2 log likelihood and AIC were 14617758 and 14617798 respectively. Results of the adjusted logistic regression among women in the model with BMI as one of the covariates are presented in Table 23.

Table 22
Adjusted Logistic Regression of Major Depression and Insulin Resistance among Men in the Model with Waist Circumference

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	-1.2219	0.4160	8.6297	.0033	0.295	[0.130, 0.666]
Age	-0.0394	0.0198	3.9639	.0465	0.961	[0.925, 0.999]
Race						
NH-White					0.000	
NH-Black	0.6368	0.6368	0.2817	.0238	1.890	[1.088, 3.283]
Mexican American	0.7116	0.2422	8.6344	.0033	2.037	[1.267, 3.275]
Other	0.4468	0.3343	1.7859	.1814	1.563	[0.812, 3.010]
Waist circumference	0.0909	0.00909	99.8234	<.0001	1.095	[1.076, 1.115]
SBP	0.0190	0.0106	3.2425	.0718	1.019	[0.998, 1.041]
Triglyceride level	1.1323	0.1890	35.9100	<.0001	3.103	[2.142, 4.494]
hs-CRP						
Low					0.000	
High	-0.7842	0.9049	0.7511	.3861	0.456	[0.077, 2.689]
Moderate	0.5258	0.4240	1.5378	.2149	1.692	[0.737, 3.884]
Smoking						
Nonsmoker					0.000	
Current	-0.1032	0.2439	0.1791	.6721	0.902	[0.559, 1.455]
Former	0.9585	0.2269	17.8394	<.0001	2.608	[1.671, 4.068]
LTPA						
Moderate					0.000	
High	-0.3090	0.3246	0.9061	.3412	0.734	[0.389, 1.387]
Low	0.0045	0.3166	0.0002	.9887	1.005	[0.540, 1.868]
No	-0.2865	0.3080	0.8648	.3524	0.751	[0.411, 1.373]
Drinking						
Nondrinker					0.000	
Former	0.3088	0.5551	0.3094	.5780	1.362	[0.459, 4.042]
Light	0.0472	0.5841	0.0065	.9356	1.048	[0.334, 3.294]
Moderate	-0.3947	0.6054	0.4250	.5144	0.674	[0.206, 2.208]
Heavy	-0.5721	0.6831	0.7015	.4023	0.564	[0.148, 2.153]

Note. n = 1021; -2 log likelihood = 18446247; AIC = 18446287. SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

Table 23

Adjusted Logistic Regression of Major Depression and Insulin Resistance among Women in the Model with Body Mass Index

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	0.5733	0.5181	1.2245	.2685	1.774	[0.643, 4.898]
Age	-0.0306	0.0227	1.8191	.1774	0.970	[0.928, 1.014]
Race						
NH-White					0.000	
NH-Black	0.8988	0.3438	6.8336	.0089	2.457	[1.252, 4.820]
Mexican American	0.4701	0.3159	2.2140	.1368	1.600	[0.861, 2.972]
Other	-0.2504	0.3931	0.4059	.5241	0.778	[0.360, 1.682]
BMI	0.1990	0.0163	149.1019	<.0001	1.220	[1.182, 1.260]
SBP	0.0306	0.0119	6.6868	.0097	1.031	[1.007, 1.055]
Triglyceride level	1.5321	0.1763	75.5465	<.0001	4.628	[3.276, 6.538]
hs-CRP						
Low					0.000	
High	-0.0172	0.6701	0.0007	.9795	0.983	[0.264, 3.655]
Moderate	0.4643	0.2922	2.5249	.1121	1.591	[0.897, 2.821]
Smoking						
Nonsmoker					0.000	
Current	-0.2730	0.3329	0.6723	.4122	0.761	[0.396, 1.462]
Former	-0.3164	0.3707	0.7283	.3934	0.729	[0.352, 1.057]
LTPA						
Moderate					0.000	
High	0.1527	0.3467	0.1940	.6596	1.165	[0.591, 2.298]
Low	-0.0228	0.4332	0.0028	.9581	0.977	[0.418, 2.285]
No	0.0431	0.3466	0.0154	.9011	1.044	[0.529, 2.059]
Drinking						
Nondrinker					0.000	
Former	0.3281	0.4908	0.4470	.5038	1.388	[0.531, 3.633]
Light	0.1278	0.2998	0.1819	.6698	1.136	[0.631, 2.045]
Moderate	0.5477	0.4265	1.6493	.1991	1.729	[0.750, 3.989]
Heavy	-0.6933	0.7505	0.8534	.3556	0.500	[0.115, 2.176]

Note. n = 1173; -2 log likelihood = 14617758; AIC = 14617798. SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; BMI = body mass index; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

Compared to non-Hispanic Whites, non-Hispanic Black women were more likely to be insulin resistant (*B* = 0.8988, *p* = .0089, *OR* = 2.457, 95% *CI* = [1.252, 4.820]). However, no significant association between Mexican American women and insulin resistance was found (*B* = 0.4701, *p* = .1368, *OR* = 1.600, 95% *CI* = [0.861, 2.972]). Similarly, being of other race/ethnicity was not associated with insulin resistance (*B* = -0.2504, *p* = .5241, *OR* = 0.778, 95% *CI* = [0.360, 1.682]).

BMI was a significant predictor for insulin resistance among women (*B* = 0.1990, *p* < .0001, *OR* = 1.220, 95% *CI* = [1.182, 1.260]). For every 1 unit change in BMI, the risk of insulin resistance increases 22%, controlling for age, race/ethnicity, major depression, systolic blood pressure, triglyceride level, hs-CRP, smoking, LTPA and alcohol consumption.

A significant positive relationship between systolic blood pressure and insulin resistance also was found among women (*B* = 0.0306, *p* = .0097, *OR* = 1.031, 95% *CI* = [1.007, 1.055]), after adjusting for age, race/ethnicity, major depression, triglyceride level, hs-CRP, BMI, smoking, LTPA and alcohol consumption. Triglyceride level was significantly associated with insulin resistance among women (*B* = 1.5321, *p* < .0001, *OR* = 4.628, 95% *CI* = [3.276, 6.538]). Hs-CRP was not associated with insulin resistance, regardless of hs-CRP levels. Similarly, there was no association between smoking status and insulin resistance in women. No significant association was found between LTPA and insulin resistance. The

association between alcohol consumption and insulin resistance also was not significant either.

Adjusted Logistic Regression among Women in the Model with Waist Circumference

Waist circumference was entered into the adjusted logistic regression model to replace BMI to examine the strength of the association with insulin resistance among women. Compared to the adjusted logistic regression model with BMI as one of the covariates, the significances of the model with waist circumference were: 1) the relationship between major depression and insulin resistance remained insignificant (B = 0.5034, p = .2590, OR = 1.654, 95% CI = [0.690, 3.965]); 2) the association between being non-Hispanic Black and insulin resistance remained significant, but the strength of the association increased (B = 0.9415, p = .0030, OR = 2.564, 95% CI = [1.376, 4.776]); 3) waist circumference was significantly associated with insulin resistance (B = 0.0808, p < .0001, OR = 1.084, 95% CI = [1.064, 1.105]), however, the strength of this relationship was less than the strength of relationship of BMI to insulin resistance; 4) systolic blood pressure and triglyceride level continued to be significant predictors for insulin resistance; 5) moderate level of hs-CRP became a significant predictor for insulin resistance (B = 0.5924, p < .0295, OR = 1.808, 95% CI = [1.061, 3.083]). The model fit statistics of -2 log likelihood and AIC were 14868518 and 14868558 respectively. The complete results of the adjusted logistic regression model with waist circumference among women are presented in Table 24.

Table 24

Adjusted Logistic Regression of Major Depression and Insulin Resistance among Women in the Model with Waist Circumference

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	0.5034	0.4460	1.2740	.2590	1.654	[0.690, 3.965]
Age	-0.0273	0.0217	1.5864	.2078	0.973	[0.933, 1.015]
Race						
NH-White					0.000	
NH-Black	0.9415	0.3174	8.7973	.0030	2.564	[1.376, 4.776]
Mexican American	0.5179	0.3102	2.7882	.0950	1.679	[0.914, 3.083]
Other	-0.0270	0.3982	0.0046	.9460	0.973	[0.446, 2.125]
Waist Circumference	0.0808	0.00971	69.3127	<.0001	1.084	[1.064, 1.105]
SBP	0.0373	0.0117	10.2282	.0014	1.038	[1.015, 1.062]
Triglyceride level	1.1726	0.2100	31.1834	<.0001	3.230	[2.140, 4.875]
hs-CRP						
Low					0.000	
High	0.2241	0.6693	0.1121	.7377	1.251	[0.337, 4.646]
Moderate	0.5924	0.2721	4.7388	.0295	1.808	[1.061, 3.083]
Smoking						
Nonsmoker					0.000	
Current	-0.1983	0.3181	0.3888	.5329	0.820	[0.440, 1.530]
Former	-0.3482	0.4051	0.7391	.3900	0.706	[0.319, 1.562]
LTPA						
Moderate					0.000	
High	0.1350	0.3411	0.1566	.6923	1.145	[0.587, 2.234]
Low	-0.0951	0.4494	0.0448	.8325	0.909	[0.377, 2.194]
No	0.0575	0.3363	0.0292	.8642	1.059	[0.548, 2.047]
Drinking						
Nondrinker					0.000	
Former	0.2888	0.4785	0.3644	.5461	1.335	[0.523, 3.410]
Light	0.1662	0.3116	0.2846	.5937	1.181	[0.641, 2.175]
Moderate	0.5716	0.4400	1.6878	.1939	1.771	[0.748, 4.195]
Heavy	-0.4370	0.6775	0.4161	.5189	0.646	[0.171, 2.437]

Note. n = 1163; -2 log likelihood = 14868518; AIC = 14868558. SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

Interaction between Race/Ethnicity and Major Depression

Major depression was not significantly associated with insulin resistance (B = 0.1909, p = .5420) in the model when major depression, race/ethnicity and the interaction term for major depression and race/ethnicity were entered. Although there was a significant association between race/ethnicity and insulin resistance (Wald χ^2 = 30.7612, p < .0001), the interaction between race/ethnicity and major depression was not statistically significant (Wald χ^2 = 4.2927, p = .2315).

Because of the nonsignificant interaction between race/ethnicity and major depression, no separate multivariate logistic regression models were conducted by race/ethnicity. However, the alternative, as identified in the list of research questions and statistical analysis was logistic regression analysis to examine the association between major depression and insulin resistance (main effect), controlling for age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, BMI or waist circumference, LTPA, smoking, and alcohol consumption. BMI and waist circumference were tested in separate models. The results of these logistic regression analyses are presented below.

Adjusted Logistic Regression Model among the Study Sample in the Model with BMI

Logistic regression model was performed in the whole study sample, adjusted for age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, BMI, LTPA, smoking, and alcohol consumption. Major depression was not associated with

insulin resistance (*B* = -0.1878, *p* = .6360, *OR* = 0.829, 95% *CI* = [0.381, 1.804]), when adjusting for age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, BMI, smoking, leisure-time physical activity (LTPA), and alcohol consumption. Age was not associated with insulin resistance (*B* = -0.0217, *p* = .1113, *OR* = 0.979, 95% *CI* = [0.953, 1.005]). The model fit statistics of -2 log likelihood and AIC were 34159478 and 34159520 respectively. Table 25 demonstrates the results of adjusted logistic regression analyses among the whole study sample with BMI as one of the covariates.

Compared to non-Hispanic Whites, Mexican Americans were more likely to be insulin resistant (*B* = 0.5014, *p* = .0040, *OR* = 1.651, 95% *CI* = [1.174, 2.322]). Similarly, a significant association between non-Hispanic Black and insulin resistance was found (*B* = 0.5252, *p* = .0149, *OR* = 1.691, 95% *CI* = [1.108, 2.581]). However, being of other race/ethnicity was not associated with insulin resistance (*B* = 0.00925, *p* = .9716, *OR* = 1.009, 95% *CI* = [0.606, 1.608]).

BMI was positively associated with insulin resistance (*B* = 0.2091, *p* < .0001, *OR* = 1.233, 95% *CI* = [1.201, 1.265]). For every 1 unit change in BMI, the likelihood of having insulin resistance increases 23.3%, after controlling for other variables including age, gender, race/ethnicity, major depression, systolic blood pressure, triglyceride level, hs-CRP, smoking, LTPA and alcohol consumption.

A significant positive relationship between systolic blood pressure and insulin resistance was observed (*B* = 0.0244, *p* = .0023, *OR* = 1.025, 95% *CI* = [1.009,

Table 25
Adjusted Logistic Regression of Major Depression and Insulin Resistance in the Study Sample with Body Mass Index

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	-0.1878	0.3969	0.2240	.6360	0.829	[0.381, 1.804]
Age	-0.0217	0.0136	2.5358	.1113	0.979	[0.953, 1.005]
Gender						
Males					0.000	
Females	-0.4357	0.1971	4.8877	.0270	0.647	[0.440, 0.952]
Race						
NH-White					0.000	
NH-Black	0.5252	0.2157	5.9267	.0149	1.691	[1.108, 2.581]
Mexican American	0.5014	0.1741	8.2999	.0040	1.651	[1.174, 2.322]
Other	0.00925	0.2600	0.0013	.9716	1.009	[0.606, 1.680]
BMI	0.2091	0.0132	249.6534	<.0001	1.233	[1.201, 1.265]
SBP	0.0244	0.00802	9.2672	.0023	1.025	[1.009, 1.041]
Triglyceride level	1.1962	0.1128	112.4474	<.0001	3.307	[2.651, 4.126]
Hs-CRP						
Low					0.000	
High	-0.2331	0.4774	0.2384	.6254	0.792	[0.311, 2.019]
Moderate	0.5047	0.2638	3.6602	.0557	1.656	[0.988, 2.778]
Smoking						
Nonsmoker					0.000	
Current	-0.1776	0.1700	1.0923	.2960	0.837	[0.600, 1.168]
Former	0.4754	0.1928	6.0784	.0137	1.609	[1.102, 2.347]
LTPA						
Moderate					0.000	
High	-0.1774	0.2068	0.7365	.3908	0.837	[0.558, 1.256]
Low	-0.0272	0.2060	0.0174	.8951	0.973	[0.650, 1.457]
No	-0.0648	0.1606	0.1630	.6864	0.937	[0.684, 1.284]
Drinking						
Nondrinker					0.000	
Former	0.2453	0.3211	0.5836	.4449	1.278	[0.681, 2.398]
Light	0.0397	0.2623	0.0229	.8797	1.041	[0.622, 1.740]
Moderate	-0.2150	0.2994	0.5156	.4727	0.807	[0.448, 1.450]
Heavy	-0.6697	0.4180	2.5668	.1091	0.512	[0.226, 1.161]

Note. *n* = 2199; -2 log likelihood = 34159478; AIC = 34159520. SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; BMI = body mass index; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

1.041]), after adjusting for age, gender, race/ethnicity, major depression, triglyceride level, hs-CRP, BMI, smoking, LTPA and alcohol consumption.

There was a strong positive association between triglyceride level and insulin resistance (*B* = 1.1962, *p* < .0001, *OR* = 3.307, 95% *CI* = [2.651, 4.126]). Hs-CRP was not significantly associated with insulin resistance, regardless of hs-CRP levels.

Compared to nonsmokers, former smokers were more likely to have insulin resistance (*B* = 0.4754, *p* = .0137, *OR* = 1.609, 95% *CI* = [1.102, 2.347]). LTPA was not associated with insulin resistance, regardless of level. No significant association between alcohol consumption and insulin resistance was observed.

Adjusted Logistic Regression among the Study Sample in the Model with Waist Circumference

Logistic regression modeling was performed again after removing BMI from the model and replacing this variable with waist circumference to examine the strength of the association with insulin resistance. The modeling procedure adjusted for age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, waist circumference, LTPA, smoking, and alcohol consumption in the analyses. Compared to the adjusted logistic regression model with BMI, the significance of the model with waist circumference were: 1) the negative association between major depression and insulin resistance remained insignificant (*B* = -0.1451, *p* = .6660, *OR* = 0.865, 95% *CI* = [0.447, 1.672]); 2) age became a significant predictor for insulin resistance (*B* =

-0.0278, p = .0434, OR = 0.973, 95% CI = [0.947, 0.999]); 3) the association between Mexican Americans and insulin resistance remained significant, but the strength of the relationship increased (B = 0.6330, p = .0005, OR = 1.883, 95% CI = [1.319, 2.689]); 4) being a non-Hispanic Black remained a significant predictor for insulin resistance (B = 0.7604, p = .0004, OR = 2.139, 95% CI = [1.402, 3.264]); 5) waist circumference was significantly associated with insulin resistance (B = 0.0849, p < .0001, OR = 1.089, 95% CI = [1.077, 1.101]), however, the strength of the relationship to insulin resistance was less than for BMI (B = 0.2091, p < .0001, OR = 1.233, 95% CI = [1.201, 1.265]); 6) systolic blood pressure and triglyceride level continued to be significant predictors for insulin resistance; 7) moderate hs-CRP was positively associated with insulin resistance (B = 0.5887, p = .0109, OR = 1.802, 95% CI = [1.145, 2.834]); 8) former smoker remained as a significant predictor for insulin resistance. The model fit statistics of -2 log likelihood and AIC were 34080111 and 34080153 respectively. The complete results of the adjusted logistic regression model among the whole study sample with waist circumference are presented in Table 26.

Univariate Logistic Regression by Measures of Depression

The relationship between major depression and insulin resistance was investigated by type of depression measures to examine the influence of measurement type in the results. Univariate logistic regression analyses showed that major depression measured by the CIDI was not significantly associated with insulin resistance (B = 0.1083, p = .7470, OR = 1.114, 95% CI = [0.577, 2.152]). No

Table 26
Adjusted Logistic Regression of Major Depression and Insulin Resistance in the Study Sample with Waist Circumference

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	-0.1451	0.3362	0.1863	.6660	0.865	[0.447, 1.672]
Age	-0.0278	0.0137	4.0807	.0434	0.973	[0.947, 0.999]
Gender						
Males					0.000	
Females	0.0700	0.2071	0.1142	.7354	1.072	[0.715, 1.609]
Race						
NH-White					0.000	
NH-Black	0.7604	0.2155	12.4476	.0004	2.139	[1.402, 3.264]
Mexican American	0.6330	0.1817	12.1339	.0005	1.883	[1.319, 2.689]
Other	0.2552	0.2711	0.8864	.3465	1.291	[0.759, 2.196]
Waist Circumference	0.0849	0.00559	230.4969	<.0001	1.089	[1.077, 1.101]
SBP	0.0260	0.00811	10.2812	.0013	1.026	[1.010, 1.043]
Triglyceride level	1.0414	0.1245	69.9153	<.0001	2.833	[2.220, 3.617]
hs-CRP						
Low					0.000	
High	-0.1504	0.5785	0.0676	.7949	0.860	[0.277, 2.674]
Moderate	0.5887	0.2312	6.4863	.0109	1.802	[1.145, 2.834]
Smoking						
Nonsmoker					0.000	
Current smoker	-0.1497	0.1728	0.7500	.3865	0.861	[0.614, 1.208]
Former smoker	0.4124	0.2013	4.1983	.0405	1.510	[1.018, 2.241]
LTPA						
Moderate					0.000	
High	-0.1317	0.1966	0.4485	.5030	0.877	[0.596, 1.289]
Low	-0.0746	0.2167	0.1185	.7306	0.928	[0.607, 1.419]
No	-0.0864	0.1583	0.2977	.5853	0.917	[0.673, 1.251]
Drinking						
Nondrinker					0.000	
Former	0.3063	0.3078	0.9903	.3197	1.358	[0.743, 2.483]
Light	0.1084	0.2680	0.1638	.6857	1.115	[0.659, 1.884]
Moderate	-0.0740	0.3123	0.0562	.8127	0.929	[0.504, 1.713]
Heavy	-0.4789	0.4268	1.2587	.2619	0.619	[0.268, 1.430]

Note. n = 2184; -2 log likelihood = 34080111; AIC = 34080153. SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

significant relationship was observed between major depression assessed by the PHQ-9 and insulin resistance, but the *B* coefficient became larger (*B* = 0.4816, *p* = .1556, *OR* = 1.619, 95% *CI* = [0.833, 3.146]).

Adjusted Logistic Regression in the Model with BMI by Measures of Depression

When adjusting for age, gender, race/ethnicity, BMI, systolic blood pressure, triglyceride level, hs-CRP, smoking status, LTPA, and alcohol consumption, the direction of the relationship between major depression and insulin resistance became negative but remained nonsignificant (*B* = -0.1621, *p* = .7560, *OR* = 0.850, 95% *CI* = [0.306, 2.364]) among participants whose measure of major depression was the CIDI. BMI, systolic blood pressure, and triglyceride level were significant predictors for insulin resistance, after controlling for major depression, age, gender, race/ethnicity, hs-CRP, smoking status, LTPA, and alcohol consumption. The model fit statistics of -2 log likelihood and AIC were 12849175 and 12849217 respectively. The results of the adjusted logistic regression analyses with BMI as one of the covariates among NHANES 1999-2004 participants who had measure of major depression by the CIDI are presented in Table 27.

When major depression was measured by the PHQ-9 in NHANES 2005-2008, the direction of the relationship between major depression and insulin resistance changed but remained insignificant (*B* = -0.0634, *p* = .9043, *OR* = 0.939, 95% *CI* = [0.334, 2.640]), after adjusting for age, gender, race/ethnicity, BMI, systolic blood pressure, triglyceride level, hs-CRP, smoking status, LTPA, and alcohol consumption.

Table 27

Adjusted Logistic Regression of Major Depression and Insulin Resistance with Body Mass Index among NHANES 1999-2004 Participants who had Measures of Major Depression by the Composite International Diagnostic Interview

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	-0.1621	0.5216	0.0965	.7560	0.850	[0.306, 2.364]
Age	-0.0264	0.0222	1.4213	.2332	0.974	[0.933, 1.071]
Gender						
Males					0.000	
Females	-0.3862	0.2614	2.1829	.1396	0.680	[0.407, 1.134]
Race						
NH-White					0.000	
NH-Black	0.5348	0.3387	2.4934	.1143	1.707	[0.879, 3.316]
Mexican American	0.4882	0.3185	2.3496	.1253	1.629	[0.873, 3.042]
Other	0.1360	0.4332	0.0986	.7535	1.146	[0.490, 2.678]
BMI	0.2387	0.0229	108.6106	<.0001	1.270	[1.214, 1.328]
SBP	0.0308	0.0112	7.5902	.0059	1.031	[1.009, 1.054]
Triglyceride level	0.9225	0.2071	19.8444	<.0001	2.516	[1.676, 3.775]
hs-CRP						
Low					0.000	
High	-0.1500	0.7675	0.0382	.8450	0.861	[0.191, 3.874]
Moderate	0.4549	0.4050	1.2617	.2613	1.576	[0.713, 3.485]
Smoking						
Nonsmoker					0.000	
Current	-0.1772	0.3037	0.3403	.5596	0.838	[0.462, 1.519]
Former	0.4744	0.3578	1.7583	.1848	1.607	[0.797, 3.240]
LTPA						
Moderate					0.000	
High	0.0880	0.2547	0.1195	.7296	1.092	[0.663, 1.799]
Low	0.1649	0.3243	0.2587	.6110	1.179	[0.625, 2.227]
No	-0.1818	0.3367	0.2914	.5893	0.834	[0.431, 1.613]
Drinking						
Nondrinker					0.000	
Former	0.6608	0.5249	1.5847	.2081	1.936	[0.692, 5.417]
Light	0.2479	0.4013	0.3815	.5368	1.281	[0.584, 2.813]
Moderate	-0.2681	0.5212	0.2647	.6069	0.765	[0.275, 2.124]
Heavy	-0.3170	0.7389	0.1840	.6679	0.728	[0.171, 3.099]

Note. n = 904; -2 log likelihood = 12849175; AIC = 12849217. NHANES = National Health and Nutrition Examination Survey; SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; BMI = body mass index; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

Non-Hispanic Blacks, Mexican Americans, BMI, triglyceride level, and former smokers were significant positive predictors for insulin resistance. The model fit statistics of -2 log likelihood and AIC were 20839533 and 20839575 respectively. The results of the adjusted logistic regression analyses with BMI as one of the covariates among NHANES 2005-2008 participants who had measure of major depression by the PHQ-9 are reported in Table 28.

Adjusted Logistic Regression with Waist Circumference by Measures of Depression

Major depression was insignificantly associated with insulin resistance (*B* = -0.0884, *p* = .8380, OR = 0.915, 95% *CI* = [0.392, 2.137]) among participants whose measure of major depression was the CIDI, after adjusting for age, gender, race/ethnicity, waist circumference, systolic blood pressure, triglyceride level, hs-CRP, smoking status, LTPA, and alcohol consumption. Being non-Hispanic Black, waist circumference, systolic blood pressure, and triglyceride level were significant predictors for insulin resistance, after controlling for major depression, age, gender, hs-CRP, smoking status, LTPA, and alcohol consumption. The model fit statistics of -2 log likelihood and AIC were 12824610 and 12824652 respectively. The results of the adjusted logistic regression analyses with waist circumference as one of the covariates among NHANES 1999-2004 participants who had measure of major depression by the CIDI are presented in Table 29.

When major depression was measured by the PHQ-9 in NHANES 2005-2008, major depression was not associated with insulin resistance (*B* = 0.1406, *p* = .7174,

Table 28

Adjusted Logistic Regression of Major Depression and Insulin Resistance with Body Mass Index among NHANES 2005-2008 Participants who had Measures of Major Depression by Patient Health Questionnaire-9

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	-0.0634	0.5276	0.0144	.9043	0.939	[0.334, 2.640]
Age	-0.0177	0.0170	1.0906	.2963	0.982	[0.950, 1.016]
Gender						
Males					0.000	
Females	-0.4308	0.2703	2.5404	.1110	0.650	[0.383, 1.104]
Race						
NH-White					0.000	
NH-Black	0.5581	0.2777	4.0380	.0445	1.747	[1.041, 3.012]
Mexican American	0.5992	0.2200	7.4178	.0065	1.821	[1.183, 2.802]
Other	-0.0986	0.3302	0.0892	.7652	0.906	[0.474, 1.731]
BMI	0.1928	0.0177	119.0253	<.0001	1.213	[1.171, 1.255]
SBP	0.0212	0.0114	3.4783	.0622	1.021	[0.999, 1.044]
Triglyceride level	1.3647	0.1248	119.6155	<.0001	3.915	[3.065, 4.999]
hs-CRP						
Low					0.000	
High	-0.4107	0.6661	0.3801	.5375	0.663	[0.180, 2.447]
Moderate	0.5449	0.3530	2.3818	.1228	1.724	[0.863, 3.445]
Smoking						
Nonsmoker					0.000	
Current	-0.1566	0.2265	0.4783	.4892	0.855	[0.549, 1.333]
Former	0.5095	0.2406	4.4842	.0342	1.664	[1.039, 2.667]
LTPA						
Moderate					0.000	
High	-0.2934	0.2906	1.0200	.3125	0.746	[0.422, 1.318]
Low	-0.0802	0.2781	0.0831	.7731	0.923	[0.535, 1.592]
No	0.0421	0.1840	0.0524	.8189	1.043	[0.727, 1.496]
Drinking						
Nondrinker					0.000	
Former	-0.0939	0.4543	0.0427	.8363	0.910	[0.374, 2.218]
Light	-0.0950	0.3294	0.0831	.7731	0.909	[0.477, 1.734]
Moderate	-0.2667	0.3754	0.5049	.4774	0.766	[0.367, 1.598]
Heavy	-0.9463	0.5213	3.2951	.0695	0.388	[0.140, 1.078]

Note. *n* = 1295; -2 log likelihood = 20839533; AIC = 20839575. NHANES = National Health and Nutrition Examination Survey; SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; BMI = body mass index; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

Table 29

Adjusted Logistic Regression of Major Depression and Insulin Resistance with Waist Circumference among NHANES 1999-2004 Participants who had Measures of Major Depression by the Composite International Diagnostic Interview

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	-0.0884	0.4326	0.0418	.8380	0.915	[0.392, 2.137]
Age	-0.0329	0.0217	2.3022	.1292	0.968	[0.927, 1.010]
Gender						
Males						
Females	0.2914	0.2637	1.2207	.2692	1.338	[0.798, 2.244]
Race						
NH-White					0.000	
NH-Black	0.8186	0.3487	5.5093	.0189	2.267	[1.145, 4.491]
Mexican American	0.6320	0.3262	3.7541	.0527	1.881	[0.993, 3.566]
Other	0.3605	0.4708	0.5863	.4439	1.434	[0.570, 3.608]
Waist Circumference	0.0963	0.0104	85.3024	<.0001	1.101	[1.079, 1.124]
SBP	0.0354	0.0110	10.4463	.0012	1.036	[1.014, 1.059]
Triglyceride level	0.7101	0.2321	9.3564	.0022	2.034	[1.291, 3.206]
hs-CRP						
Low					0.000	
High	0.0134	0.6544	0.0004	.9836	1.014	[0.281, 3.655]
Moderate	0.5243	0.3870	1.8347	.1756	1.689	[0.791, 3.607]
Smoking						
Nonsmoker					0.000	
Current	-0.2269	0.3187	0.5069	.4765	0.797	[0.427, 1.489]
Former	0.4084	0.3653	1.2499	.2636	1.504	[0.735, 3.079]
LTPA						
Moderate					0.000	
High	0.1063	0.2289	0.2155	.6425	1.112	[0.710, 1.742]
Low	-0.0532	0.3588	0.0220	.8822	0.948	[0.469, 1.916]
No	-0.3283	0.3403	0.9310	.3346	0.720	[0.370, 1.403]
Drinking						
Nondrinker					0.000	
Former	0.5545	0.4945	1.2572	.2622	1.741	[0.660, 4.590]
Light	0.1572	0.4062	0.1499	.6987	1.170	[0.528, 2.594]
Moderate	-0.1929	0.5081	0.1441	.7042	0.825	[0.305, 2.232]
Heavy	-0.3235	0.6976	0.2150	.6429	0.724	[0.184, 2.840]

Note. n = 901; -2 log likelihood = 12824610; AIC = 12824652. NHANES = National Health and Nutrition Examination Survey; SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

OR = 1.151, 95% *CI* = [0.538, 2.464]), after adjusting for age, gender, race/ethnicity, waist circumference, systolic blood pressure, triglyceride level, hs-CRP, smoking status, LTPA, and alcohol consumption. Being non-Hispanic Blacks or Mexican American, waist circumference, triglyceride level, and moderate hs-CRP were significant positive predictors for insulin resistance. The model fit statistics of -2 log likelihood and AIC were 20735491 and 20735533 respectively. The results of the adjusted logistic regression analyses with waist circumference as one of the covariates among NHANES 2005-2008 participants who had measure of major depression by the PHQ-9 are reported in Table 30.

Table 30

Adjusted Logistic Regression of Major Depression and Insulin Resistance with Waist Circumference among NHANES 2005-2008 Participants Who had Measures of Major Depression by the Patient Health Questionnaire-9

Variables	*B*	*SE*	Wald χ^2	*p*-value	*OR*	95% CI
Major depression	0.1406	0.3883	0.1310	.7174	1.151	[0.538, 2.464]
Age	-0.0245	0.0174	1.9997	.1573	0.976	[0.943, 1.010]
Gender						
Males					0.000	
Females	-0.0175	0.2841	0.0038	.9510	0.983	[0.563, 1.715]
Race						
NH-White					0.000	
NH-Black	0.7689	0.2745	7.8450	.0051	2.157	[1.260, 3.695]
Mexican American	0.7240	0.2310	9.8257	.0017	2.063	[1.312, 3.244]
Other	0.1609	0.3433	0.2195	.6394	1.175	[0.599, 2.302]
Waist Circumference	0.0791	0.00714	122.5780	<.0001	1.082	[1.067, 1.098]
SBP	0.0213	0.0115	3.4195	.0644	1.022	[0.999, 1.045]
Triglyceride level	1.2359	0.1351	83.7296	<.0001	3.441	[2.641, 4.484]
hs-CRP						
Low					0.000	
High	-0.3270	0.8438	0.1502	.6984	0.721	[0.138, 3.769]
Moderate	0.6091	0.3077	3.9170	.0478	1.839	[1.006, 3.361]
Smoking						
Nonsmoker					0.000	
Current	-0.0946	0.2243	0.1779	.6731	0.910	[0.586, 1.412]
Former	0.4386	0.2527	3.0124	.0826	1.551	[0.945, 2.544]
LTPA						
Moderate					0.000	
High	-0.2631	0.2778	0.8969	.3436	0.769	[0.446, 1.325]
Low	-0.0489	0.2898	0.0285	.8659	0.952	[0.540, 1.680]
No	0.0672	0.1860	0.1305	.7179	1.069	[0.743, 1.540]
Drinking						
Nondrinker					0.000	
Former	0.1081	0.4300	0.0633	.8014	1.114	[0.480, 2.588]
Light	0.0681	0.3442	0.0392	.8431	1.071	[0.545, 2.102]
Moderate	-0.0603	0.4045	0.0223	.8814	0.941	[0.426, 2.080]
Heavy	-0.6484	0.5341	1.4738	.2247	0.523	[0.184, 1.489]

Note. n = 1283; -2 log likelihood = 20735491; AIC = 20735533. NHANES = National Health and Nutrition Examination Survey; SE = standard error; OR = odds ratio; CI = confidence interval; NH = non-Hispanic; SBP = systolic blood pressure; hs-CRP = high sensitivity C-reactive protein; LTPA = leisure time physical activity.

CHAPTER V DISCUSSION, RECOMMENDATIONS AND CONCLUSIONS

The purpose of this study was to 1) determine the prevalence of major depression and insulin resistance among nondiabetic adults aged 20-39 years in the United States; 2) examine the relationship between major depression and insulin resistance among nondiabetic U.S. adults aged 20-39 years; and 3) investigate the role of gender, race/ethnicity, and measure of depression on the relationship between major depression and insulin resistance. Data obtained from nondiabetic adults aged 20-39 years who participated in the National Health and Nutrition Examination Survey (NHANES) 1999-2008 were analyzed for the prevalence of major depression and insulin resistance and their relationship. This chapter discusses the results of the study, identifies limitations to the study, conclusions and implications of the study, and makes recommendations for future research.

Prevalence of Major Depression

The overall prevalence of major depression among nondiabetic adults aged 20-39 years was 3.8%. This 3.8% prevalence rate is lower than the 6.9% (Aalto-Setala, et al., 2001) to 9% prevalence of depression reported by previous studies in young adults aged 20-39 years (Gwynn, et al., 2008). The rate also is lower than the 6.6% prevalence of major depression among nondiabetic adults aged 20-39 years who

participated in NHANES 1999-2002 (Shen, et al., 2011). This finding is surprising as previous research reported that the prevalence of depression among young adults was higher than middle- and older-age adults in a review by Jorm (2000).

When measured by the CIDI, the prevalence of major depression in the current study was 6.6%. This is lower than the 9% prevalence of 12-month major depression among adults aged 20-39 years reported by Gwynn et al. (2008), but comparable to the 6.6% prevalence of major depression among nondiabetic adults aged 20-39 years who participated in NHANES 1999-2002 reported by Shen et al. (2011). The prevalence of major depression evaluated by the PHQ-9 was 1.8%, which is surprisingly lower than the 7% found among adults aged 20 and older (Pratt & Brody, 2010).

Differences in reported depression rates for nondiabetic adults aged 20-39 years may result from variations in the definition of major depression and measures of depression. In Aalto-Setala et al.'s study (2001), major depression for the previous 4 weeks was measured by the Schedules for Clinical Assessment in Neuropsychiatry (SCAN). Gwynn et al. (2008) examined the 12-month prevalence of major depression using the CIDI. However, in the study by Prat and Brody (2010), depression was assessed by the PHQ-9 and defined as a PHQ-9 score of 10 or higher which included moderate, moderately severe, and severe depression. In comparison, DSM-IV diagnostic criteria for major depression were applied in the current study by using the

CIDI which includes DSM-IV diagnostic criteria in its algorithm for a diagnosis of major depression (yes/no) and evaluating depressive symptoms reported in the PHQ-9 according to DSM-IV criteria to establish a diagnosis of major depression (yes/no); although the PHQ-9 may have underestimated the prevalence of major depression relative to the CIDI. In addition, it is possible that individuals experiencing major depression may have declined participation in NHANES, which may have contributed to the potential underestimation of the prevalence of major depression among nondiabetic adults aged 20-39 years. Further, the much lower prevalence rate of major depression, when evaluated by the PHQ-9, may be attributed to a time effect. The CIDI evaluates symptoms of depression present in the past 12 months; while the PHQ-9 examines the presence of depressive symptoms in the past two weeks. Estimation of the prevalence rate of major depression by each NHANES period should be examined in future studies.

Females had a higher overall prevalence rate of major depression (4.3%) than males (3.3%). Results are consistent with those from Gwynn et al. (2008), who found a 9% prevalence of depression in females and a 6% prevalence of depression among community-based adults in New York. This higher prevalence of major depression among females may be from gender differences in genetic predisposition, hormonal, and responses to adverse life events (CDC, 2010b). However, the 4.3% prevalence of major depression among females found in the current study is nearly half the 9% found in the study by Gwynn et al. (2008). The 3.3% prevalence of major depression found in males also is much lower than the 6% reported by Gwynn et al. (2008). The

discrepancies in the prevalence of major depression among females and males may be attributed to differing definitions of depression. The prevalence of depression reported by Gwynn et al. (2008) was estimated from any type of depression; while only major depression was included to calculate the prevalence rate in this study. Without delineation of the severity of depression, the prevalence rate of major depression was possibly overestimated in the study by Gwynn et al. (2008).

The prevalence of major depression varied by race/ethnicity in the current study. Major depression was found to be the most prevalent among non-Hispanic Whites aged 20-39 years (4.4%). Compared to non-Hispanic Whites, non-Hispanic Blacks had a slightly lower prevalence rate of major depression (4.0%). The 2.5% rate of major depression found among Mexican Americans in the study was surprisingly lower than the 7% reported by Gwynn et al. (2008) in a community-based study among New York adults aged 20 years and older. Despite the 2.5% to 4.4% difference in prevalence rates, there was no significant interaction effect of race/ethnicity on the relationship between major depression and insulin resistance found in the study.

The pattern of highest prevalence of major depression among non-Hispanic Whites, followed by non-Hispanic Blacks and Mexican Americans varied from the study conducted by Gwynn et al. (2008) that found the prevalence of major depression was highest among Black Americans (9%), followed by Whites (8%), Hispanics (7%), and Asians (5%). The race/ethnicity composition of the population for the current study also differed from that of the community-based New York adult

population in Gwynn et al.'s study. The sample in the current study consisted of 11.8% non-Hispanic Blacks, and 12.0% Mexican Americans, in contrast to the 26.6% Blacks and 27.0% Hispanics in Gwynn et al.'s study. Therefore, the findings from Gwynn et al.'s study may not be generalizable to general population in other regions. The different definitions of major depression also may have contributed to the discrepancies of prevalence rate across race/ethnicity.

Prevalence of Insulin Resistance

The prevalence of insulin resistance among nondiabetic adults aged 20-39 years who participated in NHANES 1999-2008 was 22.5%. This is slightly higher than the reported 21.5% of insulin resistance among Thai adults aged 35 years and older (Do, et al., 2010), but much lower than the 32.2% prevalence rate of insulin resistance among adults aged 20 to 85 years old found by Ioannou, Bryson, and Boyko (2007). The variations in the prevalence of insulin resistance may result from age differences in the study samples. Subjects in this study were younger than those in previous studies. Findings provide further evidence that insulin resistance can be present in young adults with euglycemia (Reaven, 1988).

Insulin resistance was found to be significantly more prevalent among males (24.5%) than females (20.5%). This contradicts findings from previous research which showed that females are more insulin resistant than males from birth throughout adulthood (Wilkin & Murphy, 2006). Findings also were surprising given

that males had a higher level of self-reported leisure time physical activity than females in the study. Contextual information to explain these results were not collected and warrant further study.

Both nondiabetic Mexican Americans and non-Hispanic Blacks aged 20-39 years had higher prevalence rates of insulin resistance than non-Hispanic Whites. The prevalence of insulin resistance among Mexican Americans was 31.0%, the rate of insulin resistance among non-Hispanic Blacks was 30.1%, and the prevalence of insulin resistance among non-Hispanic Whites was 20.0%. This 10% higher rate of insulin resistance among non-Hispanic Blacks and Mexican Americans is consistent with previous research, showing that Mexican Americans and non-Hispanic Blacks were the two racial/ethnic groups that have higher prevalence rates of insulin resistance and type 2 diabetes (Aguirre, et al., 1997; Karim, et al., 2005). The higher prevalence of insulin resistance among these two racial/ethnic groups may be attributed to genetic variants and environmental factors.

The 75 percentile of HOMA-IR scores among normal healthy population is the most commonly used definition of insulin resistance in epidemiological research (Balkau & Charles, 1999). The current study used the 75 percentile of HOMA-IR scores (P_{75} = 3.4351) among nondiabetic adults aged 20 and above who participated in NHANES 1999-2008 and had complete data on fasting glucose and insulin levels to define insulin resistance. The cutoff value of HOMA-IR used in the study is lower than the value of 3.8 suggested by Ascaso et al. (2001). If the value of 3.8 were used

in the study, fewer subjects would have been classified as insulin resistance and the prevalence of insulin resistance would have been lower. Appel (2005) recommended a HOMA-IR of 2.8 - 3.0 as the cut point for insulin resistance to be used in clinical practice. This range of 2.8 - 3.0 is lower than the value of 3.4351 found in the current study. More individuals would have been defined as insulin resistant in the current study if this range of 2.8 - 3.0 had been applied. Also the prevalence of insulin resistance would have been higher. Since there is no standardized insulin assay available, it is impossible to establish a universal cutoff HOMA-IR score to define insulin resistance.

Risk Factors Associated with Insulin Resistance

Univariate analyses of risk factors for insulin resistance revealed that eight variables were significantly associated with insulin resistance in the study. Discussion of results of univariate analyses are presented by risk factors.

Systolic Blood Pressure

The average systolic blood pressure in the study sample was 113.9 mmHg and was within the normal range of systolic blood pressure (< 120 mmHg) (Chobanian, et al., 2003). However, 75 of 2,222 subjects (3.3%) had a systolic blood pressure ≥ 140 mmHg. Among males, 59 out of 1,042 had a systolic blood pressure ≥ 140 mmHg (5.4%), in contrast to the 1.1% of females. Although both proportions are small, this finding is consistent with results from a previous study which identified that

hypertension was more prevalent among men than women in Europe (49.7% vs 38.6%), Canada (31.0% vs 23.8%), and the United States (29.8% vs 25.8%) (Wolf-Maier et al., 2003). Hypertension is a known risk factor for insulin resistance (Lima, et al., 2009). Consequently, the higher average systolic blood pressure among males in the current study may partially explain the higher prevalence of insulin resistance in males relative to females in this study. The gender difference in systolic blood pressure may begin at puberty (Dasgupta et al., 2006). However, the prevalence of hypertension among women increases as sex hormones (i.e., estrogens and progesterone) decline during the peri- and postmenopausal period (Boschitsch, Mayerhofer, & Magometschnigg, 2010).

Findings from this study also showed that the mean systolic blood pressure of non-Hispanic Blacks was 4 mmHg higher than that of Mexican Americans, non-Hispanic Whites, or other race/ethnicity. The highest prevalence of systolic blood pressure ≥ 140 mmHg (5.4%) also was observed among non-Hispanic Blacks. Results parallel those reported by the National Center for Health Statistics in the publication of *Health, United States, 2010: With Special Feature on Death and Dying* (National Center for Health Statistics, 2011, p. 268) that found the highest prevalence of hypertension was among non-Hispanic Blacks. Other research also has found that race/ethnicity is a risk factor for hypertension with non-Hispanic Blacks at increased risk for hypertension and more likely to have higher blood pressure compared to non-Hispanic Whites (Kurian & Cardarelli, 2007). The trend of higher blood pressure in non-Hispanic Blacks than that of non-Hispanic Whites was even observed among

children at as early as 13 years old (Brady, Fivush, Parekh, & Flynn, 2010). This may be partially explained by the genetic predisposition for alterations in the renin-angiotensin-aldosterone system among non-Hispanic Blacks.

The average systolic blood pressure among insulin resistant subjects was about 7 mmHg higher than that of non-insulin resistant subjects. Also, significantly more insulin resistant subjects (7.3%) had an average systolic blood pressure > 140 mmHg, compared to non-insulin resistant individuals (2.0%). This is consistent with results from previous research that found a positive relationship between hypertension and insulin resistance. However, the percentage of subjects with hypertension who were insulin resistant in the current study is much lower than the 50% or higher rate estimated by Lima et al. (2009). This makes sense given the average age of subjects in the 2009 study was above 50 years old, whereas subjects in the current study were age 20-39 years with a mean of 29.5 years. Hypertension was also defined as a systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, or use of antihypertensive medications in the study by Lima et al. (2009). This study defined hypertension as a systolic blood pressure ≥ 140 mmHg only. The difference in definitions also may help explain the lower prevalence of hypertension among insulin resistant subjects found in the current study. In addition, the cutoff value of 140 mmHg in this study was higher than the 130 mmHg recommended by NCEP ATP III (2002) to identify individuals at risk for metabolic syndrome. More subjects would have had elevated systolic blood pressure if the value of 130 mmHg were applied in the current study. Results provide support for hypertension as a significant risk factor

for insulin resistance in the conceptual schema of factors thought to be associated with insulin resistance in the current study (Figure 1).

Triglyceride Level

The study observed a high prevalence (23.1%) of triglycerides ≥ 150 mg/dl among nondiabetic U.S. adults aged 20-39 years. This is comparable to the 24.0% prevalence rate of triglycerides ≥ 150 mg/dl found among U.S. adults aged 20-39 years reported by Ford, Li, Zhao, Pearson, and Mokdad (2009), but 10% lower than the overall prevalence rate of 33.1% among U.S. adults ≥ 20 years and older found in the same study. The estimated prevalence of triglyceride level ≥ 150 mg/dl in Ford et al.'s study was based on data from 5,610 participants aged 20 years or older from the National Health and Nutrition Examination Survey (NHANES) 1999-2004.

The finding that men had a higher prevalence of triglyceride level ≥ 150 mg/dl than women also is consistent with that observed by Ford et al. (2009). However, the 27.8% rate of triglyceride level ≥ 150 mg/dl among men in the current study is lower than the 36.7% overall rate for men in Ford et al.'s study. Similarly, women in the current study had a lower rate of triglyceride level ≥ 150 mg/dl (18.5%) than the 29.6% reported by Ford et al. (2009). The disparity in findings between studies may be explained by evidence that suggests biomarkers of cardiometabolic risk (e.g., triglyceride level) increase with age.

High triglyceride levels (≥ 150 mg/dl) were the most prevalent among Mexican Americans (30.1%), followed by non-Hispanic Whites (24.0%), and non-Hispanic Blacks (13.3%). Findings are similar to those observed by Ford et al. (2009). However, the rates found in this study are generally lower than the 37.9% of Mexican Americans, the 35.2% of non-Hispanic Whites, and the 16.3% of non-Hispanic Blacks reported by Ford et al. (2009). As expected, high triglyceride levels were more prevalent among individuals with insulin resistance (44.2%) relative to those without insulin resistance (17.0%). Results support the strong positive association between triglyceride level and insulin resistance found by Avramoglu et al. (2006). The study findings also provide support for high triglyceride level as a significant risk factor for insulin resistance in the conceptual schema of factors thought to be associated with insulin resistance in the current study (Figure 1).

The high prevalence of triglyceride level ≥ 150 mg/dl found in the general U.S. population, or even nondiabetic young adults aged 20-39 years, is concerning. Many studies have shown that high triglyceride level is a significant risk factor for cardiovascular disease (Sarwar et al., 2007). Although high triglyceride level (≥ 150 mg/dl) was less prevalent among women than men in the current study, previous studies report a higher risk for cardiovascular disease among women with high triglyceride level than men (McBride, 2008). In a meta-analysis by Hokanson and Austin (1996), women were found to have 75% increased risk for cardiovascular disease for every 1 mmol/L increase in triglyceride, compared to a 30% increased risk among men. Similarly, although high triglyceride level (≥ 150 mg/dl) was less

prevalent among non-Hispanic Blacks, this does not necessarily reduce their risk for insulin resistance. Sumner and Cowie (2008) investigated the racial/ethnic differences of triglyceride concentration in predicting insulin resistance, using NHANES 1999-2002. They found that in comparison to non-Hispanic Whites or Mexican Americans, non-Hispanic Blacks were more likely to be insulin resistant, but had a lower level of triglycerides.

High Sensitivity C-Reactive Protein

As a biomarker for systemic inflammation, research has shown that elevation of high sensitivity C-reactive protein (hs-CRP) is a significant risk factor for cardiovascular disease. Hs-CRP was found to be significantly associated with insulin resistance in univariate analyses in the current study. More than 17% of insulin resistant individuals had hs-CRP equal or greater than 1mg/L, compared to only 5.2% of individuals without insulin resistance. Findings are consistent with many studies which have found a significantly positive relationship between CRP and insulin resistance (Chou, et al., 2010; Gelaye, et al., 2010; Meng, et al., 2007; Nakanishi, et al., 2005). However, these previous studies examined regular CRP, not hs-CRP. The positive association between hs-CRP and insulin resistance also was observed by Kawamoto et al. (2010) among 1,919 Japanese community-dwelling participants. The available research data demonstrate that hs-CRP is a significant predictor for insulin resistance.

Gender and race/ethnicity also were significantly associated with hs-CRP that was categorized into low (< 1.0 mg/L), moderate (1.0 to 3.0 mg/L), and high (> 3.0 mg/L) in the current study. Nearly one tenth of females had moderate levels of hs-CRP and more than 1 % of females had hs-CRP larger than 3.0 mg/L. In contrast, only about 4% males had moderate level of hs-CRP and less than 1 % of them had high hs-CRP. Females were more likely to have increased hs-CRP than males. The prevalence of elevated hs-CRP among non-Hispanic Blacks was higher than other non-Black races/ethnicities, which may indicate that non-Hispanic Blacks are at increased risk of developing cardiovascular disease due to elevation of hs-CRP.

Body Mass Index

The mean body mass index (BMI) of the study sample was 27.4 kg/m^2. This falls within the range of BMI (25-29.9 kg/m^2) that defines overweight, according to the World Health Organization (WHO) guidelines (WHO, 2000). Results suggest that subjects in the study sample were at risk for cardiovascular disease and type 2 diabetes, even though they had not yet developed diabetes at the time of NHANES participation.

The average BMI for subjects who were non-Hispanic Blacks was 29.6 kg/m^2 which was slightly higher than the average of 27.9 kg/m^2 for Mexican Americans and the average of 27.0 kg/m^2 for non-Hispanic White subjects. The prevalence rate of obesity among non-Hispanic Black subjects was 43.3%, which was the greatest among the three racial/ethnic groups. Mexican Americans had the second highest

prevalence rate of obesity (29.9%), followed by non-Hispanic Whites (25.2%). These findings are comparable to those reported by the Centers for Disease Control and Prevention (CDC), using data from the Behavioral Risk Factor Surveillance System (BRFSS) surveys conducted during 2006-2008 (CDC, 2009b). According to this CDC's report, the highest prevalence of obesity was found among non-Hispanic Blacks (35.7%), followed by Hispanics (28.7%), and non-Hispanic Whites (23.7%). However, the prevalence rates of obesity estimated from BRFSS 2006-2008 were lower than those evaluated by Ogden et al. (2006) using data from NHANES 2003-2004. The NHANES 2003-2004 study reported that 45.0% of non-Hispanic Blacks were obese as were 36.8% of Mexican Americans, and 30.6% of non-Hispanic Whites (Ogden et al., 2006). The discrepancies in the prevalence estimates for obesity between the BRFSS and NHANES studies may be attributed to measures of height and weight needed for the calculation of BMI. The height and weight in the BRFSS were self-reported; whereas they were measured by trained health technicians in NHANES. The disproportional prevalence rates of obesity across racial/ethnic populations might be explained by culture differences in behaviors related physical activity, food consumption and access to healthy food, and attitudes toward bigger body size (CDC, 2009b).

It was not surprising that insulin resistant individuals had a mean BMI of 33.8 kg/m^2 that met the WHO's definition of obesity (BMI $\geq$ 30 kg/m^2). Previous studies have shown that BMI is positively associated with insulin resistance (Skidmore, et al., 2008) and obesity is a strong risk factor for insulin resistance (Boden & Laakso,

2004). The prevalence of obesity among insulin resistant subjects found in this study was 67.1%, which was much higher than the 16.2% of non-insulin resistant individuals. The conceptual schema of factors thought to be associated with insulin resistance for the current study identifies that obesity is a significant risk factor for insulin resistance (Figure 1). Results from this study provide additional support for this relationship even among nondiabetic adults aged 20-39 years.

Waist Circumference

As an index for central obesity (NCEP ATP III, 2002), waist circumference is the distance around the abdomen between the lower rib cage and hips and is measured with minimal inspiration. Central obesity is defined as waist circumference > 35 inches (88 cm) for women and > 40 inches (102 cm) for men, according to the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) (NCEP ATP III, 2002). The subjects in this study had an average of 92.7 cm waist circumference. The mean waist circumference for males was approximately 4 cm larger than that of females, which is consistent with past literature (Stevens, Katz, & Huxley, 2010). However, females in this study had a mean of 90.5 cm in waist circumference, exceeding the cutoff value (88 cm) for central obesity. In contrast, the average of waist circumference in males was 94.9 cm that was less than 102cm, the cutoff value for central obesity for men. The finding is interesting given that both men and women were overweight as defined by their average BMI, but only women had central obesity. This probably relates to the attributes of the two obesity indexes. The

calculation of BMI is based on weight and height, thus does not account for the distribution of fat, muscle and bone mass; whereas waist circumference is a direct measure of abdominal distance and reflects subabdominal and visceral adipose tissue deposits. Having an overweight BMI but non-central obesity in men may suggest that men in this study probably had more muscles and bone mass but less centrally distributed fat, compared to women.

Similar to the pattern of BMI distributed across race/ethnicity, non-Hispanic Blacks had the largest mean waist circumference (95.1 cm), followed by Mexican Americans (94.3 cm), and non-Hispanic Whites (92.5 cm). Females across race/ethnicity had a mean waist circumference greater than 88 cm with non-Hispanic Black females having the largest waist circumference (97.2 cm). The finding is more interesting in that non-Hispanic Black females had a larger waist circumference (97.2 cm) than non-Hispanic Black males (92.6cm). This result is consistent with those from an earlier NHANES III study conducted among subjects aged 20 years old and above; however, the waist circumference of non-Hispanic Black females in the current study was 4.3 cm larger than that reported in the previous study (Zhu et al., 2005). Moreover, the mean age of the non-Hispanic black females in this study (29.9 years) was about 10 years younger than that of those in Zhu's study (41.4 years). The finding that women had a larger waist circumference than men also was observed in a Japanese population, although the definition of central obesity in this study was > 90 cm for Japanese women and > 85 cm for Japanese men (Japan Society for the Study of Obesity, 2002). More research is needed to examine whether the finding that

non-Hispanic Black females had a larger waist circumference than non-Hispanic Black males is only observed in the age group of 20-39 years.

Significant differences in waist circumference were observed between subjects with insulin resistance and those without insulin resistance. On average, the waist circumference of insulin resistant subjects was 108.8 cm, which was almost 20 cm larger than the average of 88.1 cm for non-insulin resistant individuals. Central obesity was highly prevalent among insulin resistant subjects (73%) relative to the 27.4% of non-insulin resistant subjects. This finding provides support for the positive relationship between central obesity and insulin resistance reported in previous studies (Farin, Abbasi, & Reaven, 2005; Farin, et al., 2006). The conceptual schema of factors thought to be associated with insulin resistance in the current study identifies a positive relationship between obesity and insulin resistance (Figure 1). Study findings provide support for this relationship among nondiabetic adults aged 20-39 years.

Leisure Time Physical Activity

Fewer than 50% of nondiabetic adults aged 20-39 years reported engaging in leisure time physical activity (LTPA) to meet the minimum goal of 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity physical activity per week recommended by the 2008 *Physical Activity Guidelines for Americans* (U.S. Department of Health and Human Services, 2008). About one third of subjects did not participate in any LTPA; only 21% reported participating in a low level of LTPA (<

500 MET min/week). This is concerning as previous research has demonstrated that physical inactivity may increase the risk of insulin resistance (Booth, et al., 2008; Kump & Booth, 2005). Although not fully understood, the proposed underlying mechanism of insulin resistance induced by physical inactivity is that insulin sensitivity for glucose uptake is possibly impaired when less energy-producing substrates are utilized by skeletal muscles because of physical inactivity (Booth, et al., 2008).

Men were more physically active during leisure time than women. More than 53.7% of men reported participating in at least 500 MET minute/week LTPA, compared to only 44.3% of women. The majority of men (41.0%) who were physically active, engaged in a high level of LTPA with a MET minute/week larger than 1000. In contrast, only 29.5% of women participated in a high level of LTPA. The findings are consistent with previous studies that investigated the gender differences in LTPA and found that men in both developed (Martinez-Gonzalez et al., 2001) and developing countries (Azevedo et al., 2007) engaged more time in LTPA, relative to women. Azevedo et al. (2007) explored men and women's main reasons for participating in LTPA and found that about 50% men reported that they participated in LTPA for enjoyment, whereas more women engaged in LTPA because of medical advice from health professionals.

When comparing LTPA across race/ethnicity, non-Hispanic Whites were the most physically active racial/ethnic group with 52.2% reporting participating in ≥ 500

MET minute/week LTPA. In contrast, the most physically inactive racial/ethnic group was Mexican Americans with 62.1% reporting engaging no LTPA or < 500 MET minute/week LTPA, followed by non-Hispanic Blacks (54.6%) and non-Hispanic Whites (47.9%). The findings are consistent with results from previous studies which reported that Mexican Americans and non-Hispanic Blacks were the two racial/ethnic minority groups that were more physically inactive, compared to other racial/ethnic minority groups (Crespo, Smit, Andersen, Carter-Pokras, & Ainsworth, 2000; Marshall et al., 2007). Parallel to the finding that most Mexican Americans were physically inactive was the finding that Mexican Americans had the highest mean BMI. The racial/ethnic disparities in LTPA may be related to different culture perspectives toward to body weight and body size. In addition, the low socio-economic status of minority racial/ethnic groups could restrict their time in participating in LTPA because of long working hours or limit their access to fitness facilities.

LTPA was significantly associated with insulin resistance among nondiabetic adult males and females aged 20-39 years in univariate analyses. The proportions of subjects who engaged in different levels of LTPA between insulin resistant and non-insulin resistant subjects were different. Compared to non-insulin resistant subjects, insulin resistant individuals were more physically inactive, as evidenced by the 56.4% who did not participated in LTPA or participated in LTPA that was less than 500 MET minute/week. In contrast, more than 50% of non-insulin resistant subjects met the recommended physical activity level by U.S. Department of Health and

Human Services (2008). In accordance with results from prior studies (Booth, et al., 2008; Kump & Booth, 2005), physical inactivity was a risk factor for insulin resistance in this study. Interestingly, research has been conducted to investigate the effects of two months of moderate physical exercise on insulin sensitivity among nonobese and nondiabetic individuals. A significant decrease in plasma glucose and insulin levels and an increase in insulin sensitivity were found in the study by Hasbum et al. (2006). They reported that these changes were independent of changes in body weight, BMI, waist-hip ratio, lipid profile, and oxygen consumption. The improved insulin sensitivity may result from increased transportation of glucose transporters 4 (GLU-4) to cellular membrane of the skeletal muscle during physical activity.

Smoking Status

Accumulating evidence has demonstrated that smoking has detrimental effects on many aspects of health, including increased risk of insulin resistance. Even so, smoking behavior is still highly prevalent among the U.S. population. The prevalence of current cigarette smoking among subjects in this study was over 27.6%, which is higher than the 20.6% overall prevalence rate of current cigarette smokers in U.S adults estimated in 2008 (CDC, 2009a) and two times higher than the target 12% for cigarette smoking in *Healthy People 2020* (U.S. Department of Health and Human Services, 2010a). Results indicate that efforts to reduce cigarette smoking should be

strengthened, even though various smoking prevention and smoking cessation programs have been initiated and implemented.

More men in the study smoked than women (33.0% vs 22.5%). The prevalence of smoking among men was about 10% higher than the national estimate of men's smoking rate (23.1%) from 21,781 persons aged 18 years or above in the 2008 National Health Interview Survey (NHIS) (CDC, 2009a). Similarly, the prevalence of smoking among women in the study was about 4% higher than the 18.3% for women estimated from the 2008 NHIS. The definition of current cigarette smoking applied in the 2008 NHIS was the same as the one used in the current study. Therefore, the differences in the prevalence rate of cigarette smoking between the two studies may be related to age variations. The subjects in the current study were aged 20-39 years; while the subjects in the 2008 NHIS were aged 18 years and above. Results suggest that the prevalence of cigarette smoking was higher in the younger age group, regardless of gender.

Variations in cigarette smoking prevalence also were observed by race/ethnicity. Mexican Americans had the lowest prevalence (15.8%), which was approaching the target 12% of *Healthy People 2020*. Non-Hispanic Blacks had a lower prevalence of smoking (25.8%) than non-Hispanic Whites (32.1%). These proportions are consistent with the racial/ethnic estimates of cigarette smoking from the 2008 NHIS (CDC, 2009a). However, non-Hispanic Whites in the current study had a 10% higher prevalence of smoking, compared with non-Hispanic Whites in the 2008 NHIS

(22.0%). Similarly, the prevalence of smoking among non-Hispanic Blacks in the current study was 4.5% higher than the non-Hispanic Blacks who participated in the 2008 NHIS (21.3%). Estimates of smoking prevalence for Mexican Americans in the current study and the 2008 NHIS were the same (15.8%). Again, differences in age ranges between the two studies may have contributed to the discrepancies in the prevalence of smoking in both non-Hispanic Whites and non-Hispanic Blacks. Study findings suggest that younger non-Hispanic Whites and non-Hispanic Blacks had a higher prevalence of smoking than those who were older. In contrast, the prevalence of smoking in younger and older Mexican Americans may not differ.

A significant association between smoking and insulin resistance was observed in the study. Unexpectedly, non-insulin resistant subjects had a 9.2% higher prevalence of current cigarette smoking (29.2%) than insulin resistant subjects (20.0%). This finding differs from the positive association between smoking and insulin resistance found in previous studies (Anan, et al., 2006; Bergman, et al., 2009; Daniel & Cargo, 2004; Ko, et al., 2007). Some suggest that smoking impairs the pathway of insulin action, thus increases the risk of insulin resistance. However, one study found no significant association between active smoking and insulin sensitivity (Henkin, et al., 1999). No study that reported a negative relationship between smoking and insulin resistance was found in the literature. Other contextual information is needed to better explain the negative finding observed in this current study. Inconsistencies in the relationship between smoking and insulin resistance observed across studies warrant further exploration.

Alcohol Consumption

Alcohol consumption was highly prevalent among nondiabetic adults aged 20-39 years in the study with about 90% having had at least 12 drinks in their lifetime. Overall, nearly 80% of subjects were current drinkers who consumed at least 12 drinks in their lifetime and had at least one or more drinks in the past year. This was much higher than the 65% of current drinkers among U.S. adults aged ≥ 18 years of age in the 2009 National Health Interview Survey (NHIS) (U.S. Department of Health and Human Services, 2010b). The differences in the prevalence rate of current drinkers may be attributed to the age range of subjects in the two studies. As reported by the U.S. Department of Health and Human Services (2010b), the proportion of adults who were current regular drinkers decreased as age advanced. About 86% of men were current drinkers, in contrast to 72% of women. Approximately 10% of the subjects in this study were former drinkers, which was lower than the 15% estimated from the 2009 NHIS. Women were more likely to be nondrinkers, former drinkers or light drinkers than men, whereas men were more likely to be moderate or heavy drinkers than women. Results are consistent with those found in the 2009 NHIS (U.S. Department of Health and Human Services, 2010b).

Alcohol consumption varied significantly by race/ethnicity. Specifically, 82% of non-Hispanic Whites were current drinkers compared with 76.3% of Mexican Americans and 70.9% of non-Hispanic Blacks. These rates are higher than the rates reported in the 2009 NHIS. Stratified by drinking levels, non-Hispanic Whites were

more likely to be moderate or heavy drinkers. Mexican Americans were more likely to be light drinkers than either non-Hispanic Whites or Blacks. In contrast, non-Hispanic Blacks were more likely to be nondrinkers. This pattern of alcohol consumption by race/ethnicity found in the current study is consistent with those reported by U.S. Department of Health and Human Services (2010b).

Alcohol consumption was found to be significantly associated with insulin resistance. Eighty percent of non-insulin resistant subjects were current drinkers, compared with 75.2% of insulin resistant subjects. Although significant, the prevalence of current drinkers between non-insulin resistant and insulin resistant subjects did not differ more than 5%. Non-insulin resistant individuals were more likely to be moderate (24.1%) or heavy drinkers (9.1%) than insulin resistant individuals (moderate: 20.1%; heavy: 4.4%). In contrast, insulin resistant subjects were more likely to be light drinkers (50.7%) than non-insulin resistant subjects (47.1%). The rates of nondrinkers between insulin resistant (11.3%) and non-insulin resistant subjects (10.8%) were comparable. The findings from this study are consistent with those from previous studies, which demonstrated a significantly negative relationship between alcohol consumption and insulin resistance (Fueki et al., 2007; Joosten, et al., 2008; Kawamoto et al., 2009; Player, Mainous, King, Diaz, & Everett, 2010). Alcohol consumption, especially moderate levels, may help improve insulin sensitivity, thus, decrease insulin resistance. Kawamoto et al. (2009) evaluated the effect of alcohol consumption on insulin resistance among 678 Japanese community dwelling men and found that the mean log HOMA-IR was significantly

lower in heavy drinkers. They also demonstrated that the effect of alcohol consumption on insulin resistance was independent of BMI. Player, Mainous, King, Diaz and Everett (2010) reported that moderate alcohol consumption can decrease the risk of insulin resistance among subjects with vitamin D insufficiency. Research has explored the mechanisms underlying the relationship between alcohol consumption and improved insulin resistance. A decrease in insulin resistance may be attributed to an elevation in plasma adiponectin associated with alcohol consumption. This proposed mechanism was supported by study findings from Sierksma et al. (2004) and Thamer, Haap, Fritsche, Haering, and Stumvoll (2004).

Although accumulating evidence shows that moderate alcohol consumption can improve the status of insulin resistance and decrease risk of cardiovascular disease (Brinton, 2010), healthcare providers should be cautious in making such a recommendation to patients. Initiating drinking behavior to improve health may wrongly imply that it is appropriate to drink or even drink excessively or irresponsibly. Research also has demonstrated that heavy drinking can cause a myriad of health problems such as elevation of triglycerides, which is one of the biomarkers of increased risk for cardiovascular disease and diabetes (Foerster, et al., 2009). Despite the beneficial effects of alcohol consumption, it is difficult to implement this finding in clinical practice due to lack of appropriate strategies.

Correlations among Independent Variables

The examination of the inter-correlations among independent variables showed small to moderate correlations. As expected, BMI and waist circumference were highly correlated ($r = .92$, $p < .0001$). This finding suggests that BMI may be as effective as waist circumference in identifying 20-39 years old individuals with insulin resistance. Results are consistent with the observation by Farin, Abbasi, and Reaven (2005) that BMI highly correlated with waist circumference among men ($r = .90$) and women ($r = .86$). A high correlation between BMI and waist circumference also was found among school-aged Japanese children (Ochiai et al., 2010) with a correlation coefficient of .94 for boys and .90 for girls.

Relationship between Major Depression and Insulin Resistance

The relationship between major depression and insulin resistance was investigated in univariate and multivariate logistic regression analyses. A significant interaction between gender and major depression was observed; however, no evidence was found to support the role of race/ethnicity on the relationship between major depression and insulin resistance. BMI and waist circumference were examined in separate models to investigate the strength of their relationships with insulin resistance and predicting values. The effect of depression measures on the association between major depression and insulin resistance also was explored. Discussion of univariate and multivariate results are presented by model.

Unadjusted Relationship between Major Depression and Insulin Resistance

Major depression was not significantly associated with insulin resistance in the bivariate logistic regression analysis among nondiabetic adults aged 20-39 years in the current study. This finding is consistent with results of pilot work on the topic, which reported an insignificant relationship between major depression and insulin resistance, using data from National Health and Nutritional Examination Survey (NHANES) 1999-2002 (Shen, et al., 2011). Even though the relationship between major depression and insulin resistance was not significant in either study, the direction of the *B* coefficients for major depression differed. In the current study, a positive *B* coefficient (*B* = 0.14) was found; while a negative *B* coefficient was observed in the pilot study (*B* = -0.01). In the pilot study, major depression was measured by the Composite International Diagnostic Interview (CIDI); whereas in this study, major depression was assessed by the CIDI in NHANES 1999-2004 and the Patient Health Questionnaire 9 (PHQ-9) in NHANES 2005-2008. Differences in depression measures might also have contributed to the inconsistent direction of the *B* coefficients for major depression. A positive *B* coefficient for major depression (*B* = 0.11) when measured by the CIDI and a negative *B* coefficient for major depression when measured by the PHQ-9 were found in the study, when the relationship between major depression and insulin resistance was examined by depression measures. This will be discussed in a later section. Nevertheless, both indicated nonsignificance in the relationship between major depression and insulin resistance.

Adjusted Relationship between Major Depression and Insulin Resistance by Gender

A significant interaction between gender and major depression was observed (B = 1.39, p = .0031) in this study. This finding is consistent with the earlier pilot work (Shen, et al., 2011), which also found a significant interaction between gender and major depression. Results indicate that the relationship between major depression and insulin resistance varies by gender.

Among men, major depression was significantly and negatively associated with insulin resistance, after controlling for age, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, BMI, leisure time physical activity, smoking, and alcohol consumption. The negative association between major depression and insulin resistance among men remained significant in the model when BMI was replaced by waist circumference. Both the B coefficients and odds ratio (OR) for major depression maintained relatively unchanged. The model with waist circumference had a lower -2 log likelihood (18446247) and minimum AIC (18446287), suggesting it is better than the model with BMI (18738539 and 18738579 for -2 log likelihood and AIC respectively) among men.

Results provide support for the significant negative association between major depression and insulin resistance among men found in the pilot study (Shen, et al., 2011). However, findings differ from previous studies that reported a positive relationship between depression and insulin resistance among young Finnish men

aged 18-31 years (Timonen, et al., 2006; Timonen, et al., 2007) and Australian men aged 26-36 years (Pearson, et al., 2010) or no significant relationship among Welsh men aged 45-59 years (Lawlor, et al., 2005).

All of these previous studies were cross-sectional studies with a relatively large sample size (> 1000 subjects). The variations in study findings may be attributed to differences in measurements of depression, definitions of depression, subjects' age range, or the characteristics of subjects. Depression questionnaires such as Beck's Depression Inventory (Timonen, et al., 2007), Hopkins Symptoms Checklist (Timonen, et al., 2006), or the General Household Questionnaire (Lawlor, et al., 2005) measure depressive symptoms, instead of making a clinical diagnosis of major depression. Although the CIDI was used in Pearson et al.'s study (2010), depression was defined as any depression with various degree of severity, including major depression, minor depression and depression otherwise not specified. It was different than the definition of major depression applied in this current study that was based on the diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders,* 4th edition (DSM-IV) (American Psychiatric Association, 1994). Although HOMA-IR also was used to measure insulin resistance in the study by Pearson et al (2010), HOMA-IR scored were log-transformed and used as a continuous variable. Clinical significance of a log-transformed HOMA-IR is difficult to interpret. The significantly higher ratio of mean log-transformed HOMA-IR reported by Pearson et al did not necessarily indicate the presence of insulin resistance. Age differences in subjects between Lawlor et al.'s study (2005) (45-59 years) and this current study (20-39 years)

may also explain the discrepancy in findings. In addition, factors such as low exposure to sunlight among subjects living in northern Finland and stress associated with newly recruited military young men may have mediated the relationship between major depression and insulin resistance and contributed to the inconsistency between the findings (Timonen, et al., 2006; Timonen, et al., 2007). This researcher hypothesizes it is possible that it may be the cumulative effect of insulin resistance over time that leads to depression from continued overactivity of the hypothalamus-pituitary-adrenal (HPA) system. This hypothesis requires further study.

No significant association between major depression and insulin resistance was observed among women in this study, when adjusting for age, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, BMI, leisure time physical activity, smoking, and alcohol consumption. The association between major depression and insulin resistance among women remained nonsignificant in the model when BMI was replaced by waist circumference. The model with BMI had a lower -2 log likelihood (14617758) and minimum AIC (14617798) than the model with waist circumference (14868518 and 14868558 for -2 log likelihood and AIC respectively), suggesting it was the better model than the one with waist circumference among women.

The finding of no association between major depression and insulin resistance among women is consistent with two previous studies (Roos, et al., 2007; Shen, et al., 2011), but contradicted two others (Lawlor, et al., 2003; Pearson, et al., 2010). Roos

et al. (2007) reported no association between insulin resistance and depression among Swedish women aged 50-64 years and similar findings were reported among U.S. women aged 29-39 years by Shen et al. (2011). In contrast, Lawlor et al. (2003) identified a significant negative relationship between depression and insulin resistance among British women aged 60-79 years; whereas Pearson et al. (2010) demonstrated that depression was positively associated with insulin resistance among Australian women aged 26-36 years. It is important to note that the positive relationship between depression and insulin resistance reported by Pearson et al. (2010) became insignificant, after adjustment for covariates such as age, education, polycystic ovary syndrome, fish consumption, and use of antidepressants. The mixed results of the relationship between depression and insulin resistance among women may partially be attributed to age differences, variations in depression measures, and other covariates. Future research is needed to further explore the relationship between depression and insulin resistance among women, especially those at younger age.

Adjusted Relationship between Major Depression and Insulin Resistance by Race/Ethnicity

Surprisingly, the interaction between race/ethnicity and major depression was not statistically significant, although race/ethnicity was significantly associated with insulin resistance and past studies have identified significant differences in major depression by racial/ethnic groups. The hypothesis that the relationship between major depression and insulin resistance varied by race/ethnicity was not supported by

the study findings. This hypothesis could not be examined in the pilot study because of a relatively small sample size for certain racial/ethnic groups. All previous studies that have examined the association between depression and insulin resistance were limited to one racial/ethnic group (i.e., European Caucasians or Asian population). No prior studies were found that investigated the role of race/ethnicity on the relationship between major depression and insulin resistance. Lack of such studies that focus on minority racial/ethnic groups such as non-Hispanic Blacks or Mexican Americans made it difficult to compare and contrast the findings from this study. Even so, this finding was exploratory. Future research that explores the relationship between major depression and insulin resistance among minority racial/ethnic groups are necessary.

Overall, a nonsignificant negative association between major depression and insulin resistance was observed, irrespective of racial/ethnic groups, with adjustment for age, gender, race/ethnicity, systolic blood pressure, triglyceride level, hs-CRP, BMI, leisure time physical activity, smoking, and alcohol consumption. The direction and strength of the relationship remained relatively stable, regardless of obesity index (BMI or waist circumference).

Unadjusted Relationship between Major Depression and Insulin Resistance by Measures of Depression

Major depression, as measured by the Composite International Diagnostic Interview (CIDI), was not significantly associated with insulin resistance, although

the direction of the relationship was positive. Similarly, a nonsignificant relationship was observed between major depression and insulin resistance, when measured by the Patient Health Questionnaire 9 (PHQ-9). However, the strength of the relationship between major depression and insulin resistance when measured by the PHQ-9 was stronger than when measured by the CIDI. This was evidenced by an increase in the *B* coefficient from .11 to .48 and a 50% increase in odds ratio.

No prior studies were found that compared the effects of different depression measures on the relationship between major depression and insulin resistance. In contrast to the CIDI, which is the gold standard for clinical diagnosis of major depression, the PHQ-9 is usually used as a screening tool to identify individuals who are at risk of depression. Although a diagnosis of major depression can be made according to the DSM-IV diagnostic criteria, the PHQ-9 itself does not exclude conditions that can cause depressive symptoms, for example, substance abuse, general medical condition, or bereavement. Therefore, the increased strength of the relationship between major depression, when measured by the PHQ-9, and insulin resistance may be attributed to the underlying medical conditions that caused depressive symptoms, rather than major depression itself. More studies that use gold standard diagnostic tool such as the CIDI to measure major depression are needed to investigate whether a clinical diagnosis of major depression is associated with insulin resistance. When more evidence becomes available, comparison the relationships of insulin resistance to clinical diagnosed major depression and to depressive symptoms may be possible. Otherwise, it is premature to draw the conclusion that the

relationship between depression and insulin resistance found in previous studies may be due to underlying medical conditions.

Adjusted Relationship between Major Depression and Insulin Resistance by Measures of Depression

The study found no significant relationship between major depression and insulin resistance, when measured by the CIDI, after adjusting for age, gender, race/ethnicity, BMI, systolic blood pressure, triglyceride level, hs-CRP, smoking, leisure time physical activity, and alcohol consumption. Interestingly, the direction of the insignificant relationship was inversed after adjustment for the covariates. A similar pattern was observed when major depression was measured by the PHQ-9, controlling for the same covariates. Comparison of the two models found that the strength of the negative relationship between major depression and insulin resistance, when measured by the CIDI was stronger than the relationship when major depression was assessed by the PHQ-9, although neither was statistically significant. The findings suggest a possible mediating suppression effect by the covariates. More studies are needed to further explore this effect of major depression on insulin resistance.

When controlling for waist circumference and other covariates, major depression, as evaluated by the CIDI, was not significantly associated with insulin resistance in the study. The direction of the relationship remained negative but the magnitude of the relationship was reduced relative to the model with BMI. The -2 log likelihood

and AIC were lower in the model with waist circumference, suggesting that it was the better model than the one with BMI.

In comparison, the relationship between major depression measured by the PHQ-9 and insulin resistance also was not statistically significant, after adjusting for waist circumference and the same other covariates. Even though it was nonsignificant, the trend of the association of major depression and insulin resistance unexpectedly reverted to positive. The relatively small sample of those with a positive diagnosis of major depression as measured by the PHQ-9 may have limited the power to detect significance. Thus, this result from the study should be interpreted with caution.

Summary

The 3.8% overall prevalence of major depression found among nondiabetic U.S. adults aged 20-39 years in the study sample was lower than those previously reported. Similarly, the 6.6% prevalence of major depression when measured by the CIDI also was low. The 1.8% prevalence of major depression when measured by the PHQ-9 was surprisingly low. As expected, the weighted prevalence of insulin resistance among nondiabetic U.S. adults aged 20-39 years in the study sample was 22.7%, only slightly lower than the estimated 25% prevalence rate among the general population (Reaven, 1988). Similar to previous pilot work, this study found no significant relationship between major depression and insulin resistance among nondiabetic U.S. men and women aged 20-39 years, but observed a significant negative association

between major depression and insulin resistance in men. Major depression was not significantly associated with insulin resistance among women. The role of race/ethnicity on the relationship between major depression and insulin resistance was not supported by findings from this study. There was no significant variation in the relationship between major depression and insulin resistance by measures of depression. The results of the study support that BMI and waist circumference were significant predictors for insulin resistance. Overall, -2 log likelihood and AIC values were lower for models with waist circumference relative to models with BMI, except among women, suggesting that waist circumference may be a better predictor than BMI, except among women. However, BMI had greater odds ratio for insulin resistance than waist circumference, suggesting a stronger relationship with insulin resistance. Together, results suggest that BMI and waist circumference may be equally effective for identifying insulin resistance among nondiabetic adults aged 20-39 years.

Findings provide support for the positive and significant relationship between insulin resistance and 1) systolic blood pressure; 2) triglyceride level, 3) and obesity as measured by BMI or waist circumference in multivariate analyses among nondiabetic adults aged 20-39 years.

Limitations

There are several limitations to this study that must be acknowledged. Consistent with the disadvantages of using cross-sectional data, this study cannot provide information on the temporal sequence of major depression and insulin resistance. Although various methods and techniques were applied in the National Health and Nutrition Examination Survey (NHANES) to ensure the quality of data, the characteristics of secondary data analyses of existing data induced several of the following limitations to the study.

First, 10 years of the NHANES data (1999-2008) were combined for this study to ensure a large sample size that was appropriate for the proposed statistical analyses. Time factor may have played a role in the study investigation due to a wide range of time elapsed between NHANES 1999-2000 and 2007-2008. Young adults may have become more obese over time.

Second, although 10 years of NHANES data were combined, the sample size (N = 2,265) for the current study was only one-fifth of the eligible adults aged 20-39 years (N = 11,617) who were selected to participate in NHANES 1999-2008. This may limit the generalizability of the study findings to adults aged 20-39 years. The 75.3% response rate to the home interview and health examination can also partially explain the reduction of sample size in this study. More importantly, the significant reduction in sample size was attributed to missing data on measures of major depression, fasting glucose and insulin levels. This is because fasting glucose and

insulin levels were collected from a subsample of the examined sample. However, fasting sample weights provided in NHANES data to account for nonresponse rate and additional sampling stage have been used in the study analyses to produce unbiased statistical estimates of the population.

Third, changes in laboratory methodologies for determining plasma glucose and insulin levels over NHANES periods may have imposed a threat to the internal validity of the study. However, several studies have been conducted by NHANES to compare and contrast the values. In addition, conversion equations were recommended to make the values comparable over the NHANES periods.

Fourth, there were slight changes in the questions on leisure time physical activity between NHANES 1999-2006 and NHANES 2007-2008. Participants in NHANES 2007-2008 were not asked to specify the individual leisure time physical activities in which they engaged. However, calculation of MET minutes/week was performed to minimize the impact of these changes.

Fifth, the changes in the measurement of depression imposed a threat to the internal validity of the study. The CIDI differs from the PHQ-9 that: 1) the CIDI is a clinical diagnostic tool for major depression; 2) it excludes conditions that can cause depressive symptoms such as general medical diseases, substance abuse, or bereavement; and 3) it measures depressive symptoms over the past 12 months, in contrast that the PHQ-9 evaluates symptoms of depression within the past 2 weeks. Despite these differences, the PHQ-9 has been found to be a reliable and valid

measure of depression with a pooled sensitivity of .80 and specificity of .92, in comparison to the CIDI (Gilbody, et al., 2007). In addition, the study applied the DSM-IV diagnostic criteria for major depression measured by the PHQ-9, which parallels the CIDI, hoping to make the data as comparable as possible. The results of investigating the relationship between major depression and insulin resistance separately by measure of depression showed no significant variations. However, separate logistic regression analyses among men and women by measures of depression were not conducted due to insufficient sample size for sub-analyses. In addition, the current study did not examine data on use of antidepressant medications, which could have helped detect subjects who had depression.

Sixth, the NHANES did not contain all the variables of interest for the study. For example, the study could not control for risk factors that were found to be positively associated with insulin resistance such as tumor necrosis factor-α (TNF-α), interleukin (IL)-1 and IL-6. However, hs-CRP, one of the immunoinflammatory cytokines, was examined in this study and included in the regression analyses. Since multiple factors (e.g., common cold or muscle strain) can increase hs-CRP, CDC and American Heart Association (Pearson, et al., 2003) have recommended that measurement of hs-CRP should be conducted on persons who are metabolically stable and have no obvious inflammatory or infectious conditions. Two measurements of hs-CRP should be performed at least two weeks apart and averaged to obtain a more accurate estimate of hs-CRP (Pearson, et al., 2003). However, hs-CRP was measured

for only one time in NHANES data. Therefore, a single-point elevation of hs-CRP may not suggest increased risk for cardiovascular disease.

Seventh, data on race/ethnicity collected in the NHANES were limited to non-Hispanic White, non-Hispanic Black, and Mexican American. Subjects who reported race/ethnicity other than non-Hispanic White, non-Hispanic Black, and Mexican American or reported more than one race/ethnicity were classified into "other" race/ethnicity category. Thus, the study findings could not be generalized to other minority racial/ethnic groups such as Asian Americans.

Eighth, the coefficients of variation (CV) for insulin assay across NHANES periods were relatively higher, in comparison with the CV for glucose assay. By definition, the CV is the ratio of the standard deviation to the mean and can be used to describe dispersion of a variable. The higher the CV, the greater the dispersion is in the variable. The highest range of the CV for insulin assay was found in NHANES 2007-2008 (5.5-8.8%), followed by those in NHANES 1999-2002 (3.3-5.4%), NHANES 2005-2006 (3.4-4.9%), and NHANES 2003-2004 (2.0-4.6%).

Lastly, information on demographic variables (age, gender, and race/ethnicity), health risk behaviors (smoking, leisure time physical inactivity, and alcohol consumption), and the depression questionnaires (the CIDI and the PHQ-9) were self-reported. Self-reported demographic information may be subject to the least bias, in comparison to health risk behaviors and the depression questionnaires. Social desirability bias, the tendency to report responses that are consistent with social

norms and expectations, may have impacted self-reports of health risk behaviors in the study (Davis, Thake, & Vilhena, 2010; Tourangeau & Yan, 2007). Smoking and alcohol consumption may have been underreported, while leisure time physical activity could have been over-reported. Responses to the depression questionnaires could be subject to recall bias, especially for the CIDI, in which participants were required to recall their depressive symptoms over a 12-month period. Despite these possible biases, self-reports continue to be commonly used method to gather information on demographic variables and health risk behaviors in epidemiological research because of its cost-effectiveness.

Besides the limitations induced by secondary analyses discussed above, readers also should note that the homeostasis model assessment for insulin resistance (HOMA-IR) was used to define insulin resistance in the study. The most accurate measurement of insulin resistance is the hyperinsulinemic euglycemic glucose clamp test. However, the clamp test involves complex techniques and is very time - and cost - consuming, so it is unrealistic to conduct the glucose clamp test in large epidemiological studies such as the NHANES. Previous studies have shown that HOMA-IR is highly correlated with the hyperinsulinemic euglycemic glucose clamp test (Bonora, et al., 2000; Lansang, et al., 2001; Wallace, et al., 2004). Even so, there was no consensus on a universal cutoff value of HOMA-IR to define insulin resistance. This is partially due to lack of standardization of the insulin agent. In addition, the cutoff value may vary depending on the characteristics of the studied populations. The most commonly used definition of insulin resistance is the 75

percentile of HOMA-IR among normal healthy population (Balkau & Charles, 1999). However, implementation of the definition is not without difficulties. For practical purpose, some researchers used the 75 percentile of HOMA-IR based on a nondiabetic sample; while others estimated the 75 percentile of HOMA-IR from strictly selected normal subjects. For example, Nakai et al. (2002) defined normal subjects as those who had a BMI < 25 kg/m^2, fasting plasma glucose < 6.1 mmol/L, serum total cholesterol < 5.7 mmol/L, HDL > 1.0 mmol/L, serum triglycerides < 1.7 mmol/L, systolic blood pressure < 130 mmHg, and diastolic blood pressure < 85 mmHg. This would greatly reduce the heterogeneity of the study sample. In this current study, the cutoff value of HOMA-IR to define insulin resistance was derived from the 75 percentile of HOMA-IR (P_{75} = 3.4351) among nondiabetic U.S. adults aged ≥ 20 years old who had data on plasma glucose and insulin levels. This value was comparable to the P_{75} of 3.233 found in the pilot study (Shen, et al., 2011), was relatively lower than the P_{75} of 3.8 in Ascaso et al.'s study (2001), but was fairly higher than the P_{75} of 1.7 reported by Nakai et al. (2002). The strictly and loosely defined normal healthy populations between Nakai et al.'s study and this study could have contributed to the differences. Also, the study by Ascaso et al. (2001) used the 90 percentile rather than 75 percentile as the cutoff value. In previous studies that have examined the relationship between depression and insulin resistance estimated by the HOMA-IR (Lawlor, et al., 2003; Pan, et al., 2008; Timonen, et al., 2007), no specific cutoff values of the HOMA-IR were provided, making it impossible to compare and contrast to the cutoff value found in this study. The variations in

defining normal healthy population and the cutoff value of the HOMA-IR (quartile, quintile, or decile) continue to contribute to the debates.

Subjects with borderline diabetes or prediabetes were classified as having no diabetes in the study. Except for diabetes, subjects in this study were not screened for other comorbidity that might have influenced the findings of the study. It is known that depression is closely associated with hypothyroidism with a prevalence rate of 63.5% among those who had subclinical hypothyroidism (Demartini, Masu, Scarone, Pontiroli, & Gambini, 2010). In addition, the study did not examine pregnancy status of women and could have included subjects who were pregnant. Insulin resistance has been shown to be related to pregnancy, which may result from the significant changes in hormones during pregnancy (Mastrogiannis, Spiliopoulos, Mulla, & Homko, 2009).

The relatively small number of subjects with major depression as measured by the PHQ-9 was a potential limitation to the study. The study adjusted a large number of risk factors for insulin resistance in the multivariate logistic regression analyses relative to the number of with a diagnosis of major depression. This may have limited the power to detect significant relationship between major depression and insulin resistance in the model.

Another possible limitation to the study is that the age range of the study subjects was 20-39 years old. This limits the generalizability of the study findings to other age groups. However, this was the purpose of the study to investigate if the relationship

between major depression and insulin resistance was present among young adults aged 20-39 years.

The use of SAS 9.2 for the statistical analyses may have been a potential limitation to the study. The complex survey design of the NHANES was accounted for by using the survey procedures in SAS 9.2. In contrast, SUDDAN is the software that was designed specifically for survey data and is the ideal statistical program to be used when analyzing survey data like NHANES. Even so, SAS is one of the three programs (SUDDAN, SAS, STATA) that are deemed to be appropriate to use when conducting analyses of NHANES data (CDC/NCHS, 2006a). Furthermore, one study has been conducted to compare results of logistic regression analyses generated by SAS and SUDDAN and found that identical model parameters and variance estimates were produced by SAS and SUDDAN (Chen, 2006).

Recommendations for Further Research

The findings of this study stimulated additional research questions that can be explored in the future research. Recommendations for further research related to depression and insulin resistance are presented by research questions.

The Role of Depression Measures on the Relationship between Major Depression and Insulin resistance

This study examined the relationship between major depression and insulin resistance by measures of depression due to the changes in the instruments over the NHANES periods. Results suggest that the clinical diagnoses of major depression made from a screening tool such as the PHQ-9 may underestimate the diagnoses of major depression made from the CIDI. Moreover, the relatively small sample size that had a positive diagnosis of major depression when measured by the PHQ-9 (30 out of 1,134) may have modified the relationship between major depression and insulin resistance in unknown ways in the study. When data from NHANES 2009-2010 become available, new studies can be conducted to investigate if there is an association between major depression and insulin resistance, when measured by the PHQ-9. Since the PHQ-9 can be used as a diagnostic tool as well as a severity tool, it would be interesting to compare and contrast the models when depression is operationalized as a diagnosis, categorized by severity (mild, moderate, or severe), or even used as a continuous score.

The Role of Age on the Relationship between Major Depression and Insulin Resistance

Exploration of the relationship between major depression and insulin resistance by age categories may provide additional information in understanding if the relationship varies by age. As previous studies reported mixed results from subjects

aged 18-79 years, analyses of the relationship stratified by age categories in one study may reveal additional information that is helpful in explaining the inconsistency of results. Age can be categorized into three groups: young adults (20-39 years), middle-aged adults (40-59 years), and older adults (60-79 years).

The Cutoff Value of the HOMA-IR for Insulin Resistance

Another area that is needed for further investigation is the cutoff value of the HOMA-IR for insulin resistance. The wide variations in the threshold of the HOMA-IR for insulin resistance and factors used to define the general healthy population made it difficult to compare and contrast results across studies. Future research can focus on if the universal definition of insulin resistance by 75 percentile of HOMA-IR among general population should be age-, gender-, or race/ethnicity-specific. Studies also can be conducted to compare and contrast the 75 percentiles of HOMA-IR when general healthy population is defined by different factors. The goal of investigating the cutoff value of the HOMA-IR for insulin resistance is not to find a universal cut point, but make recommendations for the range. In addition, studies can apply more restricted definition of insulin resistance using the 80 or 90 percentile of HOMA-IR to examine if the relationship between depression and insulin resistance varies.

Implications for Theory

The study findings suggest that some risk factors for insulin resistance identified in other populations also are applicable to nondiabetic adults aged 20-39 years. Figure 4 depicts modifications to the conceptual schema of factors thought to be associated with insulin resistance for nondiabetic adults aged 20-39 years. Factors positively associated with insulin resistance in univariate analyses are in bold. Factors negatively associated with insulin resistance in univariate analyses are underlined. Factors positively associated with insulin resistance in both univariate and multivariate analyses are in bold and italicized. Factors negatively associated with insulin resistance in multivariate analyses are underlined and italicized.

Implications for Practice

The insignificant association between major depression and insulin resistance found in the study does not necessarily indicate that individuals with major depression are not at risk for insulin resistance. Similarly, the significant negative relationship between major depression and insulin resistance among men does not imply that men with major depression are protected from having insulin resistance. Previous studies showed that other risk factors of insulin resistance such as obesity and physical inactivity were prevalent among patients with major depression. Thus, particular attention should be paid to patients with major depression who appear to have risk factors for insulin resistance. Assessment of these risk factors may help

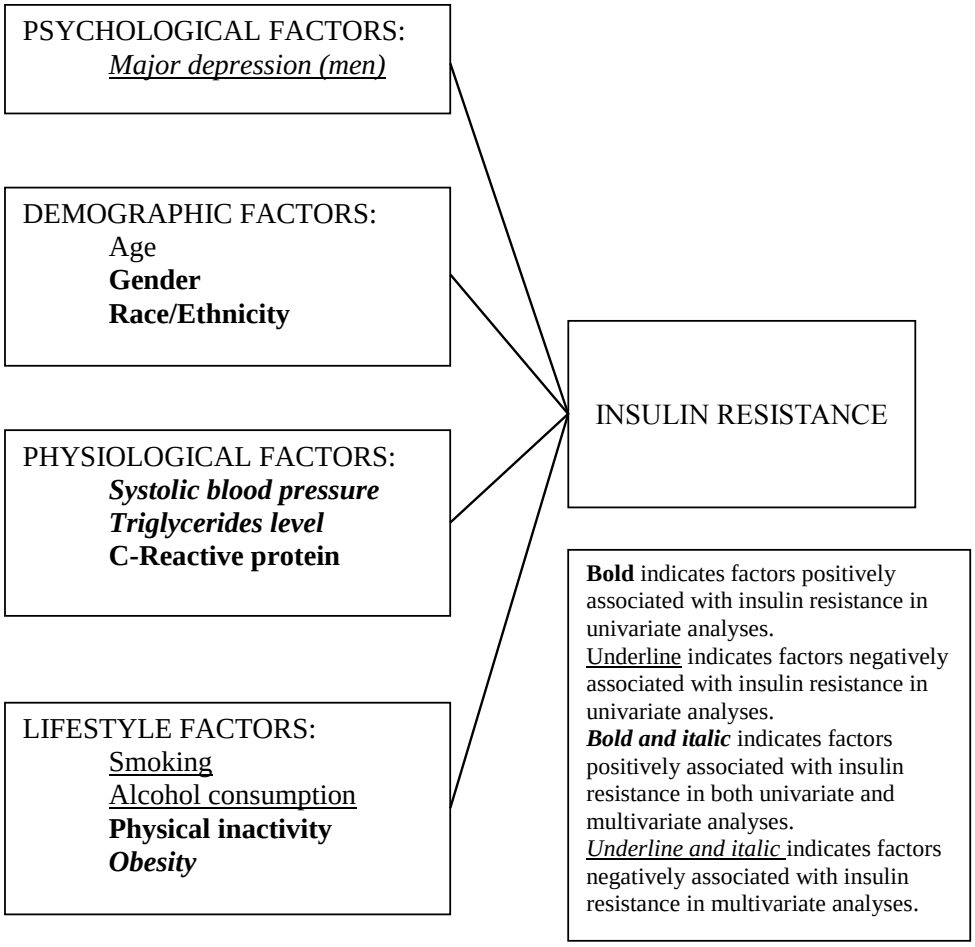


Figure 4. Modified Conceptual Schema of Risk Factors for Insulin Resistance among Nondiabetic Adults Aged 20-39 Years

healthcare providers identify patients at risk for insulin resistance and intervene at an early stage to prevent its progression to type 2 diabetes.

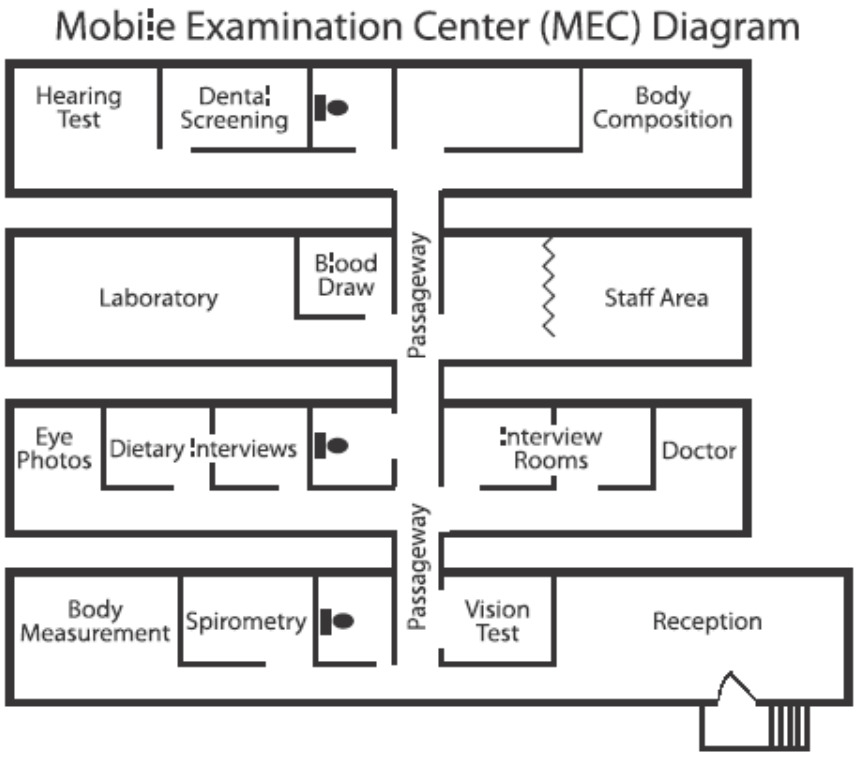
According to the findings of this study, systolic blood pressure, triglyceride level, hs-CRP, BMI, waist circumference, leisure time physical activity, and alcohol consumption were significant risk factors for insulin resistance. Further, the positive associations of systolic blood pressure, triglyceride level, BMI and waist circumference to insulin resistance were independent of other risk factors. Hypertension, high triglyceride level, and obesity or central obesity are the main components of metabolic syndrome. Results from a previous study suggest that behavioral risk factors are usually clustered among individuals (Klein-Geltink, Choi, & Fry, 2006). Multiple exposures to these risk behaviors may potentially strengthen their individual effects on the development of insulin resistance and cardiovascular disease. Identification of persons with one or more of these risk factors can help alert healthcare professionals to target this group of individuals with appropriate interventions. Healthy lifestyle can help decrease the risk of insulin resistance. Nurses are in an ideal position to educate patients the risks of unhealthy lifestyles such as overeating and physical inactivity to the development of insulin resistance. Strategies and intervention should be developed to help patients initiate and make positive changes for healthy lifestyles.

Conclusion

The overall findings of this study suggest that major depression is not associated with insulin resistance among nondiabetic adults aged 20-39 years. However, gender differences in this relationship were observed. No evidence was found to support the role of race/ethnicity in the relationship between major depression and insulin resistance. Study findings provide support for the significant positive relationships between insulin resistance and 1) systolic blood pressure, 2) triglyceride level, and 3) obesity as measured by BMI or waist circumference among nondiabetic adults aged 20-39 years.

APPENDIX A. MOBILE EXAMINATION CENTER (MEC).

National Health and Nutrition Examination Survey (NHANES) Mobile Examination Center



(Source: Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey, 2007-2008 overview. Hyattsville, MD: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. Retrieved from: http://www.cdc.gov/nchs/data/nhanes/nhanes_07_08/overviewbrochure_0708.pdf)

APPENDIX B. COMPOSITE INTERNATIONAL DIAGNOSTIC INTERVIEW - MAJOR DEPRESSION

COMPOSITE INTERNATIONAL DIAGNOSTIC INTERVIEW (CIDI)

12 MONTH MAJOR DEPRESSION

PROGRAMMER: ROTATE WITH ANXIETY SECTIONS. RANDOM 50% OF TIME ASK PANIC AND GAD BEFORE DEPRESSION; THE OTHER 50% OF THE TIME ASK DEPRESSION BEFORE PANIC AND GAD.

COMMENT: THE E1 SERIES IS THE FIRST OF THREE STEM QUESTION SEQUENCES. IF THE RESPONDENT ENDORSES THE FIRST STEM QUESTION AND SAYS IT LASTED MOST OF THE DAY NEARLY EVERY DAY FOR TWO WEEKS WE CONTINUE WITH THAT STEM FOR THE REMAINDER OF THE SECTION. IF NOT, WE GO TO THE SECOND STEM QUESTION SEQUENCE (E2 SERIES). IF R FAILS THIS SECOND CHANCE, WE GIVE A THIRD CHANCE IN THE E2.1 SERIES. ONLY AFTER FAILING ALL THREE CHANCES TO ENDORSE A STEM QUESTION DO WE SKIP R OUT OF THE MD SECTION.

E1. [THIS IS THE INTRO FOR THE 50% WHO START WITH PANIC: The next questions are about periods of being sad or depressed]/[THIS IS THE INTRO FOR THE 50% WHO START WITH DEPRESSION AND THEN GO TO PANIC AND GAD: The next questions are about emotional problems that many people have. The first question is about periods of being sad or depressed.]

(READ SLOWLY.) In the past 12 months, have you had a period of two weeks or longer when you felt sad or depressed or empty?

1. YES
5. NO GO TO E2
8. DK GO TO E2
9. REF GO TO E2

E1a. Think of the two weeks during the past 12 months when this feeling was most persistent. During that two-week period, did you feel sad or depressed or empty every day, nearly every day, most days, about half the days, or less than half the days? (PROBE DK: What's your best estimate? REPEAT RESPONSE CATEGORIES)

1. EVERY DAY
NEARLY EVERY DAY
MOST DAYS
4. ABOUT HALF THE DAYS GO TO E2
5. LESS THAN HALF THE DAYS GO TO E2

DK GO TO E2
REF GO TO E2

E1b. And did this feeling usually last all day long, most of the day, about half the day, or less than half the day? (PROBE DK: What's your best estimate? REPEAT RESPONSE CATEGORIES)

1. ALL DAY LONG
2. MOST OF THE DAY
3. ABOUT HALF THE DAY
4. LESS THAN HALF THE DAY GO TO E2
DK GO TO E2
REF GO TO E2

E1c. (IVR: HAND CARD C TO R.) (NOTE: COMPLEX QUESTION. READ CAREFULLY.) Please look at Card C. People who have periods of being sad, depressed, or empty often have other problems on this list at the same time, like changes in sleep or energy or appetite or concentration or feelings of low self-worth. During the time you were sad, depressed or empty, did you also have any of these other problems?

YES
5. NO GO TO E2
8. DK GO TO E2
9. REF GO TO E2

E1c.1 For the next questions, please think of the two weeks during the past 12 months when you were sad, depressed, or empty and had the largest number of these other problems. During that two-week period, did you lack energy or feel tired all the time nearly every day, even when you had not been working very hard? (IF R SAYS THERE WAS NO SINGLE TWO-WEEK PERIOD THAT STANDS OUT, SAY: Then think of the most recent two weeks of this sort.)

1. YES
5. NO
8. DK
9. REF

E1d. During that two-week period, did you lose interest in most things like work, hobbies, and other things you usually enjoy?

1. YES
5. NO
8. DK

9. REF

E1e. During that two-week period, did you feel irritable or grouchy or in a bad mood most of the time?

1. YES
5. NO
8. DK
9. REF

GO TO E3

COMMENT: THE E2 SERIES IS THE SECOND STEM QUESTION SEQUENCE

E2. (READ SLOWLY) In the past 12 months, have you had a period of two weeks or longer when you lost interest in most things like work, hobbies, and other things you usually enjoy?

1. YES
5. NO GO TO E2.1
8. DK GO TO E2.1
9. REF GO TO E2.1

E2a. Think of the two weeks when this loss of interest was most persistent. During that two-week period, did you lose interest in things every day, nearly every day, most days, about half the days, or less than half the days? (PROBE DK: What's your best estimate? REPEAT RESPONSE CATEGORIES).

1. EVERY DAY
NEARLY EVERY DAY
MOST DAYS
4. ABOUT HALF THE DAYS GO TO E2.1
5. LESS THAN HALF THE DAYS GO TO E2.1
DK GO TO E2.1
REF GO TO E2.1

E2b. And did this feeling usually last all day long, most of the day, about half the day, or less than half the day? (PROBE DK: What's your best estimate? REPEAT RESPONSE CATEGORIES).

1. ALL DAY LONG
2. MOST OF THE DAY
3. ABOUT HALF THE DAY
4. LESS THAN HALF THE DAY GO TO E2.1

DK GO TO E2.1
REF GO TO E2.1

E2c.
CAN: IF E1c = (NO,DK,REF) USE THIS VERSION:
(NOTE: COMPLEX QUESTION. READ CAREFULLY.) Please look at Card C again. People who have periods of losing interest in most things often have other problems on this list at the same time. During the time that you lost interest in most things, did you also have any of these other problems?

ELSE USE THIS VERSION:
(IVR: HAND CARD C TO R.) (NOTE: COMPLEX QUESTION. READ CAREFULLY.) Please look at Card C. People who have periods of losing interest in most things often have other problems on this list at the same time, like changes in sleep or energy or appetite or concentration or feelings of low self-worth. During the time that you lost interest in most things, did you also have any of these other problems?

YES
5. NO GO TO E2.1
8. DK GO TO E2.1
9. REF GO TO E2.1

E2c.1 For the next questions, please think of the two weeks during the past 12 months when you lost interest in most things and had the largest number of these other problems. During that two-week period, did you lack energy or feel tired all the time nearly every day, even when you had not been working very hard? (IF R SAYS THERE WAS NO SINGLE TWO-WEEK PERIOD THAT STANDS OUT, SAY: Then think of the most recent two weeks of this sort.)

1. YES
5. NO
8. DK
9. REF

E2d. During that two-week period, did you feel irritable or grouchy or in a bad mood most of the time?

1. YES
5. NO
8. DK
9. REF

GO TO E3

COMMENTS: THE E2.1 SEQUENCE IS THE THIRD AND FINAL STEM QUESTION SERIES

E2.1. (READ SLOWLY) In the past 12 months, Did you have a period of two weeks or longer when you were irritable or grouchy or in a bad mood most of the time?

1. YES
5. NO GO TO NEXT SECTION
8. DK GO TO NEXT SECTION
9. REF GO TO NEXT SECTION

E2.1a. Think of the two weeks when this bad mood was most persistent. During that two-week period, did you feel irritable or grouchy or in a bad mood every day, nearly every day, most days, about half the days, or less than half the days? (PROBE DK: What's your best estimate? REPEAT RESPONSE CATEGORIES).

1. EVERY DAY
NEARLY EVERY DAY
MOST DAYS
4. ABOUT HALF THE DAYS GO TO NEXT SECTION
5. LESS THAN HALF THE DAYS GO TO NEXT SECTION
DK GO TO NEXT SECTION
REF GO TO NEXT SECTION

E2.1b. And did this feeling usually last all day long, most of the day, about half the day, or less than half the day? (PROBE DK: What's your best estimate? REPEAT RESPONSE CATEGORIES).

1. ALL DAY LONG
2. MOST OF THE DAY
3. ABOUT HALF THE DAY
4. LESS THAN HALF THE DAY GO TO NEXT SECTION
DK GO TO NEXT SECTION
REF GO TO NEXT SECTION

E2.1c.
CAN: IF E1c=(NO,DK,REF) or E2c=(NO, DK, REF), USE THIS VERSION:
(NOTE: COMPLEX QUESTION. READ CAREFULLY.) Please look at Card C again. People who have periods of being irritable or grouchy often have other problems on this list at the same time. During the time you were irritable or grouchy, did you also have any of these other problems?

ELSE USE THIS VERSION:
(IVR: HAND CARD C TO R.) (NOTE: COMPLEX QUESTION. READ CAREFULLY.) Please look at Card C. People who have periods of being irritable or grouchy often have other problems on this list at the same time, like changes in sleep or energy or appetite or concentration or feelings of low self-worth. During the time you were irritable or grouchy, did you also have any of these other problems?

YES
5. NO GO TO NEXT SECTION
8. DK GO TO NEXT SECTION
9. REF GO TO NEXT SECTION

E2.1c.1 For the next questions, please think of the two weeks during the past 12 months when you were irritable and had the largest number of these other problems. During that two-week period, did you lack energy or feel tired all the time nearly every day, even when you had not been working very hard? (IF R SAYS THERE WAS NO SINGLE TWO-WEEK PERIOD THAT STANDS OUT, SAY: Then think of the most recent two weeks of this sort.)

1. YES
5. NO
8. DK
9. REF

E3. CHECKPOINT

CAN: DO NOT RANDOMIZE

E4. (During that two-week period,) Did you have less appetite than usual almost every day?

1. YES
5. NO
8. DK
9. REF

E5. (During that two-week period,) Did you lose weight without trying to?
(IF VOL: "On diet" OR "I tried to lose weight," CODE NO)

1. YES
5. NO IF E4 EQ YES, GO TO E8. ELSE GO TO E6
8. DK IF E4 EQ YES, GO TO E8. ELSE GO TO E6
9. REF IF E4 EQ YES, GO TO E8. ELSE GO TO E6

E5a. How much weight did you lose during that two week period? (IF RESPONSE ≥ 100, ENTER 100. IF RESPONSE = DK, ENTER 998. IF RESPONSE = REF, ENTER 999).

_____ NUMBER OF POUNDS

GO TO E8

E6. Did you have a much larger appetite than is usual for you almost every day during that two weeks?

IF VOL: IF ONLY BECAUSE PREGNANT, CODE NO
IF VOL: ONLY REGAINED WEIGHT LOST, CODE NO

1. YES
5. NO
8. DK
9. REF

E7. (During that two-week period,) Did you gain weight?

1. YES
5. NO GO TO E8
8. DK GO TO E8
9. REF GO TO E8

E7a. How much did you gain during that two week period? (IF RESPONSE ≥ 100, ENTER 100. IF RESPONSE = DK, ENTER 998. IF RESPONSE = REF, ENTER 999).

_____ NUMBER OF POUNDS

E8. Did you have a lot more trouble than usual sleeping for these two weeks -- either trouble falling asleep, waking in the middle of the night, or waking up too early?

1. YES
5. NO GO TO E9
8. DK GO TO E9
9. REF GO TO E9

E8.1. Did this happen every night, nearly every night, or less often during those two weeks?

1. EVERY NIGHT

2. NEARLY EVERY NIGHT GO TO E9
3. LESS OFTEN GO TO E9
8. DK GO TO E9
9. REF GO TO E9

E8a. Did you wake up at least two hours before you wanted to every day during these two weeks?

1. YES
5. NO
8. DK
9. REF

E9. Did you sleep too much almost every day?

1. YES
5. NO
8. DK
9. REF

E22. (During that two-week period,) Did you feel particularly bad when you first got up, but felt better later in the day?

1. YES
5. NO
8. DK
9. REF

E23. (During that two-week period,) Was your interest in sex a lot less than usual?

1. YES
5. NO
8. DK
9. REF

E2.4. (During that two-week period,) Did you lose the ability to enjoy having good things happen to you, like winning something or being praised or complimented?

1. YES
5. NO
8. DK
9. REF

E10. Did you talk or move more slowly than is normal for you almost every day

during these two weeks?

1. YES
5. NO GO TO E11
8. DK GO TO E11
9. REF GO TO E11

E10a. Did anyone else notice that you were talking or moving slowly?

1. YES
5. NO
8. DK
9. REF
GO TO E12

E11. (During that two-week period,) Did you have to be moving all the time -- that is, you couldn't sit still and paced up and down or couldn't keep your hands still when sitting?

1. YES
5. NO GO TO E12
8. DK GO TO E12
9. REF GO TO E12

E11a. Did anyone else notice that you were moving all the time?
1. YES
5. NO
8. DK
9. REF

E12. (During that two-week period,) Did you feel worthless nearly every day?

1. YES
5. NO
8. DK
9. REF

E12a. Did you feel guilty?

1. YES
5. NO
8. DK
9. REF

IF E12 OR E12a = YES, GO TO E12b. ELSE GO TO E13.

E12b. Was there a particular reason for feeling (worthless/or/guilty)? (PROBE: Any other reason?) RECORD OPEN-ENDED RESPONSE

If E12b= DK/REF, GO TO E13.

E12c. INTERVIEWER QUERY: DID R FEEL WORTHLESS OR GUILTY ONLY ABOUT BEING IMPAIRED BY DEPRESSION?

1. YES
NO
8. DK

E13. Did you feel that you were not as good as other people?

1. YES
5. NO
8. DK
9. REF

E14. Did you have so little self-confidence that you wouldn't try to have your say about anything?

1. YES
5. NO
8. DK
9. REF

E15. (During that two-week period,) Did you have a lot more trouble concentrating than is normal for you?

1. YES GO TO E15a
5. NO GO TO E16
8. DK GO TO E15a
9. REF GO TO E15a

E15a Were you unable to read things that usually interest you or watch television or movies you usually like because you couldn't pay attention to them?

1. YES
5. NO
8. DK
9. REF

E16. (During that two-week period,) Did your thoughts come much slower than usual or seem mixed up?

1. YES
5. NO
8. DK
9. REF

E17. (During that two-week period,) Were you unable to make up your mind about things you ordinarily have no trouble deciding about?

1. YES
5. NO
8. DK
9. REF

E18. (During that two-week period,) Did you think a lot about death?

1. YES
5. NO
8. DK
9. REF

E19. Did you feel so low you thought a lot about committing suicide?

1. YES
5. NO GO TO E20.1
8. DK
9. REF

E19a. Did you make a suicide plan?

1. YES
5. NO
8. DK
9. REF

E20. Did you attempt suicide?

1. YES
5. NO
8. DK
9. REF

E20.1 CHECKPOINT
PROGRAMMER: SUM THE FOLLOWING: E1c.1 = YES, E1d = YES, E1e = YES, E2c.1 = YES, E2.d = YES. E2.1c.1 = YES, E4 = YES, E5a GT OR EQ 10, E6 = YES, E7a GT OR EQ 10, E8.1 = 1-2, E9 = YES, E22 = YES, E23 = YES, E2.4 = YES, E10 = YES, E11 = YES, E12c = NO, E13 = YES, E14 = YES, E15 = YES, E16 = YES, E17 = YES, E18 = YES, E19 = YES.

IF SUM IS 0, GO TO THE NEXT SECTION. IF SUM IS GT 0, GO TO E66.

USE THESE PHRASES IN PADDING

E1c.1 = E2c.1 = E2.1c.1	felt tired all the time
E1d	lost interest in most things
E1e = E2d	felt irritable most of the time
E4	had less appetite than usual
E5a	lost weight
E6	had a larger appetite than usual
E7a	gained weight
E8.1	had trouble sleeping
E9	slept too much
E23	were less interested in sex than usual
E2.4	lost the ability to enjoy things
E10	talked or moved more slowly than usual
E11	had to be moving all the time
E12	felt worthless
E12a	felt guilty
E13	felt like you weren't as good as other people
E14	had low self-confidence
E15	had trouble concentrating
E16	had your thoughts come much more slowly than
usual E17	had trouble making up your mind,
E18	thought a lot about death,
E19	thought about killing yourself
E20	attempted suicide

STEM PHRASES FOR PADDING

IF E1b = 1-3	felt sad, depressed or empty most of the time
ELSE IF E2b = 1-3	lost interest in most things
ELSE IF E2.1b = 1-3	were irritable most of the time

E66. (NOTE: COMPLEX QUESTION. READ CAREFULLY.) I'm going to review what you told me. You had a period of two weeks or longer when you (stem phrase)?

IF E20.1 SUM = (1,2,3): ? and also (fill with all phrases endorsed on list).
IF E20.1 SUM ≥ 4: ? . You also had other problems at the same time. For example, you (fill with first 3 phrases endorsed on list), and had other problems you mentioned.

Think about all the weeks in the past 12 months when you (stem phrase) and also had (this/these/some of these) other problem(s) nearly every day. About how many weeks of this sort out of 52 did you have in the past 12 months? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____ NUMBER OF WEEKS

E66.3 CHECKPOINT:

IF E66 LT 2, GO TO NEXT SECTION. IF E66 EQ 2-3, GO TO E24a. IF E66 GT 3, GO TO E24. IF E66 = (DK, REF), GO TO E24.1. IF E66 EQ (51 OR 52), GO TO E24a.

E24. Was this one period of ("NUMBER FROM E66 weeks") in a row, or was it two or more periods that add up to ("NUMBER FROM E66 weeks").
1. ONE PERIOD GO TO E24a
2. TWO OR MORE PERIODS GO TO E25
DK GO TO E26x
REF GO TO E26x

E24.1 Was this one period or was it two or more periods?

ONE PERIOD GO TO E24a
TWO OR MORE PERIODS GO TO E25
8. DK GO TO E26x
REF GO TO E26x

COMMENT: THE E24 SERIES IS ONLY FOR PEOPLE WITH EXACTLY ONE 12-MONTH EPISODE

E24a. Is this period still going on or has it ended?

1. STILL GOING ON
5. ENDED
DK
REF

CHECKPOINT:

IF E24a = (8,9), SET E24a = 1 FOR THIS CHECKPOINT CALCULATION (RETAIN ORIGINAL VALUE IN DATAFILE).

IF E24a = 1 AND E66 = (52 WEEKS, DK, REF), WE KNOW REC = PAST MONTH, BUT WE DO NOT KNOW HOW LONG IT HAS BEEN GOING ON. THEREFORE, WE NEED TO ASK ABOUT DUR: GO TO E24b.

IF E24a = 1 AND E66 = 2-51 WEEKS, WE KNOW REC = PAST MONTH AND WE KNOW DURATION OF EPISODE IS LESS THAN ONE YEAR AND WE KNOW EXACT NUMBER OF WEEKS DURATION. THEREFORE, WE DO NOT NEED TO ASK ANY MORE DURATION OR RECENCY QUESTIONS AND CAN GO TO THE QUESTIONS ABOUT NORMAL BEREAVEMENT AND POSTPARTUM: GO TO E24f

IF E24a = 5 AND E66 = 48-52, WE KNOW IT ENDED IN THE PAST MONTH, WHICH MEANS THAT REC = PAST MONTH. BUT WE DO NOT KNOW HOW LONG IT WENT ON. THEREFORE, WE SHOULD SKIP REC AND GO TO THE DUR QUESTION: GO TO E24e.

IF E24a = 5 AND E66 = 27-47, WE DO NOT KNOW REC COMPLETELY, BUT WE KNOW IT CANNOT BE MORE THAN SIX MONTHS AGO. THEREFORE, WE SHOULD GO TO A TRUNCATED REC QUESTION: GO TO E24c.

IF E24a = 5 AND E66 LT 27, WE DO NOT KNOW REC. THEREFORE, WE SHOULD GO TO THE
REC QUESTION: GO TO E24d.

E24b. How long has this period been going on so far? (IF RESPONSE = DK, ENTER 998, IF RESPONSE = REF, ENTER 999).

_____# OF MONTHS OR YEARS

GO TO E24f

E24c. When did it end -- in the past month or more than a month ago?

1. PAST MONTH GO TO E24f
2. MORE THAN A MONTH AGO GO TO E24e
DK GO TO E24e
REF GO TO E24e

COMMENT:

IF E24c = 1, WE KNOW DURATION REPORTED IN E66 COULD NOT HAVE

BEEN BEYOND THE PAST 12 MONTHS. THEREFORE, WE CAN SKIP THE DURATION

QUESTION AND GO TO THE NORMAL BEREAVEMENT AND POSTPARTUM QUESTIONS: GO TO E24f

IF E24c = 2, WE HAVE NO WAY OF KNOWING WHETHER DURATION WENT BEYOND THE PAST 12 MONTHS. THEREFORE, WE HAVE TO ASK DUR: GO TO E24e.

E24d. When did it end -- in the past month, past six months, or more than six months ago?

1. MONTH GO TO E24f
2. SIX MONTHS GO TO E24f
3. MORE THAN SIX MONTHS AGO GO TO E24e
DK GO TO E24e
REF GO TO E24e

COMMENT:

EVERYONE ASKED E24d HAD A RECENCY LT 27 WEEKS. THEREFORE, IF E24d = 1-2, WE KNOW THE DURATION IN E66 IS WITHIN THE PAST YEAR. THEREFORE, WE CAN SKIP THE DURATION QUESTION: GO TO E24f

IF E24d = 3, WE NEED TO ASK DURATION BECAUSE IT MIGHT HAVE BEEN OUTSIDE THE PAST YEAR. GO TO E24e

E24e. How long did this period go on before it ended? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____# OF WEEKS OR MONTHS OR YEARS

E24f. Did this period begin just after someone close to you died?

1. YES GO TO E24g
5. NO IF MALE, GO TO E24i. IF FEMALE AGE 50+, GO TO E24i. IF FEMALE LT 50, GO TO E24h
DK IF MALE, GO TO E24i. IF FEMALE AGE 50+, GO TO E24i. IF FEMALE LT 50, GO TO E24h
9. REF IF MALE, GO TO E24i. IF FEMALE AGE 50+, GO TO E24i. IF FEMALE LT 50, GO TO E24h

E24g. (IF NEC: Who was it that died?) IF MULTIPLE RESPONSES, RECORD

ONLY FIRST MENTION.

1. SPOUSE
2. CHILD
3. PARENT/SIBLING
4. OTHER RELATIVE
5. NONRELATIVE
DK
REF

GO TO E27

E24h. Did this period begin within a month of you having a baby?

1. YES GO TO E27
5. NO
DK
REF

E24i. Did anything else happen shortly before this period began that might have caused it to happen?

1. YES
5. NO GO TO E27
DK GO TO E27
REF GO TO E27

E24j. (IF NEC: Briefly, what happened?)

GO TO E27

E25. (IF NEC: How many periods?) (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____ NUMBER OF PERIODS

IF E25 = 2, GO TO E25a
IF E25 = 3 OR MORE, GO TO E26x
IF E25 = (DK,REF), GO TO E26x

COMMENT: THE E25 SERIES IS FOR PEOPLE WITH EXACTLY 2 12-MONTH EPISODES

E25a. How many weeks, months or years did the first of these periods go on before

it ended? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____# OF WEEKS OR MONTHS OR YEARS

E25b. Did this first period begin just after someone close to you died?

1. YES GO TO E25c
NO IF MALE, GO TO E25e. IF FEMALE AGE 50+, GO TO E25e. IF FEMALE LT 50, GO TO E25d
8. DK IF MALE, GO TO E25e. IF FEMALE AGE 50+, GO TO E25e. IF FEMALE LT 50, GO TO E25d
9. REF IF MALE, GO TO E25e. IF FEMALE AGE 50+, GO TO E25e. IF FEMALE LT 50, GO TO E25d

E25c. (IF NEC: Who was it that died?) IF MULTIPLE RESPONSES, RECORD ONLY FIRST MENTION.

1. SPOUSE
2. CHILD
3. PARENT/SIBLING
4. OTHER RELATIVE
5. NONRELATIVE
DK
REF

GO TO E25g

E25d. Did this period begin within a month of you having a baby?

1. YES GO TO E25g
5. NO
DK
REF

E25e. Did anything else happen shortly before this period began that might have caused it to happen?

1. YES
5. NO GO TO E25g
DK GO TO E25g
REF GO TO E25g

E25f. (IF NEC: Briefly, what happened?)

E25g. How much time went on between the end of this first period and the beginning of the second? (IF RESPONSE = DK, ENTER 998. IF RESPONSE = REF, ENTER 999).

_____# OF DAYS OR WEEKS OR MONTHS

PROGRAMMER: CONVERT RESPONSE IN E25g TO WEEKS FOR PURPOSES OF LATER CALCULATIONS

IF E25g IS LESS THAN 8 WEEKS, GO T0 E25o. ELSE GO TO E25h

E25h. Did you feel OK for at least two months between the two periods?

1. YES
5. NO
DK
REF

E25i. Between these two periods, did you have at least two months when you were able to carry out your daily activities and enjoy being with other people as much as before the first period began?

1. YES
5. NO
DK
REF

E25o. Is the second period still going on now or has it ended?

1. STILL GOING ON GO TO E25j
5. ENDED
DK GO TO E25j
REF GO TO E25j

E25p. How long did it go on before it ended? (IF RESPONSE = DK, ENTER 998. IF RESPONSE = REF, ENTER 999).

_____# OF DAYS OR WEEKS OR MONTHS

COMMENT

WE CAN NARROW THE RANGE OF UNCERTAINTY ABOUT REC FOR MANY Rs.

IF FIRST EPISODE BEGAN MORE THAN 12 MONTHS AGO, WE CAN CALCULATE REC EXACTLY BY NOTING THAT # OF WEEKS IN EPISODE IN PAST YEAR MINUS DUR OF SECOND EPISODE = DUR OF THE PART OF FIRST EPISODE IN THE PAST 12 MONTHS. ADD THE LATTER TO TIME BETWEEN EPISODES AND ADD THIS TO DUR OF SECOND EPISODE, AND WE KNOW EXACTLY HOW MANY WEEKS AGO SECOND EPISODE ENDED. THEREFORE, IF WE KNOW FIRST EPISODE STARTED BEFORE 12 MONTHS AGO, WE CAN SKIP THE REC QUESTION. THIS CAN BE DONE EXACTLY AS FOLLOWS:

"a". PART OF EPISODE #1 THAT OCCURRED IN PAST 12 MONTHS = E66 - E25p. PROGRAMMER: BE SURE TO SET NEGATIVE NUMBERS EQUAL TO ZERO AT LEAST STAGE BEFORE CONTINUING BECAUSE THERE WILL BE SOME INCONSISTENCY IN REPORTING.

"b". PART OF EPISODE #1 THAT OCCURRED PRIOR TO PAST 12 MONTHS = E25a - PART THAT OCCURRED IN PAST 12 MONTHS.

IF "b" IS GT 0, THEN RECENCY OF EPISODE #2 IN DEFINED EXACTLY IN WEEKS AS [52 - ("a" EXPRESSED IN WEEKS + E25g EXPRESSED IN WEEKS + E25p EXPRESSED IN WEEKS). THEREFORE, IF "b" IS GT 0, SKIP THE REC QUESTION AND GO TO E25j

IF "b" IS 0 (OR NEGATIVE, REMEMBERING TO SET ALL NEGATIVE VALUES TO ZERO), AND ("a" EXPRESSED IN WEEKS + E25g EXPRESSED IN WEEKS + E25p EXPRESSED IN WEEKS) = "SUM" = 48 OR MORE, REC = PAST MONTH. IN THIS CASE, SKIP THE REC QUESTION AND GO TO E25j

IF "B" IS 0 AND "SUM" = 27-47, REC HAS TO BE EITHER ONE MONTH OR SIX MONTHS. IN THI

IF "B" IS 0 AND "SUM" = LESS THAN 27, REC IS UNKNOWN> IN THIS CASE, GO TO THE REC QUESTION: GO TO E25r

E25q. When did it end -- in the past month or more than a month ago?

1. PAST MONTH
2. MORE THAN A MONTH AGO
DK
REF
GO TO E25j

E25r. When did it end -- in the past month, past six months, or more than six months ago?

1. PAST MONTH
2. PAST SIX MONTHS
3. MORE THAN SIX MONTHS AGO
DK
REF

E25j. Did this second period begin just after someone close to you died?

1. YES GO TO E25k
5. NO IF MALE, GO TO E25m. IF FEMALE AGE 50+, GO TO E25m. IF FEMALE LT 50, GO TO E25l
DK IF MALE, GO TO E25m. IF FEMALE AGE 50+, GO TO E25m. IF FEMALE LT 50, GO TO E25l
9. REF IF MALE, GO TO E25m. IF FEMALE AGE 50+, GO TO E25m. IF FEMALE LT 50, GO TO E25l

E25k. (IF NEC: Who was it that died?) IF MULTIPLE RESPONSES, RECORD ONLY FIRST IN LIST.

1. SPOUSE
2. CHILD
3. PARENT/SIBLING
4. OTHER RELATIVE
5. NONRELATIVE
DK
REF

GO TO E27

E25l. Did this second period begin within a month of you having a baby?

1. YES GO TO E27
5. NO
DK
REF

E25m. Did anything else happen shortly before this second period began that might have caused it to happen?

1. YES
5. NO GO TO E27

DK GO TO E27
REF GO TO E27
E25n. (IF NEC: Briefly, what happened?)

GO TO E27

COMMENT: THE E26 SERIES IS FOR Rs WITH 3 OR MORE 12-MONTH EPISODES

E26x. In the past 12 months, what was the longest number of weeks in a row that you felt that way? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).
(RECORD FRACTIONAL RESPONSE ROUNDED TO LOWEST NUMBER OF WEEKS.)

_____ # of weeks

E26. Is the most recent of these (NUMBER FROM E25) periods still going on or has it ended?

1. STILL GOING ON
5. ENDED
DK
REF

CHECKPOINT:

IF E26 = 1, WE KNOW REC = PAST MONTH. SO WE CAN GO TO E26c

IF E26 = 5 AND E66 = 48-52, WE KNOW IT ENDED IN THE PAST 4 WEEKS, WHICH MEANS THAT REC = PAST MONTH. SO WE CAN GO TO E26c

IF E26 = 5 AND E66 = 27-47, WE DO NOT KNOW REC COMPLETELY, BUT WE KNOW IT CANNOT BE MORE THAN SIX MONTHS AGO. THEREFORE, WE SHOULD GO TO A TRUNCATED REC QUESTION: GO TO E26a

IF E26 = 5 AND E66 LT 27, WE DO NOT KNOW REC. THEREFORE, WE SHOULD GO TO THE REC QUESTION: GO TO E26b

E26a. When did it end -- in the past month or more than a month ago?

1. PAST MONTH
2. MORE THAN A MONTH AGO
DK

REF

GO TO E26c

E26b. When did it end -- in the past month, past six months, or more than six months ago?

1. PAST MONTH
2. PAST SIX MONTHS
3. MORE THAN SIX MONTHS AGO
DK
REF

E26c. In between any of these (NUMBER FROM E25) periods were you feeling OK for at least two months?

1. YES, FELT OK BETWEEN EPISODES GO TO E26e
2. NO , DID NOT FEEL OK BETWEEN EPISODES GO TO E26g
DK GO TO E26e
REF GO TO E26e

E26e. Between these periods, did you have at least two months when you were able to carry out your daily activities and enjoy being with other people as much as before the first period began?

1. YES
5. NO
DK
REF

E26g. Think about what was going on in your life shortly before each of your (# from E25) periods of (being sad, depressed, or empty/losing interest in most things/being irritable) in the past 12 months. Did any of these (# from E25) periods occur just after someone close to you died?

1. YES
5. NO FEMALES GO TO E26j, MALES TO E26l
DK FEMALES GO TO E26j, MALES TO E26l
REF FEMALES GO TO E26j, MALES TO E26l

E26h. (IF NEC: Who was it that died?) IF MULTIPLE RESPONSES, RECORD ONLY FIRST IN LIST.

1. SPOUSE

2. CHILD
3. PARENT/SIBLING
4. OTHER RELATIVE
5. NONRELATIVE
DK
REF

E26i. Were all these (# from E25) periods shortly after the death of someone close to you?

1. YES GO TO E27
5. NO FEMALES GO TO E26j, MALES TO E26l
DK FEMALES GO TO E26j, MALES TO E26l
REF FEMALES GO TO E26j, MALES TO E26l

E26j. Did any of these (#from E25) periods in the past 12 months occur within a month of you having a baby?

1. YES
5. NO
DK
REF

E26l. Did anything else happen shortly before any of these periods began that might have caused them to happen?

1. YES
5. NO GO TO E27
DK GO TO E27
REF GO TO E27

E26m. (IF NEC: Briefly, what happened?)

COMMENT: THE E27 SERIES IS WHERE ALL Rs COME BACK TOGETHER NO MATTER HOW MANY EPISODES THEY HAD IN THE PAST 12 MONTHS

E27. Think about how your life and activities were affected in the past 12 months by your (being sad, depressed or empty/losing interest in most things/being irritable) and other related problems. Did these problems interfere with your life or activities -- a lot, some, a little, or not at all?

1. A LOT
2. SOME
3. A LITTLE

4. NOT AT ALL GO TO E28
DK GO TO E27a
REF GO TO E27a

E27a. About how many days in the past 12 months were you totally unable for the whole day to work and carry out your other normal activities because of (being sad, depressed or empty/losing interest in most things/being irritable) and other related problems? You can answer with any number between 0 and 365. (IF RESPONSE = DK, ENTER 998. IF RESPONSE = REF, ENTER 999).

_____ NUMBER OF DAYS

E27a.a3 CHECKPOINT:

IF E27a = 0 GO TO E27b. IF E27a = 1, GO TO E27a.1. ELSE GO TO E27a.2

E27a.1. Did that day occur in the past 4 weeks?
1. YES
5. NO
DK
REF
GO TO E27b

E27a.2. How many of these (# FROM E27a) days occurred in the past 4 weeks? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____ NUMBER OF DAYS

E27b. [Not counting the day(s) you were totally unable to work,] about how many (other) days in the past 12 months did you cut back either on the amount of work you got done or on the quality of your work because of these problems? (Again, you can use any number between 0 and 365.)(IF RESPONSE = DK, ENTER 998. IF RESPONSE = REF, ENTER 999).

_____ NUMBER OF DAYS

E27b.b3 CHECKPOINT: IF E27b = 0, GO TO E27x. ELSE GO TO E27c.

E27c. Thinking about (that cutback day/those # FROM 27b cutback days), on a scale from 0 to 100 where zero means being totally unable to work and 100 means working a full high quality day, what number describes the quantity and quality of your work during (that day/those # FROM E27b days)? (IF RESPONSE = DK, ENTER 998. IF RESPONSE = REF, ENTER 999).

_____ RECORD NUMBER BETWEEN 0 AND 100

IF E27b = 1, GO TO E27c.1. ELSE GO TO E27c.2

E27c.1. Did that cutback day occur in the past 4 weeks?

1. YES
5. NO
DK
REF
GO TO E27x

E27c.2. How many of these (# FROM E27b) cutback days occurred in the past 4 weeks? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____ NUMBER OF DAYS

E27x [Not counting the day(s) you were totally unable to work /(or)/(you cut back on work,) about how many (other) days in the past 12 months did it take an extreme effort to perform up to your usual level at work or at your other normal daily activities because of (being sad/losing interest/being irritable)? (Again, you can use any number between 0 and 365.)

(IF RESPONSE = DK, ENTER 998. IF RESPONSE = REF, ENTER 999).

_____ NUMBER OF DAYS

E27x.x3 CHECKPOINT

IF E27x = 0 GO TO E27d.
IF E27x = 1, GO TO E27x.1 ELSE GO TO E27x.2

E27x.1 Did that day occur in the past 4 weeks?

YES
5. NO
DK
REF

GO TO E27d

E27x.2 How many of these (#FROM E27x) days occurred in the past 4 weeks? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____ NUMBER OF DAYS

E27d. And about how many days in the past 12 months did (being sad/losing interest/being irritable) and other related problems seriously interfere with your personal or social life? (Again, you can use any number between 0 and 365.) (IF RESPONSE = DK, ENTER 998. IF RESPONSE = REF, ENTER 999).

_____ NUMBER OF DAYS

E27d.d3 CHECKPOINT

IF E27d = 0, GO TO E28. IF E27d = 1, GO TO E27d.1. ELSE GO TO E27d.2
E27d.1. Did that day occur in the past 4 weeks?

1. YES
5. NO
DK
REF

GO TO E28

E27d.2. How many of these (# FROM E27d) days occurred in the past 4 weeks? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____ NUMBER OF DAYS

E28. In the past 12 months, did you tell a doctor about (feeling sad, empty, or depressed/losing interest in most things/being irritable)?

PFC PRB 2 3 4 5

E29. Can you remember your exact age the very first time in your life you had a period lasting two weeks or longer of (being sad, depressed, or empty/losing interest in most things/being irritable) and having some of the other problems we reviewed?

1. YES
5. NO GO TO E29.1
8. DK GO TO E29.1
9. REF GO TO E29.1

E29a. (IF NEC: How old were you?) (IF RESPONSE = REF, ENTER 99).

_____ YEARS OF AGE

GO TO NEXT SECTION

E29.1. About how old were you the first time you had a period of this sort? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____ YEARS OF AGE

E29.2. What's the earliest age you can clearly remember a particular time when you had a period of this sort? (IF RESPONSE = DK, ENTER 98. IF RESPONSE = REF, ENTER 99).

_____ YEARS OF AGE

SPLICING RULES

E27b IF E27a = (DK, REF) THEN: INCLUDE OPTIONAL PHRASES USING THE PLURAL FORM.

E27c IF E27b = (DK, REF) THEN: ?those cutback days?; ?those days?

E27x IF E27b OR E27c = (DK, REF) THEN: INCLUDE OPTIONAL PHRASES USING PLURAL FORM

(*Sources:* Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Questionnaire. Hyattsville, MD: U.S. Department of Health and Human Services, Center for Disease Control and Prevention. Retrieved November 1, 2010 from: http://www.cdc.gov/nchs/data/nhanes/cidi_quex.pdf)

APPENDIX C: PATIENT HEALTH QUESTIONNAIRE - 9

DEPRESSION SCREEN – DPQ

Target Group: SPs 12+

05BOX 1

CHECK ITEM 05DPQ.001:

- IF INTERVIEW DONE ONLY WITH SURVEY PARTICIPANT (CODED '1' IN RIQ.005), CONTINUE.
- OTHERWISE, GO TO NEXT SECTION.

05DPQ.010 Over the **last 2 weeks**, how often have you been bothered by the following problems: little interest or pleasure in doing things? Would you say . . .

NOT AT ALL..... 0

SEVERAL DAYS 1

MORE THAN HALF THE DAYS..... 2

NEARLY EVERY DAY..... 3

REFUSED 7

DON'T KNOW 9

05DPQ.020 [Over the **last 2 weeks**, how often have you been bothered by the following problems:] feeling down, depressed, or hopeless?

NOT AT ALL..... 0

SEVERAL DAYS 1

MORE THAN HALF THE DAYS..... 2

NEARLY EVERY DAY..... 3

REFUSED 7

DON'T KNOW 9

05DPQ.030 [Over the **last 2 weeks**, how often have you been bothered by the following problems:] trouble falling or staying asleep, or sleeping too much?

NOT AT ALL..... 0

SEVERAL DAYS 1

MORE THAN HALF THE DAYS..... 2

NEARLY EVERY DAY..... 3

REFUSED 7

DON'T KNOW 9

05DPQ.040 [Over the **last 2 weeks**, how often have you been bothered by the following problems:] feeling tired or having little energy?

NOT AT ALL..... 0

SEVERAL DAYS 1

MORE THAN HALF THE DAYS..... 2

NEARLY EVERY DAY..... 3

REFUSED 7

DON'T KNOW 9

05DPQ.050 [Over the **last 2 weeks**, how often have you been bothered by the following problems:] poor appetite or overeating?

NOT AT ALL..... 0

SEVERAL DAYS 1

MORE THAN HALF THE DAYS..... 2

NEARLY EVERY DAY..... 3

REFUSED 7

DON'T KNOW 9

05DPQ.060 [Over the **last 2 weeks**, how often have you been bothered by the following problems:] feeling bad about yourself – or that you are a failure or have let yourself or your family down?

NOT AT ALL..... 0

SEVERAL DAYS 1

MORE THAN HALF THE DAYS..... 2

NEARLY EVERY DAY..... 3

REFUSED 7

DON'T KNOW 9

05DPQ.070 [Over the **last 2 weeks**, how often have you been bothered by the following problems:] trouble concentrating on things, such as reading the newspaper or watching TV?

NOT AT ALL..... 0

SEVERAL DAYS 1

MORE THAN HALF THE DAYS..... 2

NEARLY EVERY DAY..... 3

REFUSED 7

DON'T KNOW 9

05DPQ.080 [Over the **last 2 weeks**, how often have you been bothered by the following problems:] moving or speaking so slowly that other people could have

noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual?

NOT AT ALL..... 0

SEVERAL DAYS 1

MORE THAN HALF THE DAYS..... 2

NEARLY EVERY DAY..... 3

REFUSED 7

DON'T KNOW 9

05DPQ.090 [Over the last 2 weeks, how often have you been bothered by the following problem]: thoughts that you would be better off dead or of hurting yourself in some way?

INTERVIEWER INSTRUCTION: IF DPQ.090 CODED 1, 2, OR 3, PLEASE COMPLETE MENTAL HEALTH OBSERVATION FOR PHYSICIAN REVIEW AT CONCLUSION OF INTERVIEW.

NOT AT ALL..... 0

SEVERAL DAYS 1

MORE THAN HALF THE DAYS..... 2

NEARLY EVERY DAY..... 3

REFUSED 7

DON'T KNOW 9

05BOX 2

CHECK ITEM 05DPQ.095:

- IF RESPONSE TO ANY OF QUESTIONS 05DPQ.010 – 05DPQ.090 = 1, 2, OR 3, GO TO 05DPQ.100.
- OTHERWISE, GO TO NEXT SECTION.

05DPQ.100

How **difficult** have these problems made it for you to do your work, take care of things at home, or get along with people?

Not at all difficult, ... 0

Somewhat difficult,..... 1

Very difficult, ... 2

Extremely difficult?.....3

REFUSED 7

DON'T KNOW 9

(*Sources*: Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Health and Nutrition Examination Survey Questionnaire. Hyattsville, MD: U.S. Department of Health and Human Services, Center for Disease Control and Prevention. Retrieved November 1, 2010 from: http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/mi_dpq_d.pdf.)

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