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# The relationship among serum levels of manganese superoxide dismutase and mtDNA 8-hydroxy-2'-deoxyguanosine, and dietary antioxidants intake in Type 2 Diabetes

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FLORIDA INTERNATIONAL UNIVERSITY

Miami, Florida

THE RELATIONSHIP AMONG SERUM LEVELS OF MANGANESE  
SUPEROXIDE DISMUTASE AND MITOCHONDRIAL DNA 8-HYDROXY-2'-  
DEOXYGUANOSINE, AND DIETARY ANTIOXIDANTS INTAKE IN  
TYPE 2 DIABETES

A dissertation submitted in partial fulfillment of the

Requirements for the degree of

DOCTOR OF PHILOSOPHY

in

DIETETICS AND NUTRITION

by

Michael Andrew McLean

2014

To: Dean Michele Ciccazzo  
R.Stempel College of Public Health and Social Work

This dissertation, written by Michael Andrew McLean, and entitled The Relationship among Serum Levels of Manganese Superoxide Dismutase and mitochondrial DNA 8-hydroxy-2'-deoxyguanosine, and Dietary Antioxidants Intake in Type 2 Diabetes, having been approved in respect to style and intellectual content, is referred to you for judgment.

We have read this dissertation and recommend that it be approved.

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Fatma G. Huffman, Major Professor

Date of Defense: October 3, 2014

The dissertation of Michael Andrew McLean is approved.

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Dean Michele Ciccazzo  
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Dean Lakshmi N. Reddi  
University Graduate School

Florida International University, 2014

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## DEDICATION

I dedicate this dissertation to my wife Zunilda, my daughter Kasey Diana, my two sons Adrian Luis and Michael (AJ), and my parents. Without their sacrifices, understanding, motivation, and encouragement the completion of this project would not have been possible.

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encouragement and understanding. She always stood with me throughout the good and bad times and for sacrifice and understanding when I was away from the family, whether I am at the university or at the library. And of course, my daughter the princess Kasey Diana McLean and my two sons Adrian Luis McLean and Michael McLean (AJ) who were the men of the house when I am away working on my dissertation.

## ABSTRACT OF THE DISSERTATION

# THE RELATIONSHIP AMONG SERUM LEVELS OF MANGANESE SUPEROXIDE DISMUTASE AND MITOCHONDRIAL DNA 8-HYDROXY-2'- DEOXYGUANOSINE, AND DIETARY ANTIOXIDANTS INTAKE IN TYPE 2 DIABETES

By

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Florida International University, 2014

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Oxidative stress plays a key role in the development of Type 2 Diabetes (T2D). This cross-sectional study examined the relationship among serum levels of manganese superoxide dismutase (MnSOD), 8-hydroxy-2'-deoxyguanosine (8OHdG), dietary antioxidant intakes and glycemic control in African Americans (n=209) and Haitian Americans (n=234) with and without T2D.

African Americans had higher BMI (32.8 vs. 29.3 kg/m<sup>2</sup>), higher energy intake (2148 vs. 1770 kcal), and were more educated as compared to Haitian Americans; all variables were significant at  $p < .001$ . Serum levels of 8OHdG and MnSOD for African Americans ( $1691.0 \pm 225.1$  pg/ml,  $2538.0 \pm 1091.8$  pg/ml; respectively) were significantly higher than for Haitian Americans ( $1626.2 \pm 222.9$ ,  $2015.8 \pm 656.3$  pg/ml; respectively). 8OHdG was negatively correlated with MnSOD ( $r = -.167$ ,  $p < .001$ ) in T2D. Having T2D was negatively correlated with MnSOD ( $r = -.337$ ;  $p < .01$ ) and positively correlated with 8OHdG ( $r = .500$ ;  $p < .01$ ). African Americans and Haitian Americans with T2D had fasting plasma glucose (FPG) levels of  $143.0 \pm 61.0$  mg/dl and



157.6 ± 65.5 mg/dl, and A1C of 7.5 ± 1.8 % and 8.4 ± 2.4 %, respectively. African Americans and Haitian Americans without T2D had FPG levels of 95.8 ± 13.2 mg/dl and 98.7 ± 16.9 mg/dl, and A1C of 5.9 ± 0.4% and 6.0 ± 0.5%, respectively. Dietary intakes of vitamin C and vitamin D were negatively correlated with FPG ( $r = -.21$ ;  $r = -.19$ ,  $p < .05$ ) respectively. Carotenoids negatively correlated with A1C ( $r = -.19$ ,  $p < .05$ ). Lower levels of MnSOD were associated with lower levels of zinc,  $r = .10$ ,  $p < .05$ , and higher levels of carotenoids  $r = -.10$ ,  $p < .05$ . Higher levels of 8OHdG were associated with lower levels of Vitamin D,  $r = -.14$ ,  $p < .01$ , and carotenoids,  $r = -.09$ ,  $p < .05$ .

The results demonstrate greater oxidative mtDNA damage in persons with T2D compared to those without T2D and in African Americans compared with Haitian Americans. The inverse relationship between dietary intake of antioxidants and oxidative stress implies a potential to reduce oxidative stress with diet.

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# **CHAPTER I**

## **INTRODUCTION**

The United States Census Bureau (2009) reported that the Haitian American population in the United States (U.S.) is approximately 830,000, two thirds of whom live in Florida and New York. An intensive search of the literature resulted in very little health care information about the population of Haitian descent and it is unclear how their glycemic control, dietary intake of antioxidants, and oxidative stress biomarkers compare with African Americans. African Americans have higher mean A1C (Kirk et al., 2006; Manickham et al., 2013), lower dietary antioxidants plasma biomarkers (Arab et al., 2011), and increased oxidative stress biomarkers and inflammation (Fairheller et al., 2011; Cook et al., 2013) than whites. There are no studies on glycemic control, oxidative stress biomarkers, or dietary antioxidant in Haitians. In addition, there are no studies that compared African Americans with Haitian Americans with and without Type 2 Diabetes (T2D) as investigated by this study.

Diabetes is of epidemic proportions, and T2D accounts for 90% - 95% of all diabetes cases (Centers for Disease Control [CDC], 2011; O'Brien, Patrick, & Caro, 2000). According to the American Diabetes Association (ADA), there are 23.6 million children and adults in the United States who are afflicted with diabetes, with approximately 50% of whom are not aware that they have the disease. It is estimated that 5-10% of these patients have Type 1 (T1D), or insulin-dependent diabetes, and that the remaining have T2D, or non-insulin dependent diabetes mellitus (NIDDM; ADA, 2013; Demmer et al., 2013). T2D is the focus of the current research.

The prevalence of diabetes in the United States is 8.3%, of which 12.6% of those diagnosed with T2D are of African descent (ADA, 2013; Demmer et al., 2013). In 2007, Rosen et al. investigated the prevalence of T2D in the Haitians. The investigators used fasting glucose to determine the prevalence of T2D and found that the prevalence of T2D was 33% (Rosen et al., 2007) in Haitians in the Miami-Haitian community. A report prepared by The Health Council of South Florida for the Miami-Dade County Health Department (2008) documented that death rates for Blacks were twice that of Whites and Hispanics with T2D. It is clear that health disparity exist between African Americans and Whites. There are gaps in scientific literature regarding health biomarkers in Haitians and it is imperative to investigate the differences observed in the prevalence of T2D in African Americans and Haitians.

Diabetes is clinically diagnosed by the use of a fasting plasma glucose (FPG) test or oral glucose tolerance test (OGTT), and a diagnosis of diabetes is made when the fasting plasma level of glucose is greater than or equal to 126 mg/dl (ADA, 2013). The symptoms that are associated with diabetes are frequent urination, excessive thirst, extreme hunger, unusual weight loss, increased fatigue, irritability, and blurry vision. Diabetes risks may be categorized as either modifiable or non-modifiable. The modifiable risk factors associated with diabetes are high blood glucose, obesity, hypertension, abnormal lipid metabolism, smoking, physical inactivity, and inflammation (ADA, 2013). The non-modifiable risk factors are age, ethnicity, gender, and family history (Vanuzzo, Pilotto, Mirolo, & Pirelli, 2008; Giovannucci et al., 2010).

Oxidative stress plays an important role in the progression of complications associated with diabetes and the severity of the complications may be reduced with dietary antioxidant supplements (Gopaul et al., 2001; Kiss & Szabo, 2005; Rains & Jain, 2011; West, 2000; Daien et al., 2013). Montonen, Järvinen, Knekt, and Reunanen (2004) studied dietary antioxidant intakes and the development of T2D and found a negative relationship between T2D symptoms and dietary intake of antioxidants in the form of food or supplements.

High levels of glucose contribute to an increase in reactive oxygen species (ROS) that up-regulate 8-oxoguanosine DNA glycosylase (OGG1) and decrease manganese superoxide dismutase (MnSOD), both of which are indicators of enzymatic antioxidants (Bolajoko et al., 2008; Ruchko et al., 2011). This effectively induces mtDNA damage, whereby there is an increase in the byproduct mtDNA 8-hydroxy-2'-deoxyguanosine (8OHdG; Bolajoko et al., 2008). 8OHdG is a byproduct of the DNA repair mechanism, which has been used worldwide as a non-invasive method of identifying oxidative DNA damage that can occur both *in vivo* and in cell cultures (Harri et al., 2007; Patel, Bevan, Mistry, & Lunec, 2007; De Iuliis et al., 2009). The mitochondrion also produces superoxide via reverse electron transport, and the body will normally up-regulate the antioxidant enzyme MnSOD to neutralize its damaging effects (Ceriello, 2003; Abraham et al., 2013).

Other studies have shown that riboflavin (Cobianchi et al., 2008; Schramm et al., 2013), n-acetylcysteine (Deneke, 2000), and vitamin E (Clarke, Burnett, & Croft, 2008; Niki, 2013) may all down-regulate the production of reactive oxygen species and assist

the body's antioxidant defense system. As such, the therapeutic use of antioxidant nutrients as food or supplements can prevent oxidative damage (Jat et al., 2013; Landete, 2013).

The mechanism of DNA damage appears to be directly associated with oxidative stress and impairment of mitochondrial oxidative phosphorylation (Lee & Pervaiz, 2011; Suzuki et al., 1999). This impairment and defect results in the generation of the byproduct 8OHdG, which has been documented as a sensitive biomarker of oxidative stress, associated with a biochemical damaging effect on mitochondrial DNA (Ishikawa, Fujioka, Ishimura, Takenaka, & Fujisawa, 2007; Johnston et al., 2010). 8OHdG is the most frequently studied and validated biomarker of oxidative stress damage of the mitochondrial DNA (Cooke, Henderson, & Evans, 2009). 8OHdG has been shown to be stable in blood circulation and is measureable by the Enzyme-Linked Immunosorbent Assay (ELISA) methodology using serum (Breton, Sichel, Bianchini, & Prevost, 2003). There is a strong relationship between serum 8OHdG and creatine, but there is no relationship between serum levels of 8OHdG and urinary 8OHdG (Soini et al., 2011). It is believed that 8OHdG excretion from the urine may be dependent on kidney function, which would justify not using urinary 8OHdG analysis in the T2D population (Soini et al., 2011).

### **Statement of the Problem and Justification of the Study**

The prevalence of T2D in the general population is well documented, and research shows a disproportionate prevalence in ethnic/minority groups (Kim & Caprio, 2011; Richard, Alexandre, Lara, & Akamigbo, 2011), who experience poor outcomes and



increased rates of complications associated with T2D (Richard et al., 2011). There are no studies, however, that looked at 8OHdG and MnSOD in African Americans and Haitian Americans, two ethnically different groups that are normally grouped together. This study provides data on the serum levels of 8OHdG, MnSOD, dietary antioxidant and A1C in African Americans and Haitian Americans. The relationship between these variables was also determined. The literature provides strong evidence of a protective effect of MnSOD on cell apoptosis. Improvement in the deficient level of MnSOD may provide an ameliorative effect on diabetes complications resulting from programmed cell death (Kannan & Jain, 2000; Kowluru, Atasi, & Ho, 2006; Kaminski et al., 2012).

This study also investigated the levels of dietary intake of antioxidants in African Americans and Haitian Americans, in addition to establishing a relationship between dietary intake of antioxidant nutrients and the serum levels of MnSOD. Finally, this study provides valuable information for potential intervention studies on therapeutic approaches (Li & Zhou, 2011) to reduce progressive disorders associated with T2D.

### **Purpose of the Study**

The purpose of this study was to determine the relationship between oxidative stress biomarkers that included mitochondrial DNA damage and serum MnSOD and to explore the relationship between these parameters of oxidative stress and dietary antioxidant intake. Another purpose was to identify whether there are ethnic differences in these biomarkers in participants with and without T2D. The study provides information on dietary intakes of antioxidant nutrients and their relationship with circulating oxidative stress biomarkers in persons with and without T2D.

## **Hypotheses and Specific Aims**

Aim 1: To determine differences in the serum levels of MnSOD and 8OHdG by diabetes status and ethnicity.

Hypothesis 1a: Serum levels of MnSOD will be lower in participants with T2D as compared to those without T2D, independent of ethnicity.

Hypothesis 1b: Serum levels of 8OHdG will be higher in participants with T2D when compared to those without T2D, independent of ethnicity.

Hypothesis 1c: There will be an inverse relationship between serum levels of MnSOD and 8OHdG in participants with T2D, independent of ethnicity.

Aim 2: To determine the relationships of serum MnSOD and 8OHdG with various dietary antioxidants by diabetes status and ethnicity..

Hypothesis 2a: Serum 8OHdG levels will be negatively associated with dietary intake of antioxidants, independent of diabetes status and ethnicity.

Hypothesis 2b: Serum MnSOD levels will be negatively associated with dietary intake of antioxidants, independent of diabetes status and ethnicity.

Aim 3: To examine the relationships of glycemic control (A1C) and fasting plasma glucose levels with various dietary antioxidants in T2D by ethnicity.

Hypothesis 3a: There will be no relationship of A1C with any dietary antioxidants in T2D independent of ethnicity.

Hypothesis 3b: There will be no relationship of fasting plasma glucose level and any dietary antioxidants in T2D independent of ethnicity.

## **CHAPTER II**

### **LITERATURE REVIEW**

#### **Oxidative Stress and Diabetes**

The literature shows that oxidative stress plays an important role in the progression of complications associated with diabetes and that there is the potential to reduce the complications of diabetes via supplementation with antioxidant therapeutics (Gopaul et al., 2001; Kiss & Szabo, 2005; Rains & Jain, 2011; West, 2000; Ren et al., 2013). High levels of glucose contribute to an increase in ROS that up-regulates 8-oxoguanine DNA glycosylase (OGG1) and decreases superoxide dismutase (SOD) (Bolajoko et al., 2008). A decrease in serum levels of SOD reduces the efficiency of neutralizing free radicals, which leads to an induction of mtDNA damage. The result of the mtDNA damage is an increase in the byproduct 8OHdG (Bolajoko et al., 2008; De Iuliis et al., 2013).

In the mitochondria, the reverse electron transport chain produces harmful superoxide radical ( $O_2^-$ ) and other ROS (Wen et al., 2013). The body responds to the production of  $O_2^-$  by up-regulating the antioxidant enzyme SOD in order to neutralize the oxidizing effects from the superoxide (Ceriello, 2003; Di Naso et al., 2011). Antioxidants such as riboflavin, n-acetylcysteine, and vitamin E may down-regulate the production of ROS and assist the body's antioxidant defensive system, which has therapeutic implications (Clarke et al., 2008; Cobianchi et al., 2008; Deneke, 2000; Lee et al., 2013; Landete, 2013).

Endothelial dysfunction and insulin resistance may result from oxidative stress (Pereira et al., 2008; Petocco et al., 2010). Additionally, there is a positive relationship of insulin resistance with 8-epi-PGF2-alpha, an indicator of oxidative stress, among persons with and without diabetes (Gopaul et al., 2001). Gopaul et al. (2001) also examined individuals with diabetes who had endothelial dysfunction, assessed by a non-invasive digital pulse wave photoplethysmography. The finding suggested an increase in arterial stiffness with the duration of diabetes. There was an increase in 8-epi-PGF2alpha in subjects with diabetes when compared to controls without diabetes. 8-epi-PGF2alpha positively correlated with fasting blood glucose, triglycerides, and insulin resistance. Gopaul et al. (2001) showed that, in T2D, development of endothelial dysfunction and insulin resistance are preceded by oxidative stress.

Oxidative stress is considered a common pathway for such health conditions as neurological degenerative disorders, diabetes, and various cancers. A number of studies have documented the role of oxidative stress in T2D and in MetS in both adults and children (Abate, Vatansev, & Erkul, 2004; Baines, 1991; Block et al., 2002; Ren et al., 2013). Ren et al. (2013) observed that ROS may contribute to the T2D by damaging the normal function of islet  $\beta$  cells via apoptosis of mitochondrial structure. Block et al. (2002) found that increased fruit consumption correlated with decreased lipid peroxidation and that the levels of the oxidative stress biomarker malondialdehyde (MDA) positively correlated with inflammation, as determined by C-reactive protein. They also found that oxidative stress biomarkers were inconsistent among races; i.e., African Americans had higher levels of thiobarbituric acid-reactive substances (TBARS), no difference in levels of MDA, and lower levels of Iso-P levels as compared to

Caucasians. The level of oxidative stress appears to correlate with the degree of mitochondrial dysfunction in Asian Indians with T2D compared to healthy controls (Khan et al., 2011).

Khan et al. (2011) studied lymphocytes which were harvested by a density gradient centrifugation technique and were then used for DNA studies and immunophenotyping. The researchers used mtDNA/nDNA as a biomarker for the pathophysiology of the disease. Oxidative DNA damage and cell death were determined via ELISA. In this way, Khan et al. (2011) examined the role of mitochondrial dysfunction in immune pathophysiology and were able to identify a strong association between lymphocytic nuclear DNA damage and T2D as well as an increase in levels of circulating pro-inflammatory cytokines in subjects with T2D as compared to controls. Khan et al. (2011) hypothesized that the inconsistency of oxidative stress biomarkers between ethnicities may be due to differences within an ethnic group. Researchers normally recruit and classify participants into one group based upon shared distinctive physical appearance with ancestral origin, such as African Americans, Afro-Caribbean, and Africans may be classified as Blacks or African Americans. However these ethnic groups may have large health disparities and different associated risk factors which may influence the serum levels of oxidative stress biomarkers (VanEenwyk, 2010).

Three factors that contribute to oxidative stress are an increase in oxidant generation, such as catechols, semiquinones, and reactive quinones; antioxidant protection degeneration; and oxidative damage repair dysfunction. Free radicals that contribute to oxidative stress status (OSS) include, but are not limited to, catechol, 2,3

DHBA, lipid peroxides, reduced glutathione, glutathione peroxidase (GSH-Px), and SOD (Nelson et al., 2006). Oxidative stress factors may contribute to mtDNA damage inside the cell. The byproduct of this DNA damage is an endonuclease repair nucleotide called 8OHdG, which is facilitated by an endonuclease repair enzyme (Nelson et al., 2006).

### **Oxidative Stress and Obesity**

Obesity is the accumulation of excessive fat that have been correlated with increased mortality and health impairment (WHO, 2012). Abdominal fat is a major risk factor for diseases which are related to obesity and BMI, total body fat and waist circumference have been shown to be positively correlated with oxidative stress. It is clear that there is a positive relationship of oxidative stress with obesity, regardless of the etiology of obesity (Savini et al., 2013).

There is evidence of an increased chance of developing health related diseases with increasing obesity and BMI, and these findings are higher among some ethnic groups (Pan et al., 2004; Shai et al., 2006). Since BMI is correlated with oxidative stress levels and Vimalananda et al. (2011) reported that Haitians had lower mean BMI than African Americans, determining the relationship between oxidative stress levels in these two ethnic groups is warranted.

### **Oxidative Stress and Dietary Antioxidants**

It has been proposed that the root cause and complications of T2D is associated with oxidative stress and that dietary intakes of antioxidants nutrients have been shown to have beneficial effect on the body's natural defense mechanisms by inhibiting ROS (Han

et al., 2007) and preventing mitochondrial dysfunction. Published studies have shown that accumulated oxidative stress biomarkers and free radicals damages lipid membranes, DNA and influences insulin resistance and  $\beta$ -cell dysfunction (Morris, et al., 2002; Ceriello et al., 2004; Wright Jr. et al., 2006) and there is growing body of evidence to support the theory that oxidative stress may be reduced by dietary antioxidant intakes (Frei, 2004; Siedlak et al., 2009; Mullner et al., 2013 ).

In the review by Frei, a number of studies have shown that dietary antioxidants such as vitamin C, E,  $\beta$ -carotene provide protection against ROS in various biological systems. He reported that several case-controlled studies have shown an increase in the DNA oxidation marker, 8OHdG, in subjects with certain types of cancers, cigarette smokers, and persons with diabetes and suggested that dietary antioxidants may be a viable therapeutic option. His suggestion was supported by a number of observational studies that reported an inverse relationship between dietary antioxidant intake and oxidative DNA damage.

Another dietary antioxidant that has been well studied and has been shown to be inversely correlated with oxidative stress is vitamin D. It has been reported that vitamin D deficiency have been correlated with an increased risk of cardiovascular disease and have been reported to be associated with obesity (Codoner-Franch et al., 2012; Earthman, et al., 2012; Alemzadeh et al., 2008; Pacifico et al., 2011). Codoner-Franch et al. (2012). The researchers studied the relationship between relationship of vitamin D and oxidative stress biomarkers in Caucasians. Overall, these researchers found a significant relationship of insufficient vitamin D levels and obesity, a risk factor for T2D.



Similarly, Gradinaru et al. (2012) studied vitamin D status and oxidative stress in T2D and reported an inverse relationship of vitamin D status with oxidative stress biomarkers.

Siedlak et al. (2009) studied the effect of a diet rich in alpha-lipoic acid in a mouse model expressing amyloid- $\beta$  protein precursors. The oxidative stress biomarkers used in this study was heme-oxygenase -1 and 4-hydroxynonenal. The researchers reported a significant decrease in the level of these oxidative stress biomarkers in the animals fed the diet of alpha-lipoic acid compared to wild-type mice which served as controls.

Mullner et al. (2013) studied the effect of vegetables and PUFA-rich plant oils on DNA strand breaks in T2D subjects. Diabetes and non-diabetes participants were assigned to either a intervention or control group. Participants from the intervention group were provided vegetable rich and PUFA-rich oils. Blood samples were collected at baseline, and at 4, 8, and 16 weeks and oxidative stress assessment was conducted to determine DNA damage in mononuclear cells. The study showed that participants with diabetes had statistically significant reduced levels of DNA strand breaks and it appears that the healthy oils provided some protection to the DNA in the participants with diabetes.

Other research provided evidence of an association between diet and oxidative stress and the possible role of dietary antioxidants in the reduction of complications associated with T2D. Additionally, some foods may have powerful antioxidant properties which have been reported to have health benefits such as the Mediterranean diet (Savini et al., 2013). The effect of this diet on health conditions is related to the

dietary benefits from fruits, vegetables, whole-grains, nuts, fish, moderate wine consumption and olive oil. A study by Ortega-Azorin et al. (2012) provided evidence that dietary patterns were more beneficial than specific foods and that adherence to one such dietary pattern, the Mediterranean diet, provided the health benefits of a high quality diet.

The dietary intake of antioxidant foods or supplements may reduce oxidative stress and, subsequently, lessen mtDNA damage (Weissenberger et al., 2010). Generally it is believed that the identification of dietary factors that play a key role in the protection of the mitochondria and the alleviation of symptoms associated with diabetes is crucial to the development of preventive measures. Due to the variability in ethnic dietary choices and food preparation, it is important to determine whether there are ethnic differences in oxidative stress biomarkers and mtDNA damage. There are few published studies on the relationship of antioxidant nutrient intake and mtDNA damage among different ethnic groups. This study identified the differences in dietary intakes of antioxidants for African Americans and Haitian Americans and also investigated the relationships between the dietary antioxidants and oxidative stress biomarkers.

### **Oxidative Stress and Biochemical Mechanism**

There is convincing clinical and experimental evidence of the biochemical mechanism of oxidative stress. Experimental evidence establishes that there is a significant reduction in glutathione levels and erythrocyte CuZn-SOD activity in individuals with diabetes, with or without cardiovascular disease (CVD) (Chen, Osio, & Anderson, 1999; Chatuphonprasert et al., 2013). The underlying mechanism of oxidative

stress is a reduction of oxygen ( $O_2$ ) that can have reversible or irreversible effect on cells, organs, or tissues. This biochemical effect results from intermediate compounds that are produced from the reduction of  $O_2$ , which produces  $O_2^-$ , hydrogen peroxide, and hydroxyl anions.

There is strong evidence that oxidative stress is increased by several physiological conditions such as hyperglycemia, exposure to environmental pollutants, and the generation of ROS by DNA during its normal biochemical functions (Poljsak & Fink, 2014). Oxidative Stress may also be generated from different sources in the body such the oxidation of polyunsaturated fatty acid (PUFA; West, 2000; Bae et al., 2011) and calcified regions of stenotic aortic valves and atherosclerotic arteries (Miller et al, 2008).

In the mitochondrial membrane, ROS is generated during the production of nicotinamide adenine dinucleotide phosphate (NADPH) and catalyzed by the enzyme NADPH oxidase (Bae, 2011). There are two biochemical pathways for the production of NADPH. The first pathway is the hexose monophosphate shunt, where the insulin-induced enzyme glucose-6-phosphate-dehydrogenase (G-6PD) is required to oxidize glucose-6-phosphate (G-6P) to produce 6-phosphogluconate. The second pathway is driven by another insulin-dependent enzyme, 6-phosphogluconate dehydrogenase (6-PGD), to oxidize 6-phosphogluconate, which produces more NADPH. The enzyme isocitrate dehydrogenase (ICD) is critical to the oxidative decarboxylation of isocitrate to alpha-ketoglutarate, utilizing either  $NAD^+$  or  $NADP^+$  as cofactors. In a rat model, superoxide dismutase (SOD) inactivates the NADP-dependent isocitrate dehydrogenase (ICD), resulting in a statistically significant reduction in ICD activity (Batini-Haberle &

Benov, 2008). Since  $\text{NAD}^+$  and  $\text{NADH}^+$  are both key components of cellular respiration and energy metabolism, then a reduction in ICD activity would profoundly affect apoptosis and increase oxidative stress levels.

Batini-Haberle & Benov (2008) studied the reduction in ICD activity levels and found that it was due to the neutralizing and reducing effects of SOD on the production of NADPH. NADPH, a reducing agent, is involved in immunological reactions in immune cells and in respiratory burst reactions where there is a production of ROS. A similar mechanism is observed in immune response to the presence of bacteria or fungi in the blood stream (Omori et al., 2008). In persons with diabetes, it is observed that neutrophils which participate in the respiratory burst require priming by NADPH oxidase (Omori et al., 2008). Abnormal insulin production will impair the hexose monophosphate shunt and reduces the rate of NADPH production. This reduction in NADPH influences the oxidative defense systems, e.g., the glutathione peroxidase and catalase enzymatic system (Bono, 1987). This is because NADPH plays a crucial role in the activities of enzymes such as catalase and SOD, which are anti-oxidative defense systems whose function is to reduce ROS. The effect of the impairment is the elevation of the levels of serum ROS, which results in oxidative cell damage (Bono, 1987).

Miller et al. (2008) studied the biochemical mechanism that may contribute to the stenotic aortic valves and atherosclerotic arteries and he found that a major contributor is the activity of uncoupled nitrous oxide species (NOS). In addition, uncoupled nitrous oxide contributes to the production of superoxide and ROS and may assist in the disruption of cell membranes, proteins, lipids, and cellular constituents. The

mitochondrion is a cellular component that is responsible for a vast majority of ROS production (Bae, 2011).

### **Diabetes and Manganese Superoxide Dismutase (MnSOD)**

The major defense from free radical damage in the mitochondria is provided by the manganese superoxide dismutase (MnSOD), which is an enzyme unique to the inner mitochondrial space (Curtis et al., 2007). Manganese superoxide dismutase is regarded as the most powerful enzyme in the defense against active oxygen species, producing hydrogen peroxide and oxygen (Curtis et al., 2007). The mitochondria are the source of superoxide, which has been shown to be a major contributor to the progression of diabetes complications in persons with diabetes (Kowluru et al., 2006).

There is evidence that MnSOD may provide protection to diabetic cardiomyopathy in a diabetic mouse model by reducing ROS and improving mitochondrial function (Shen et al., 2006). The researchers identified that ROS participate in diabetes-induced heart muscle apoptosis, and they reported that this pathology was preventable with adequate antioxidants.

Manganese superoxide dismutase (MnSOD) is an enzyme that is encoded by a single-copy gene. Its expression is controlled by the GC-rich promoter region that contains numerous specificity protein 1 (SP-1) and activating protein 2 (AP-2) binding sites (Hitchler, Oberley, & Domann, 2008). Hitchler et al. (2006) have shown that the MnSOD expression is regulated by epigenetic factors rather than just variations in DNA sequence. This enzymatic regulatory mechanism may provide an explanation of the

reduction in MnSOD enzyme activity and that its production is influenced by both genetic and environmental factors (Hitchler et al., 2006).

Madsen-Bouterse, Zhong, Mohammad, Ho, and Kowluru (2010) conducted research on retinal endothelial cells and found evidence for the protection of mitochondrial DNA by the nuclear specific enzyme MnSOD. The researchers examined the DNA damage caused by hyperglycemia using a q-PCR method and identified the genes which were expressed using RT-PCR methodology. Madsen-Bouterse et al. (2010) found that there was an increase in mtDNA damage in retinal endothelial cells which were exposed to hyperglycemia and that MnSOD play a significant role in preventing mtDNA damage. A similar protective role of MnSOD on mtDNA damage was reported by Sadi, Eryilmaz, Tutuncuoglu, Cingir, and Guray (2011). In another study (Zhong & Kowluru, 2011) that used rats, the results indicated that hyperglycemia reduced MnSOD activity, which, in turn, resulted in a 60% decrease in gene transcription. Overall, there are few studies that examine the relationship between MnSOD and mtDNA damage, and most were conducted using cell cultures or animal models. Because these experimental designs used animals, it is not known whether the results are generalizable to humans.

In an animal study, Kowluru et al. (2006) investigated the effects of diabetes complications in MnSOD-transfected rats. Wister rats were caused to be diabetic with the use of streptozotocin and were maintained as such through the 11-month duration of the study. The control group of transfected rats was fed a diet that was void of the antioxidant lipoic acid, while the experimental group had a diet that was supplemented with lipoic acid. Both groups were fed for 11 months, after which time they were

sacrificed, and the retina was harvested and serum was collected and stored for analytical studies. The researchers used commercially available ELISA kits to determine MnSOD activity and 8OHdG levels; they also determined the development of retinopathy by pathological examination of the harvested retina. They observed an increase in the level of MnSOD and the progression of diabetic retinopathy in MnSOD-transfected rats when compared to the non-transfected rats.

In the same study Kowluru et al. (2006) also examined the effect of lipoic acid therapy on the MnSOD activity in the rats with diabetic retinopathy. They found a significant decrease in the enzymatic activity of MnSOD within the mitochondria of diabetic rats compared to rats without diabetes. In addition, there was similar cytosolic SOD activity between diabetic rats and non-diabetic rats. A statistically significant increase in the MnSOD level in the plasma of rats that consumed diets with lipoic acid was also found. They concluded that there was a decrease in oxidative stress in the lipoic acid-supplemented group, as determined by a decrease in 8OHdG level.

Garcia-Ramirez et al. (2008) have shown that subjects with diabetes, with or without CVD, had significantly reduced SOD activity when compared to a control group. The participants with diabetes were in the late stages of diabetes complications. Mitochondrial DNA was then determined via a real-time peripheral blood mononuclear cells (PBMC). MnSOD activity was determined from homogenized PBMC via an assay that measured inhibition of the reduction of cytochrome C by moving oxygen. Mitochondrial DNA damage and mitochondrial content were used as indicators of the

degree of oxidative stress. MnSOD activity was used as a mitochondrial antioxidant defense index.

Mitochondrial DNA damage was significantly greater in the subjects with diabetes than without diabetes. MnSOD activity was significantly increased in the peripheral blood mononuclear cells (PBMC) of persons with T2D, as compared to the controls without diabetes. The researchers concluded that the increased MnSOD activity was due to an adaptive response to oxidative stress. Overall, the results showed that there was a reduction in mtDNA damage due to the degree of mtDNA oxidation (a result of oxidative stress) and that MnSOD was up-regulated as a response to the oxidative DNA damage.

The literature shows that there is an inverse relationship between serum MnSOD levels and T2D complications; i.e., the over production of serum levels of MnSOD levels were observed in subjects with diabetes complications as compared to subjects without diabetes complications. There is accumulating evidence that mitochondrial substrate sensitivity is increased in the skeletal muscle of subjects with T2D when compared to subjects without T2D. A decrease in mitochondrial substrate sensitivity correlates with reduced extracellular MnSOD levels (Larsen et al., 2011). In addition, it appears that mitochondria do not function efficiently in the skeletal muscle of subjects with T2D, and the size of the mitochondria, as measured by electron microscope, is smaller than that seen in a control group (Kelley, He, Menshikova, & Ritov, 2002).



There were no recent studies found in the literature that evaluated the relationship between the serum levels of MnSOD and either African American or Haitian American subjects with and without T2D.

### **Diabetes and 8-hydroxy-2'-deguanosine (8OHdG)**

Diabetes contributes to numerous health complications such as neuropathies, blindness, and macular degeneration. The major mechanisms that cause the complications are the activation of protein kinase C (PKC), advanced glycation end products (AGE), and an increase in polyol and hexosamine pathway flux (Rolo & Palmeira, 2006). The progression of diseases which are associated with T2D may be due to mutations in the mtDNA and mtDNA copy reduction. Rolo and Palmeira (2006) have shown an association between the mitochondrial nuclear-encoded glucose transporters, glucose-stimulated insulin secretion, and nuclear-encoded uncoupling proteins.

One of the effects of oxidative stress is the damage to the mitochondria. The damage is associated with an increase in mitochondrial reactive oxygen and the generation of nitrogen species, i.e. Nitrogen oxide. MnSOD plays a key role in the protection of the mtDNA damage from oxidative stress (Li & Zhou, 2011). Lumini, Magalhaes, Oliveira, and Ascensao (2008) stated that the dysfunction of the mitochondria produces reduced uncoupling proteins (UCPs). UCPs are located in the inner membrane of mitochondria that function as transporters. UCP1 is predominantly found in brown adipose tissue and is involved in respiration, UCP2 is ubiquitous and is highly expressed in the lymphoid system, and UCP3 is solely expressed in skeletal muscle and heart. The UCP2 that is expressed in the pancreas has been linked to hyperinsulinemia (Fleury et al.,

1997). In addition, under-expressed UCP2 is associated with a reduction in glucose-induced insulin secretion (Saleh, Wheeler, & Chan, 2002). Lumini et al. (2008) indicated that exercise may reverse the mitochondrial defect, but the mechanism by which this occurs is not clearly understood. This finding was corroborated by Jun et al. (2009) in a study of male and female Koreans between the ages of 20 and 70 years. From the 1,500 subjects, the researchers collected data on dietary intake, physical activity, anthropometrics, and biochemical analysis, including single-nucleotide polymorphism genotype, using fasting blood specimen. Low physical activity was correlated with under-expression of UCP2, BMI, and waist circumference. The polymorphism in the UCP2 gene was related to T2D.

In hyperglycemic subjects, elevated levels of oxidative stress contribute to the progression of diabetes complications. Research has shown an association between diabetes complications and mitochondrial DNA damage (Madsen-Bouterse et al., 2010; Kowluru et al., 2006). The effect of oxidative stress on the mitochondria is evidenced by an increase in the conversion of deoxyguanine (dG) to 8OHdG in DNA (Suzuki et al., 1999; Xu et al., 2004). Suzuki et al. (1999) investigated mtDNA4977 deletion in muscle DNA and 8OHdG content in diabetes and found that there was an increase in delta-mtDNA4977. The study showed that an increase in mtDNA4977 was proportional to the severity of the diabetes complications. The study also showed that increased 8OHdG was related to the severity of diabetes complications (Suzuki et al., 1999). The mechanism of DNA damage appears to be directly associated with oxidative stress and defects in the mitochondrial oxidative phosphorylation (Lee & Pervaiz, 2011; Suzuki et al., 1999).

## **Diabetes and Diet**

According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDKD), the improvement of the quality of the diet may reduce the risk of T2D by lowering blood glucose and cholesterol levels, lower BMI, and in some cases it is preventable by early detection of insulin resistance and subsequent high quality dietary intervention. In persons with T2D, the risk of T2D may be reduced by including daily exercise and physical activity, abstaining from smoking and alcohol, and maintaining a healthy weight, and dietary management (Martin-Timon et al., 2014; ADA, 2013; Izandi et al, 2013). Of these cofactors of T2D, dietary management is probably the most difficult therapeutic intervention for individuals with T2D (Evert et al., 2014).

Several studies have demonstrated that T2D may be prevented with dietary modifications and lifestyle changes (Bazzano, Serdula, & Liu, 2005; Caro, Ward, & O'Brien, 2002; O'Brien et al., 2000; Tuomilehto et al., 2011). According to Bazzano et al. (2002), the development of T2D may be influenced by a combination of environmental factors, such as low dietary fiber and high fat intakes, high glycemic index and high glycemic load of the diet, being overweight or obese, and physical inactivity. Tuomeliheto et al. (2011) observed that T2D may be prevented when several lifestyle targets were followed, such as loss of weight, decrease fat intake, increase dietary fiber intake, and increased physical activity. Participants who followed a healthy diet had favorable health outcomes.

A healthy diet is defined as being of high quality when it includes whole grains, healthy fats and proteins, unrefined foods, and fruits and vegetables (Akbaraly et al.,

2011; McCullough et al., 2002; Larsen et al., 2010). Harvard School of Public Health provided evidence that eating more whole grains, fruits, and vegetables will reduce the risk of T2D by 20 percent (ADA, 2014). In this study, the researchers determined the quality of diet with the use of the 110-point Alternate Healthy Eating Index 2010.

The inability to follow a recommended high quality diet may be influenced by ethnic culture, lifestyles, and beliefs (Anderson-Loftin et al., 2005). African Americans (Liburd, 2003) and Haitian Americans may find it challenging to follow a high quality diet because of cultural and ritualized nature of food choices and socio-economic status (Huffman et al, 2013). The adherence to a high quality diet has been shown to influence glycemic control in African American women with T2D (Skelly et al., 2009) and thereby the possible delay of the onset of complications (ADA, 2013).

The effect of diet and environmental factors on the progression of disorders associated with T2D has been well documented (Kallio et al., 2007; Tuomeliheto et al., 2011). In the Kallio et al. (2007) study, participants had a body mass index (BMI) ( $\text{Kg/m}^2$ ) of 26-40, were between the ages of 40 and 70, and satisfied at least three criteria for a diagnosis of MetS, using National Cholesterol Education Program (NCEP, 2011) guidelines. The researchers examined the effect of a carbohydrate-modified diet on gene expression in abdominal subcutaneous adipose tissue and on glucose and insulin metabolism (Kallio et al., 2007). A diet comprised of rye-pasta influenced gene expression by down-regulating genes linked to insulin signaling, which resulted in a 21% decrease in the cell size of adipocytes (Kallio et al., 2007). A diet that consisted of oat-wheat-potato appears to activate the genes that are associated with inflammation and oxidative stress,

without any observable change in adipocyte cell size (Kallio et al, 2007). The researchers established that the type of dietary carbohydrate played an important role in modulating gene expression.

### **Serum Levels of MnSOD and Oxidative Stress**

The literature reports experimental and clinical findings of a link between MnSOD, oxidative stress and impaired mitochondrial function in diabetes. MnSOD is localized in the mitochondria and serves to protect the mtDNA from oxidative stress damages (Li & Zhou, 2011). The damages to the mtDNA can impair the functions of cells (Garcia-Ramirez et al., 2008) and contribute to progressive disorders associated with diabetes. Although serum level of MnSOD is well documented in subjects with cancers (Lin et al., 2005; Nishida et al., 1993; Schadendor et al., 1995) and cardiovascular disease (Shen et al., 2006; Miriyala et al., 2011), the data for T2D is sparse and the clinical significance of serum MnSOD is yet to be determined. The data on serum MnSOD levels in T2D would provide information that may be used to guide and monitor dietary antioxidant intakes as a means to reduce oxidative stress (Garcia-Ramirez et al., 2008).

The enzyme MnSOD reduces oxidative stressors; however, it is well documented that the plasma levels of SOD in patients with T2D diabetes is markedly reduced (Garcia-Ramirez et al., 2008). Abnormally low levels of SOD may contribute to mtDNA damage (Garcia-Ramirez et al., 2008). A possible therapeutic approach to reduce or slow the mtDNA damage caused by oxidative stress is to improve the plasma levels of MnSOD, which can be accomplished through the use of hormones such as HCG or melatonin

(Kozirog et al., 2010) as well as through antioxidant micronutrients such as copper, selenium, and manganese (Otsu, Ikeda, & Fujii, 2004).

Kozirog et al. (2010) treated diabetes subjects with 5 mg of melatonin. The subjects were instructed to take one capsule of melatonin before bedtime for a period of 60 days. Blood pressure (BP) and a fasting blood specimen were taken to establish baseline data, including serum lipid profiles and oxidative stress biochemical markers such as TBARS, SOD, and glutathione peroxidase (GSH-Px). After a 2-month intervention period, BP and blood sample were taken for the determination of the effect of the melatonin intervention. The researchers observed a significant improvement in blood pressure, lipid profiles, and glutathione.

The effect of mineral supplements on SOD enzymatic activity levels has shown positive influences, including the improvement of catalase enzymatic activity, another antioxidant enzyme (Kozirog et al., 2010; Beauchamp & Fridovich, 1971). HepG2 cell lines are hepatocellular carcinoma-derived cells that are conventionally used to conduct *in-vitro* studies of the mechanism that occurs in liver cells. The researchers studied the effect of supplements, which were either replenished or depleted, of a mineral of interest. Supplements with or without Cu and Zn, which were used to feed the cell lines, and SOD activity was determined (Beauchamp & Fridovich, 1971; Otsu et al., 2004). Mineral depletion appeared to down-regulate both Cu/ZnSOD and MnSOD to 70%-80% of baseline activity level. Zn was shown to be more critical than Cu in the up-regulation of MnSOD, which may be due to Zn's involvement in MnSOD induction (Otsu et al., 2004).

Further research is needed to evaluate effect of antioxidants supplementation on plasma levels of MnSOD and on mtDNA damage.

### **Serum Levels of 8OHdG and Oxidative Stress**

Oxidative stress has been implicated in a number of diseases, including cancers and Type 2 Diabetes. It is clear that 8OHdG is an oxidative stress biomarker found to be elevated in patients with diabetes and may contribute to diabetes complications (Pan et al., 2008; Al-Aubaidy et al., 2011). Clinical studies show that serum 8OHdG is measurable by ELISA method and proven to be a reliable biomarker for oxidative DNA damage (Basavarai, et al., 2013; Pagano, et al., 2014).

The acceptable specimen for the determination of 8OHdG levels are serum, cell lysate, peripheral blood mononuclear cells, and urine (Chen et al., 2008). Urine samples for 8OHdG testing require 24-hour urine collection, and it is demanding on the subject involved in the collection process (Khadem-Ansari et al., 2011). The predominant biomarker that is used to assess the degree of mtDNA damage is 8OHdG and the accumulation of 8OHdG in serum has been reported in patients with T2D (Jamil et al., 2014). Recently, a number of 8OHdG ELISA test kits have been validated for serum specimens and the test kits have documented performance characteristics such as sensitivity, specificity, and inter- and intra-assay reproducibility. Akihiko, Odamaki, and Hishida (2003) have shown that the serum level of 8OHdG, using ELISA test kits, was significantly higher in subjects with diabetes, as compared to subjects without diabetes.

## **Oxidative Stress and Glycemic Control among Ethnic Groups**

Emerging literature shows that all Blacks should not be grouped together and identified as African Americans (Huffman et al., 2011; Huffman et al., 2013).

Fearheller, Diaz, Sturgeon, Williamson, and Brown (2011) examined total antioxidant capacity (TAC), protein carbonyls (PC), and TBARS among African Americans and Caucasians. They found that, even though there were no statistical differences between African Americans and Caucasians for age, BMI, or blood pressure (diastolic and systolic), there were statistically significantly higher levels of oxidative stress in African Americans. To examine the effect of geographical influences on oxidative stress, Deeq et al. (2008) conducted a cross-sectional study that included African Americans from Indianapolis, Indiana, and Yoruba from Nigeria. The researchers used 8-Isoprostane as the biomarker for oxidative stress. They found evidence of higher oxidative stress levels in Nigerians, which may be dietary and environmentally influenced.

Research has shown that diabetes, high blood pressure, and other cardiovascular disease (CVD) risk factors affect African Americans more than they do Caucasians (CDC, 2011; Liutkeviciene, Lesauskaite, Asmoniene, Zaliuniene, & Jasinskas, 2010). One of the most important independent risk factors for the progression of complications associated with diabetes is hemoglobin A1C (O'Connor et al., 2011). Morbidity and mortality are highest in African Americans with peripheral artery disease (PAD). A meta-analysis (Kirk et al., 2013), examined glycemic control as measured by A1C and found that African Americans values were more elevated than non-Hispanic whites with diabetes. The authors reported that the observed disproportionate A1C levels between African Americans and non-Hispanic whites may be due to access to medical care, less



optimal diabetes care, and medication affordability (Karter et al, 2002; Rhee et al., 2005; Kirk et al., 2005; Ofili, 2001). This may be related to the lack of agreement of the correlation between A1C and average glucose in certain subjects (Standards of medical care in diabetes, 2014). Glycation rates may be race dependent, consequently A1C levels may have ethnicity variability (Ziemer et al., 2010; Kumar et al, 2010). Glycation involves oxidative reactions that may adversely affect DNA function (Pun & Murphy, 2012). Since glycation rates could be dependent on ethnicity, then oxidative stress levels could cause a higher rate of DNA damage in subjects with T2D. There is evidence of a strong inverse correlation between DNA damage, oxidative stress, and apoptosis with levels of A1C (Khan et al., 2011), providing a measure of the average blood glucose level over 2-3 month period. Subjects whose diabetes status is out-of-control are more likely to developed diabetes complications. It is well documented that glycemic control influences the extent of oxidative stress (Marling, Shubrook, Vernier, Wiley, & Schwartz, 2011; Nahkjavani et al., 2010) and that A1C is a reliable biomarker and indicator of glycemic control.

### **Ethnicity and Dietary Antioxidant Intake**

The literature on dietary antioxidants intake is varied and not conclusive. Suksomboon, Poolsup, and Sinprasert (2011) reviewed nine randomized clinical trials on vitamin E supplementation and glycemic control in subjects with T2D but found no significant changes in A1C levels as a result of supplementation with vitamin E. In a study by Camargo et al. (2006), subjects with T2D were administered pharmacological dose of vitamin E supplements over a 4 month period and it was observed that it did not impact A1C. Alternatively, in a review by Unnikrishnan et al. (2012), it was reported

that high doses of Vitamin C and E have lowering effect on A1C. In their review, they reported that the mechanism for the lowering effect of A1C is related to the reduction in the rate of hemoglobin glycation. Arab et al. (2011) compared dietary antioxidant intake between African Americans and Caucasians. They found that healthy African Americans were more likely to be overweight and that being overweight contributed to inflammation and oxidative stress status. In addition, they found that 32% of African Americans, as compared to 45.2% of Caucasians, took dietary supplements. Overall, they found a significant correlation between dietary antioxidant intake and plasma concentrations of carotenoids as determined by high-performance liquid chromatography (HPLC). African Americans had a significantly lower intake of antioxidants. The researchers believed that the difference may have been due to food preparation, dietary sources, genetic variants, or BMI (Arab et al., 2011). Huffman, Serge, and Himburg (2011) found intra-racial differences in caloric intake and BMI in African Americans and Haitian Americans.

Manganese (Mn) is an important antioxidant that scavenges free radicals and is secondary to biochemical functions, behaving as a backup free radical scavenger that is similar to MnSOD, especially in regard to oxidative stress (Reddi & Culotta, 2011). Although there is a lack of data on the mechanism by which Mn participates in the cellular adaptation to oxidative stress (Reddi & Culotta, 2011), research has shown that the antioxidant activity is regulated by nutrient-sensing pathways.

The data from published works shows that diabetes status influences manganese physiological status by various etiological factors such as viral infection, autoimmunity, genetics, and obesity (Walter et al., 1991). The mechanism which may influence the

manganese status in diabetes may be related to dysfunction in mineral metabolism (Walter et al., 1991). It is well documented that Mn, an essential component of the enzyme MnSOD (Greger, 1998). Hope et al. (2006) reported that dietary Mn intakes were lower in non-tea drinkers compared with tea drinkers and that tea is a major source of dietary Mn. In their study, the levels of MnSOD were determined via RT-PCR from blood collected from volunteers who were assigned to either a tea-drinker and non-tea drinker group. This study showed that dietary Mn intake can improve the Mn status in the body and that there was an inverse relationship of Mn plasma levels and MnSOD of leucocytes.

The literature indicates an overwhelming evidence of the negative influence of oxidative stress and MnSOD in inflammation and cancer (Fu et al., 2011; Li et al., 2011; Suzuki et al., 2001). Because Mn and iron (Fe) play an important role in the biosynthesis of MnSOD (Hassan & Schrum, 1994), data on the dietary intake of Mn may provide valuable information on possible biochemical requirements for the production and up-regulation of MnSOD. There is some evidence that vitamins and minerals play an important role in slowing the progression of disease associated with T2D (Martini et al., 2010) and reducing oxidative stress levels.

## **CHAPTER III**

### **METHODOLOGY**

#### **Study Design**

This study used a cross-sectional design to explore the relationship between two biomarkers that are closely linked to oxidative stress and the biomarkers' relationship to diet and disease state. The data and specimens that were used for this study were collected previously (Huffman et al., 2007). This study was conducted with Haitian Americans and African Americans with and without T2D. The investigator of this study fully participated in data collection. After the participants signed an informed consent form, they were assigned a unique identifier, and blood was collected and processed immediately and stored for analysis at a later time by this investigator. The unique identifier was the only link between the participants' demographic information and laboratory assessment. The participants' personal information, as linked with the unique identifier, was kept in a locked cabinet. This study was approved by the Institutional Review Board at Florida International University's Office of Research Integrity under IRB exemption number 073112-01 (Appendix E).

#### **Anthropometric Measurements**

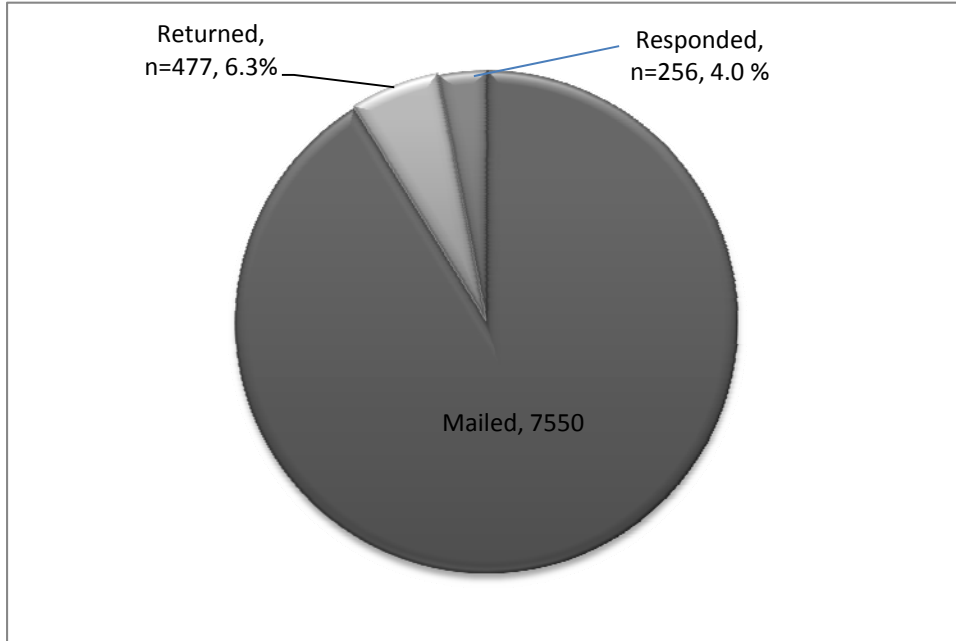
Participants had their height, weight, and waist circumference recorded by a trained research assistant. Measurements for height and weight were obtained by using a SECA balance scale (Seca Corp., MD, US). Waist circumference was measured horizontally with a measuring tape. The participants completed a standardized socio-demographic dietary assessment questionnaire (FFQ) and a medical questionnaire that included medical history, prescribed medications, and the use of supplements. The

control group participants (without T2D) underwent the same procedures as did the participants with T2D. This was a cross-sectional study that used data from male and female participants, aged 35 years or older, with and without T2D. Ethnicity (Haitian American and African American) and diabetes status (T2D or no diabetes) were self-reported but verified by blood test.

### **Recruitment of Participants**

Participants were initially recruited by randomly generated mailing lists purchased from Knowledge Base Marketing, Inc., Richardson, TX, U.S. This company provided two mailing lists generated from multiple databases of African Americans, identified as having or not having T2D, from Miami-Dade and Broward Counties, Florida, U.S. Approximately 7,550 letters were mailed to African American participants with and without T2D. Approximately, 6.3% ( $n = 477$ ) of the letters were returned due to an invalid addresses. From the remaining delivered letters, 4% ( $n = 256$ ) responded (Figure 1).

Figure 1 – Recruitment of African American Participants



1. Local diabetes educators and community health practitioners in Miami-Dade and Broward Counties. Several local diabetes educators who were either former students or who were in close contact with the Department of Dietetics and Nutrition at Florida International University (FIU) were identified. Letters of invitation, which described the study, were mailed to the diabetes educators and health professionals in Miami-Dade and Broward counties and requested their cooperation in recruiting individuals.
2. FIU faculty, staff, and students. Invitational flyers were distributed to all university faculty, staff, and students who used the university-wide e-mail system; these flyers contained an explanation of the research protocol and requested their assistance in the study.

3. Several residential and rental facilities were used to conduct interviews and complete questionnaires.
4. Advertisements. Print advertisements were placed in local Haitian newspapers and the principal gathering places of these groups, such as churches, supermarkets, and restaurants. Radio advertisements on local Creole stations also were aired.

When the target recruitment goal was reached for all ethnic groups, efforts to recruit participants were discontinued. Interested participants were initially interviewed on the phone, at which time the study's purpose was explained and the age, gender and ethnicity of the responders were determined. To ascertain T2D status, each participant who self-reported as having diabetes was asked for the age of diagnosis and initial treatment modalities. Participants who did not qualify for the study (N = 28) consisted of those who were younger than 35 years old (N = 12), another ethnicity (N = 5), or who had other chronic diseases or illnesses (N = 11). If a potential participant was determined to be eligible, then his or her participation was requested at the Human Nutrition Laboratory at FIU. Participants were instructed to refrain from smoking, consuming any food or beverages except water, and engaging in any unusual exercise for at least eight hours prior to their blood collection.

The study was approved by the Institutional Review Board at FIU. The purpose and the protocol of the study were explained to the participants, and their written consent, in either English or Creole, was obtained prior to the commencement of the study. Laboratory results showed that 12 participants (Haitian American = 8, African American

= 4) who reported as not having diabetes were reclassified as having T2D, according to American Diabetes Association standards. These participants were given their laboratory results, referred to their physician. A total of 443 (234 Haitian American, 209 African American) participants were included in the final data analysis.

### **Sample Size and Power Analysis**

In this study, multiple linear regressions were the primary statistical analysis method used. It was necessary to determine the sample size for an independent variable (e.g., total antioxidants) added to the equation explaining an additional 1.6% of the variability of the dependent variable (e.g., serum MnSOD levels) after controlling for eight covariates. Using a sample size calculator for multiple regression (GPower3, 2010, Faul et al, 2009) with eight covariates and a partial  $R^2$  of 0.18 for the added predictor, 80% power, and a 5% significance level, a sample size of 431 participants was necessary. The main study had enrolled 515 participants, and had complete data on 443 participants. This study was sufficiently powered for the statistical analysis.

### **Compliance**

A fasting specimen is an important requirement to the assessment of the biomarkers that were evaluated in this study. To ascertain that the subjects were compliant with at least an 8-hour fast, they were asked to fill out a questionnaire that included an item regarding fasting, and the researcher asked the participant about his or her fasting compliance. In addition to a fasting glucose analysis (to verify fasting), the researcher determined the level of glycosylated hemoglobin A1C. Hemoglobin A1C was



used for analysis of diabetes self-management and to help determine the presence of T2D.

### **Nutritional Assessment**

Dietary intake of calories and nutrients were measured using the semi-quantitative food frequency questionnaire (FFQ; 97GP 2006 version copyrighted at Harvard University, Boston, MA, U.S.), which has been extensively validated and standardized in several multiethnic population-based studies (Willet et al., 1985). On the FFQ, participants self-report average consumption of specified amounts of various foods over the past year, with response categories that ranged from “never” to “six or more servings per day.” In addition to food items, the FFQ included questions about type and duration of vitamin/mineral supplement use and specific details about fat, salt, and sugar used in cooking and as condiments. Each of the completed FFQs was reviewed for incomplete answers or blank responses before the interview was completed. Researchers completed the incomplete items by probing of the subjects before they left.

Daily servings for food groups were calculated by summing the frequency factors for all related food items. Macro- and micro-nutrient intakes were calculated by multiplying frequency of consumption by the nutrient value of the food item, as obtained from the Harvard University Food Composition Database (Willet et al., 1985). The calculated consumption of dietary antioxidants was used to determine the relationship between MnSOD and 8OHdG and antioxidants intakes.

### **Blood Collection and Biochemical Assessment**

Participants were asked to fast for at least 8 hours before blood was collected by a certified phlebotomist. Blood was collected by venipuncture into serum separator tube

(SST) and ethylenediaminetetraacetic acid (EDTA) tubes. Fasting Plasma Glucose levels and A1C were measured from the blood which was collected in the EDTA tube by Laboratory Corporation of America, Miami, FL (LabCorp<sup>®</sup>). Twenty milliliters of fasting venous blood was collected in serum separation tubes, centrifuged, and processed, and aliquots were stored in a -70° Celsius freezer by the researcher of this study. Biochemical studies were performed to determine total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein via a methodology from Cobas Mira, Roche Diagnostics (Bowling & Katayev, 2010). Glucose levels were measured using the hexokinase enzymatic method, and a monoclonal antibody method (Bayer Corporation, Diagnostic Division, Tarrytown, NY, USA) was used to determine glycated hemoglobin (A1C). Participants were provided with a copy of their biochemical assessment, including a cardiovascular risk analysis which was calculated from the lipid profile.

Serum levels of MnSOD and 8OHdG were determined. ELISA was used as the method of detection of these biomarkers. Presently, there are numerous ELISA kits available that can detect the levels of 8OHdG in serum. There has been good correlation between plasma levels of 8OHdG and tissue 8OHdG by this method (Park et al., 2001). These correlations support the use of plasma levels of 8OHdG to predict the degree of mtDNA damage.

The gold standard for the identification of 8OHdG in tissue, blood, and urine is high-performance liquid chromatography tandem mass spectrometry (HPLC-ms), which is as effective as the more readily available high-performance liquid chromatography-electrochemical (HPLC-EC) detection methodology (Harri et al., 2007). These methods require expensive equipment, analytical software, and highly skilled operators. The

availability of monoclonal antibodies to 8OHdG, however, provided a framework for the development of a method of detection (ELISA) that is cheaper, requires less costly equipment and reagents, and does not require highly trained experts to perform and analyze specimens. The ELISA kit platform is reliable, reproducible, and validated for the detection of 8OHdG in urine, cell lysates, and serum. In several studies, ELISA has been shown to be as effective as HPLC (Breton et al., 2003; Yoshida et al., 2003). Several manufacturers have developed highly sensitive 8OHdG ELISA kits that require a pretreatment of serum before performing the analysis.

In this study serum MnSOD was detected via the ELISA method. The literature search for the rationale in determining MnSOD in serum in T2D is missing, however the evidence is convincing that serum levels of MnSOD is a useful tool and potential clinical biomarker to predict disease associated with viruses (Tamai et al., 2011), and cancers (Schadendor et al., 1995; Nishida et al., 1993). The reagents were available on the open market and they were purchased from Cayman Chemicals (Ann Arbor, MI). The assay also requires a plate reader with a 450-nm reading capacity. All supplies and equipment were available to the investigator in the Human Nutrition Laboratory at FIU.

### **Determination of serum 8OHdG**

Several studies report an association of serum 8OHdG levels in subjects afflicted with different chronic diseases. The literature provides evidence that elevated levels of serum 8OHdG is associated with poor prognosis in patients with ovarian cancer (Pylvas et al., 2011), T2D, kidney disease (Kato et al., 2003), and also with obesity (Al-Aubaidy & Jelinek, 2011). The source of the circulating 8OHdG was not determined in neither of

these studies nor our study. Kikuchi et al. (2002) reported that elevated level of 8OHdG was observed in serum but not in cerebrospinal fluid in patients with Parkinson's disease, which suggest that 8OHdG may have originated from peripheral tissues.

The reagents used in the measurement of serum 8OHdG were manufactured by Cayman Chemicals (Ann Arbor, MI; Catalog#589320) and the analytical procedure was followed precisely according to the manufacturer's instructions. The micro titer plate found in this kit utilized an anti-mouse IgG antibody and an 8OHdG enzyme conjugate. The kits contained all reagents necessary to perform analysis except for a micro titer plate reader which was available in the Human Nutrition Laboratory at FIU.

The principle of this assay is based on the competition between oxidative damaged guanine species and an 8OHdG-acetylcholinesterase conjugate (tracer). Aliquots of standards, controls and specimen were pipetted according to micro titer plate layout and then the tracer was added. The micro titer plate was incubated for 18 hours at 4 degrees C, after which they were rinsed with a wash buffer and then an Ellman's Reagent was added. The plates were incubated for 120 minutes at room temperature and then the absorbance was measured by a micro titer plate spectrophotometer. The estimate of the oxidative DNA damage was determined by comparing the absorbance of an unknown specimen to the standard curve determined by the assay. In this study, the intra- assay and inter-Assay CV for the 8OHdG assay was calculated to be 6.2%and 4.5%, respectively, which is an acceptable range of variation.

## **Determination of serum MnSOD**

The scientific literature contains very few studies on the relationship of serum MnSOD and health related conditions in humans, however we found numerous reports on the association of MnSOD with diseases in animal models. In human models, Lin et al. (2005) studied the role of serum MnSOD in patients with gastric cancer and found a weak, but not significant, association. Tamai et al., 2011) studied the role of serum MnSOD and hepatocellular carcinoma (HCC) and reported a significantly higher level of MnSOD in subject with HCC compared with subjects without HCC. Additionally, they reported that their findings were clinically significant in that serum MnSOD may be used to predict prognosis in HCC. There were no recent studies publications that dealt with serum MnSOD with MnSOD in tissue. We found one study where Koshida et al. (1996) reported positive relationship with testicular tumors with serum MnSOD but not with tissue MnSOD. The source of circulating MnSOD is not clear (Schandendorf et al., 1995) and the limited reports suggest that serum MnSOD is a sensitive biomarker for malignant tumors (Koshida et al., 1996; Ishikawa et al., 1990).

The reagent kits used in this study were manufactured by Young In Frontier Co., Ltd (Seoul, Korea; Catalog# LF-EK0104) and the analytical procedure was followed according to the instructions found in the manufacturer's package insert. The contents of the reagent kit included all reagents necessary for the analysis, which included a micro titer plate that had been pre-coated with a monoclonal antibody specific to human MnSOD. Prior to the analyses, the samples were thawed and brought to room temperature. Aliquot of the sample, standards, and controls were pipetted into the pre-coated micro titer plate and was then incubated at room temperature with constant

agitation for 2 hours. The wells were then washed. A working antibody solution was added and then allowed to incubate for 1 hour at room temperature. After incubation, the wells were washed again and a working AV-HRP solution (conjugate) was added to each well. Wells were allowed to incubate for an additional 30 minutes at room temperature. The plate was washed and a substrate solution was added to each well and incubated for 10 minutes. A stop solution was added at the end of incubation period. The micro plate was then read on a 450nm using a micro plate reader. In this study, the intra- assay and inter-Assay CV for the MnSOD assay was calculated to be 5.5% and 3.1%, respectively.

### **Covariates**

The covariates in this study were age, gender, smoking status, education, BMI, energy intakes, ethnicity, and diabetes status. These variables were shown to be strongly associated with oxidative stress and ROS (Zhu et al., 2012; Whaley-Connell et al., 2012; Pryor, 1997; Moller et al., 1996). Oxidative stress and reactive oxygen species levels progressively increase with aging (Andriollo-Sanchez et al., 2005; Junqueira et al., 2004; Harman, 1956) and may be related to a decline in the body's primary antioxidant defense system. There is evidence of gender-related differences in oxidative stress levels and the literature report lower levels of oxidative stress in female genders than males, suggesting that the female gender have a reduced susceptibility for DNA damage than males (Hakim et al., 2012; Vina et al., 2011). Additionally, Hakim et al. reported greater levels of oxidative stress biomarkers in subjects who smoke compared to non-smokers. Oxidative stress increases with BMI and age in African Americans (Wonisch et al., 2012; Warolin et al., 2014) and oxidative stress levels have been found to be higher in African

Americans than in Whites. (Morris et al. (2012). Oxidative stress has been proposed as the root cause in T2D and excessive levels of ROS have been in subjects with T2D (Phillips et al., 2004; Wright et al., 2006).

### **Statistical Analysis**

Data were analyzed using SPSS, Version 20.0 (SPSS Inc., Chicago, IL, U.S.). Descriptive statistics were used, and the results were expressed either as means  $\pm$  standard deviations, or frequencies and percentages. The significance level was set as  $p < .05$  for all tests. The relationships between the variables were analyzed using analysis of covariance (ANCOVA), Pearson's correlations, or multiple linear regression. Since MnSOD was not normally distributed, the natural logarithm of MnSOD was used in all analyses. The ANCOVA was used to compare the levels of 8OHdG and MnSOD between ethnic groups. Pearson's correlations and multiple linear regressions were used to determine the associations between dietary antioxidant intake and MnSOD and 8OHdG by ethnicity and as well as their interaction. Full models included all potentially significant demographics (age, gender, smoking status, energy intake, and education) and the physical covariate (BMI). Final models included age, gender, and all covariates which had  $p$ -values  $\leq .20$  for the Pearson correlations with the dependent variables and diabetes status. Multiple linear regression analysis was used to compare the continuous dependent variables, i.e., enzymes and mtDNA damage byproduct, with diabetes status and ethnicity.

## CHAPTER IV

### RESULTS

This chapter is organized according to the research questions and into sections according to the aims of the study. The first section includes the general characteristics of the study participants by ethnicity and diabetes status. First, socio-demographics are presented and then oxidative stress markers, and finally glycemic control biomarkers. The second section contains correlations among socio-demographics and biomarkers. The tests of the hypotheses are presented in the last section.

#### **Section 1: General Characteristics of Participants**

This cross-section study compared African Americans and Haitian Americans by their ethnicity and diabetes status. There were complete data for 443 participants: 233 with T2D and 210 free of diabetes; 209 African Americans and 235 Haitian Americans.

Table 1 presents the socio-demographics by ethnicity. African American were significantly younger ( $M = 53.3$  vs.  $M = 55.6$ ;  $p < .018$ ), had a higher BMI ( $\text{kg/m}^2$ ) ( $M = 32.8$  vs.  $M = 29.3$ ;  $p < .001$ ), higher percentage of smokers (34% vs. 6.4%;  $p < .001$ ), a higher calculated energy intake (kcal/day) ( $Md = 1925$  vs.  $Md = 1650$ ;  $p < .001$ ) and were more educated (more than high school, 57% vs. 33%;  $p < .001$ ) as compared to Haitian Americans.



Table 1  
*General Characteristics of Participants by Ethnicity*

Variables	Ethnicity		P-value
	African Americans (n = 209)	Haitian Americans (n = 234)	
Age (years)	53.3 ± 9.5	55.6 ± 10.7	.018
Gender (male) %	50.2	47.0	.497
BMI (kg/m <sup>2</sup> )	32.8 ± 7.1	29.3 ± 4.8	< .001
Smoke (yes) %	34.4	6.4	< .001
Energy Intake (kcal/day)	1925 (1400)	1650 (1109)	< .001
Education (%)			< .001
< Grade 8	1.9	31.6	
Some high school	13.4	14.5	
High school grad/GED	28.2	20.5	
Some college/technical school	38.3	17.1	
College graduate (bachelor's degree)	11.0	12.0	
Graduate degree	7.2	4.3	

Data are median (interquartile range) or means ± SD unless otherwise indicated. BMI = body mass index.

Table 2 shows the comparison of the participants by diabetes status. Participants with T2D were significantly older than participants without diabetes ( $M = 56.3$  vs.  $M = 52.7$ ;  $p < .001$ ) and had higher BMI ( $\text{kg}/\text{m}^2$ ) ( $M = 32.1$  vs.  $M = 29.7$ ;  $p < .001$ ). Participants with T2D did not have lower calculated energy intake ( $\text{kcal}/\text{day}$ ) ( $Md = 1681$  vs.  $Md = 1834$ ;  $p = .052$ ) than those without T2D, although the difference approached significance. There were no differences in gender, percentage of smokers, or educational status for participants with and without T2D.

The participants were also compared by both ethnicity and diabetes status using two-way ANOVA or non-parametric ANOVA (Table 3). African Americans with T2D had significantly higher BMI ( $\text{kg}/\text{m}^2$ ) ( $M = 34.7$ ) than African Americans without T2D ( $M = 30.6$ ) and Haitian Americans with and without T2D ( $M_s = 29.6, 29.0$ , respectively). There were no significant differences for BMI in Haitian Americans with T2D compared to without T2D. Haitian Americans with T2D had significantly lower energy intake ( $\text{kcal}/\text{day}$ ) ( $M = 1430$ ) than Haitian Americans without T2D ( $M = 1719$ ), and both had significantly lower intakes than African Americans with and without T2D ( $Mds = 1857, 2020$ , respectively). Finally, a greater percent of Haitian Americans with T2D had less than grade 8 educations than those without T2D. Thirty six percent of Haitian Americans with T2D had less than 8 years education compared with 26.5% of Haitian Americans without T2D and African Americans with and without T2D (3.6%, 0.0%, respectively).

Table 2  
General Characteristics of Participants by Diabetes Status

Variables	Diabetes		P-value
	Yes (n = 233)	No (n = 210)	
Age (years)	56.3 ± 10.3	52.7 ± 9.8	< .001
Gender (male) %	49.5	47.6	.692
BMI (kg/m <sup>2</sup> )	32.1 ± 6.5	29.7 ± 5.7	< .001
Smoke (yes) %	18.5	20.6	.591
Energy Intake (kcal/day)	1681 (1306)	1834 (1382)	.052
Education (%)			.072
< Grade 8	14.2	20.6	
Some high school	11.4	16.3	
High school grad/GED	24.2	24.0	
Some college/technical school	28.5	25.7	
College graduate (bachelor's degree)	13.3	9.8	
Graduate degree	8.1	3.4	

Data are median (interquartile range) or means ± SD unless otherwise indicated. BMI = body mass index.

Table 3  
General Characteristics of Participants by Ethnicity and Diabetes Status

Variables	Ethnicity Diabetes Status	African Americans		Haitian Americans	
		Yes ( <i>n</i> = 112)	No ( <i>n</i> = 97)	Yes ( <i>n</i> = 121)	No ( <i>n</i> = 113)
Age (years)		54.8 ± 10.2 <sup>b</sup>	51.7 ± 8.6 <sup>a</sup>	57.6 ± 10.3 <sup>b</sup>	53.5 ± 10.7 <sup>a</sup>
Gender (male) %		50.0	50.5	45.5	48.7
BMI (kg/m <sup>2</sup> )		34.7 ± 7.1 <sup>b</sup>	30.6 ± 6.4 <sup>a</sup>	29.6 ± 4.8 <sup>a</sup>	29.0 ± 5.0 <sup>a</sup>
Smoke (yes) %		35.7 <sup>b</sup>	33.0 <sup>b</sup>	6.6 <sup>a</sup>	6.2 <sup>a</sup>
Energy Intake (kcal/day)		1857 (1457) <sup>c</sup>	2020 (1296) <sup>c</sup>	1430 (1150) <sup>a</sup>	1719 (1210) <sup>b</sup>
Education (%)					
< Grade 8		3.6 <sup>b</sup>	0.0 <sup>a</sup>	36.4 <sup>b</sup>	26.5 <sup>a</sup>
Some high school		14.3	12.4	18.2	10.6
High school grad/GED		28.6	27.8	19.8	21.2
Some college/technical school		38.4	38.1	14.0	20.4
College graduate (bachelor's degree)		8.9	13.4	10.7	13.3
Graduate degree		6.3	8.2	0.8	8.0

Data are median (interquartile range) or means ± SD unless otherwise indicated. Variables in the four groups with different superscripts are significantly different using Holm's sequential Bonferroni post hoc test,  $p < .05$ . BMI = body mass index.

The participants were also compared by both ethnicity and diabetes status using two-way ANOVA or non-parametric ANOVA (Table 3). African Americans with T2D had significantly higher BMI ( $\text{kg/m}^2$ ) ( $M = 34.7$ ) than African Americans without T2D ( $M = 30.6$ ) and Haitian Americans with and without T2D ( $M_s = 29.6, 29.0$ , respectively). Haitian Americans with T2D had significantly lower energy intake ( $\text{kcal/day}$ ) ( $Md = 1638$ ) than Haitian Americans without T2D ( $Md = 1719$ ), and both had significantly lower intakes than African Americans with and without T2D ( $Mds = 1857, 2020$ , respectively). Finally, there was a greater percent of participants with T2D who had less than grade eight educations. Thirty six percent of Haitian Americans with T2D had less than grade 8 education compared with 26.5% of Haitian Americans without T2D. Four percent of African Americans with T2D had less than grade 8 education compared to 0.0% without T2D.

### **Biomarkers**

Table 4 shows glycemic control and oxidative stress biomarkers of participants by ethnicity. African Americans had lower A1C levels (%) than Haitian Americans ( $M = 6.7$  vs.  $M = 7.1$ ;  $p = .014$ ). African Americans had higher MnSOD levels ( $\text{pg/ml}$ ) ( $M = 2538$  vs.  $M = 2016$ ), and higher 8OHdG levels ( $\text{pg/ml}$ ) ( $M = 1691$  vs.  $M = 1626$ ;  $p = .003$ ) than Haitian Americans.

Table 4  
*Biomarkers of Glycemic Control and Oxidative Stress of Participants by Ethnicity*

Variables	Ethnicity		P-value
	African Americans (n = 209)	Haitian Americans (n = 234)	
	Fasting plasma glucose (mg/dl)	121.0 ± 51.2	
Hemoglobin A1C (%)	6.7 ± 1.5	7.1 ± 2.1	.014
MnSOD (pg/ml)	2538.0 ± 1091.8	2015.8 ± 656.3	< .001
Ln-MnSOD	7.7 ± 0.5	7.6 ± 0.3	< .001
8OHdG (pg/ml)	1691.0 ± 225.1	1626.2 ± 222.9	.003

MnSOD = Manganese Superoxide Dismutase; 8OHdG = 8-hydroxy-2'-deoxyguanosine; Ln-MnSOD = Natural logarithm of Manganese Superoxide Dismutase.

Biomarkers of glycemic control and oxidative stress of participants were compared by diabetes status as shown in Table 5. Participants with T2D had higher fasting plasma glucose (mg/dl) and A1C levels (%), had lower MnSOD levels (pg/dl), and higher 8OHdG levels (pg/dl) than subjects without T2D.

The participants were also compared by both ethnicity and diabetes status as shown in Table 6. Haitian Americans with T2D had significantly higher fasting plasma glucose (mg/dl) ( $M = 158$ ) than African Americans with T2D ( $M = 143$ ), and both had significantly higher fasting plasma glucose than African Americans and Haitian Americans without T2D ( $M_s = 96, 99$ , respectively). Similarly, Haitian Americans with T2D had significantly higher A1C levels (%) ( $M = 8.4$ ) than African Americans with T2D ( $M = 7.5$ ), and both had significantly higher A1C levels than African Americans and Haitian Americans without T2D ( $M_s = 5.9, 6.0$ , respectively).

African Americans without T2D had the highest MnSOD levels (pg/ml) ( $M = 3541$ ) of the four groups, Haitian Americans with T2D had the second highest MnSOD levels ( $M = 2174$ ), Haitian Americans without T2D had the next highest MnSOD levels ( $M = 1846$ ), and African Americans without T2D had the lowest MnSOD levels ( $M = 1669$ ). These differences were all significant.

The serum levels of 8OHdG (pg/ml) in African Americans with T2D were significantly higher ( $M = 1796$ ) than those of the other three groups. Haitian Americans with T2D had significantly higher levels of 8OHdG ( $M = 1735$ ) than African Americans without T2D and Haitian Americans without T2D ( $M_s = 1570, 1510$ , respectively).

Table 5  
*Biomarkers of Glycemic Control and Oxidative Stress of Participants by Diabetes Status*

Variables	Diabetes		P-value
	Yes	No	
	(n = 233)	(n = 210)	
Fasting plasma glucose (mg/dl)	150.5 ± 63.7	97.4 ± 15.3	< .001
Hemoglobin A1C (%)	7.9 ± 2.1	5.9 ± 0.4	< .001
MnSOD (pg/ml)	1931.6 ± 630.1	2628.9 ± 1054.8	< .001
Ln-MnSOD	7.5 ± 0.3	7.8 ± 0.4	< .001
8OHdG (pg/ml)	1764.2 ± 188.6	1537.6 ± 203.5	< .001

MnSOD= Manganese Superoxide Dismutase; 8OHdG= 8-hydroxy-2'-deoxyguanosine; Ln-MnSOD = Natural logarithm of Manganese Superoxide Dismutase.



Table 6  
*Biomarkers of Participants by Ethnicity and Diabetes Status*

<b><u>Status</u></b>	<b><u>Ethnicity</u></b>	<b>African Americans</b>		<b>Haitian Americans</b>	
	<b><u>Diabetes</u></b>	<b>Yes</b>	<b>No</b>	<b>Yes</b>	<b>No</b>
<b>Variables</b>		<b>(n = 112)</b>	<b>(n = 97)</b>	<b>(n = 121)</b>	<b>(n = 113)</b>
Fasting plasma glucose (mg/dl)		143.0 ± 61.0 <sup>b</sup>	95.8 ± 13.2 <sup>a</sup>	157.6 ± 65.5 <sup>c</sup>	98.7 ± 16.9 <sup>a</sup>
Hemoglobin A1C (%)		7.5 ± 1.8 <sup>b</sup>	5.9 ± 0.4 <sup>a</sup>	8.4 ± 2.4 <sup>c</sup>	6.0 ± 0.5 <sup>a</sup>
MnSOD (pg/ml)		1669.3 ± 521.3 <sup>d</sup>	3541.1 ± 609.4 <sup>a</sup>	2174.4 ± 626.7 <sup>b</sup>	1845.9 ± 647.3 <sup>c</sup>
Ln-MnSOD		7.4 ± 0.3 <sup>a</sup>	8.2 ± 0.2 <sup>d</sup>	7.6 ± 0.3 <sup>c</sup>	7.5 ± 0.3 <sup>b</sup>
8OHdG (pg/ml)		1795.9 ± 194.7 <sup>c</sup>	1569.9 ± 196.0 <sup>a</sup>	1735.0 ± 178.7 <sup>b</sup>	1509.8 ± 206.5 <sup>a</sup>

Variables in four groups with different superscript are significantly different using Holm's sequential Bonferroni post hoc test,  $p < .05$ . MnSOD = Manganese Superoxide Dismutase; 8OHdG = 8-hydroxy-2'-deoxyguanosine; Ln-MnSOD = Natural logarithm of Manganese Superoxide Dismutase.

## Macro and Micronutrients

Table 7 presents the macro and micronutrient intake of participants by ethnicity. Non-parametric tests were conducted on all variables, since all were non-normally distributed, so results were reported with median and interquartile range (IQR). African Americans had significantly higher median calculated energy intake (kcal/day) (1925 vs. 1650;  $p < .001$ ), protein intake (g/day) (76.6 vs. 62.4;  $p < .001$ ), fat intake (g/day) (72.4 vs. 45.3;  $p < .001$ ), vitamin D intake (IU/day) (455.6 vs. 268.7;  $p < .001$ ), vitamin E intake (IU/day) (11.0 vs. 7.9;  $p = .004$ ), and zinc intake (mg/day) (12.6 vs. 9.0;  $p < .001$ ) than Haitian Americans. Conversely, Haitian Americans had a significantly higher median intake of fiber (g/day) (24.1 vs. 17.0;  $p < .001$ ) and carotenoids (IU/day) (11864 vs. 5636;  $p < .001$ ) than African Americans.

Table 8 presents the macro and micronutrients intake of participants by diabetes status. Subjects with T2D had a significantly lower median carbohydrate intake (g/day) (225.4 vs. 257.6;  $p = .012$ ), vitamin E intake (IU/day) (8.1 vs. 10.7;  $p = .030$ ), and vitamin C intake (IU/day) (156.0 vs. 201.2;  $p = .002$ ) than subjects without T2D.

Table 7  
*Macro and Micronutrients Intake of Participants by Ethnicity*

Variables	Ethnicity		P-value
	African Americans	Haitian Americans	
	(n = 209)	(n = 234)	
Energy Intake (kcal/day)	1924.8 (1400.0)	1649.9 (1109.0)	< .001
Protein intake (g/day)	76.6 (54.7)	62.4 (46.4)	< .001
Carbohydrate intake (g/day)	249.0 (192.8)	229.9 (165.0)	.107
Fat intake (g/day)	72.4 (53.4)	45.3 (40.6)	< .001
Fiber intake (g/day)	17.0 (15.8)	24.1 (19.6)	< .001
Vitamin E (IU/day)	11.0 (17.6)	7.9 (10.5)	.004
Vitamin D (IU/day)	455.6 (498.9)	268.7 (384.2)	< .001
Vitamin C (mg/day)	174.1 (221.0)	175.3 (191.6)	.938
Manganese (mg/day)	3.4 (3.1)	4.5 (3.2)	.009
Carotenoids (IU/day)	5635.7 (8240.0)	11864.4 (13762.3)	< .001
Zinc (mg/day)	12.6 (12.0)	9.0 (7.2)	< .001

Data are expressed as median (interquartile range).

Table 8  
*Macro and Micronutrients Intakes of Participants by Diabetes Status*

Variables	Diabetes		P-value
	Yes	No	
	(n=233)	(n=210)	
Energy Intake (kcal/day)	1680.7 (1306.0)	1834.1(1382.0)	.052
Protein intake (g/day)	68.5 (50.0)	69.9 (48.6)	.823
Carbohydrate intake (g/day)	225.4 (173.4)	257.6 (172.3)	.012
Fat intake (g/day)	54.1 (46.8)	57.6 (54.1)	.406
Fiber intake (g/day)	20.3 (17.6)	21.3 (19.2)	.294
Vitamin E (IU/day)	8.1 (11.5)	10.7 (16.5)	.030
Vitamin D (IU/day)	325.8 (431.5)	355.9 (509.1)	.052
Vitamin C (mg/day)	156.0 (181.2)	201.2 (241.7)	.002
Manganese (mg/day)	3.7 (3.1)	3.9 (3.1)	.334
Carotenoids (IU/day)	7153.0 (10132.5)	8435.4 (12374.0)	.214
Zinc (mg/day)	9.8 (10.0)	10.7 (10.2)	.376

Data are expressed as median (interquartile range).

### **Energy intakes of participants by ethnicity and diabetes status**

The participants were compared on the macro and micronutrient intake by ethnicity and diabetes status using non-parametric ANOVA (Table 9). As seen in Table 3, Haitian Americans with T2D had significantly lower energy intake (kcal/day) ( $Md = 1430$ ) than Haitian Americans without T2D ( $Md = 1719$ ), and both had significantly lower intakes than African Americans with and without T2D ( $Mds = 1857, 2020$ , respectively).

### **Protein, Carbohydrate, and Fat Intakes by ethnicity and diabetes status**

Haitian Americans with T2D had a significantly lower median carbohydrate intake (g/day) (206.3) than Haitian Americans without T2D (253) and African Americans with and without T2D (236.6, 259.8, respectively).

### **Vitamin and Mineral Intakes by ethnicity and diabetes status**

Haitian Americans with T2D had a significantly lower median vitamin E intake (IU/day) (7.3) than the other three groups. In addition, Haitian Americans without T2D (9.5) and African Americans with T2D (10.4) had significantly lower median vitamin E intakes than African Americans without T2D (12.3).

Haitian Americans with T2D had a significantly lower median vitamin D intake (IU/day) (236.4) than the other three groups. Haitian Americans without T2D had a significantly lower median vitamin D intake (280.5) than African Americans with and without T2D (371.8, 471.7, respectively).

Haitian Americans with T2D had a significantly lower median vitamin C intake (mg/day) (138.4) than Haitian Americans without T2D (203.9) and African Americans with and without T2D (165.6 and 198.1, respectively).

Haitian Americans without T2D had a higher median manganese intake (mg/day) (4.4) than the other three groups. Median intakes for Haitian Americans with T2D was 4.1 mg/day, for African American without T2D (3.4), and for African Americans with T2D (3.3).

Table 9

*Macro and Micronutrients Intake of Participants by Ethnicity and Diabetes Status*

<b>Variables</b>	<b>African Americans</b>		<b>Haitian Americans</b>	
	<b>Yes</b> ( <i>n</i> = 112)	<b>No</b> ( <i>n</i> = 97)	<b>Yes</b> ( <i>n</i> = 121)	<b>No</b> ( <i>n</i> = 113)
Energy Intake (kcal/day)	1857 (1457) <sup>c</sup>	2020 (1296) <sup>c</sup>	1430 (1150) <sup>a</sup>	1719 (1210) <sup>b</sup>
Protein intake (g/day)	75.9 (58.6) <sup>b</sup>	79.4 (56.4) <sup>b</sup>	60.1 (51.8) <sup>a</sup>	63.5 (42.9) <sup>a</sup>
Carbohydrate intake (g/day)	236.6 (210.0) <sup>b</sup>	259.8 (171.6) <sup>b</sup>	206.3 (145.8) <sup>a</sup>	253.4 (174.5) <sup>b</sup>
Fat intake (g/day)	70.0 (58.0) <sup>b</sup>	73.5 (49.5) <sup>b</sup>	41.9 (41.4) <sup>a</sup>	46.4 (41.2) <sup>a</sup>
Fiber intake (g/day)	16.6 (13.6) <sup>a</sup>	18.3 (17.1) <sup>a</sup>	22.4 (18.8) <sup>b</sup>	25.2 (21.1) <sup>b</sup>
Vitamin E (IU/day)	10.4 (15.7) <sup>b</sup>	12.3 (19.4) <sup>c</sup>	7.3 (8.8) <sup>a</sup>	9.5 (11.4) <sup>b</sup>
Vitamin D (IU/day)	371.8 (472.7) <sup>c</sup>	471.7 (569.9) <sup>c</sup>	236.4 (380.3) <sup>a</sup>	280.5 (425.5) <sup>b</sup>
Vitamin C (mg/day)	165.6 (208.3) <sup>b</sup>	198.1 (260.3) <sup>b</sup>	138.4 (170.0) <sup>a</sup>	203.9 (237.2) <sup>b</sup>
Manganese (mg/day)	3.3 (3.1) <sup>a</sup>	3.4 (3.4) <sup>a</sup>	4.1 (3.2) <sup>a</sup>	4.4 (2.9) <sup>b</sup>
Carotenoids (IU/day)	5618.8 (7236.7) <sup>a</sup>	5644.1 (9472.6) <sup>a</sup>	11368.3 (13612.3) <sup>b</sup>	12162.4 (14915.2) <sup>b</sup>
Zinc (mg/day)	12.2 (12.2) <sup>b</sup>	13.0 (11.9) <sup>b</sup>	9.0 (7.8) <sup>a</sup>	9.0 (6.8) <sup>a</sup>

Data are expressed as median (interquartile range). Variables in groups with different superscripts are significantly different using Holm's sequential Bonferroni post hoc test,  $p < .05$ .

## **Section 2: Correlations**

### **Correlation of Oxidative Stress Biomarkers and Socio-demographic Characteristics**

This section contains results of the correlation analysis between biomarkers and socio-demographics using Pearson's and point bi-serial correlations, depending on the type of socio-demographic variable. The associations between Ln-MnSOD and 8OHdG levels and dietary antioxidant intakes were analyzed with Pearson's correlations. Additionally, Pearson's and point bi-serial correlations measured the relationship between glycemic control with socio-demographic variables and dietary antioxidant intakes for study participants with T2D. Overall, there was a significant negative correlation between Ln-MnSOD and 8OHdG,  $r = -.17, p < .001$ , so that lower levels of Ln-MnSOD associated with higher levels of 8OHdG.

### **Correlation of Oxidative Stress Biomarkers and Study Variables**

Table 10 presents the Pearson's correlation analysis of oxidative stress biomarkers with study variables. Ln-MnSOD was negatively correlated with BMI,  $r = -.15, p < .05$ , and 8OHdG was positively correlated with BMI,  $r = .15, p < .05$ , age,  $r = .13, p < .01$ , and being male,  $r = .11, p < .05$ . Thus, lower levels of Ln-MnSOD were associated with greater BMI, while higher levels of 8OHdG were associated with greater BMI, being older and being male.



Table 10  
*Pearson's Correlations of Oxidative Stress Biomarkers with Study Variables*

<b>Participants (n = 433)</b>			
<b>Variables</b>	<b>MnSOD</b>	<b>Ln-MnSOD</b>	<b>8OHdG</b>
Age (years)	-.10*	-.09	.13**
Gender (male)	.07	.06	.11*
BMI (kg/m <sup>2</sup> )	-.15**	-.15**	.15**
Smoke (yes)	.10*	.07	.04
Energy Intake(kcal/day)	.04	.02	-.05
Education	.08	.07	.01
Less than high school	-.11*	-.10*	-.03
High school grad/GED	.07	.07	.04
Some college/technical school	.07	.06	-.01
Graduate school	-.02	-.02	.00

\*  $p < .05$ , \*\*  $p < .01$

BMI = body mass index; MnSOD = Manganese Superoxide Dismutase; 8OHdG = 8-hydroxy-2'-deoxyguanosine. Ln-MnSOD = Natural logarithm of Manganese Superoxide Dismutase.

Table 11 presents Pearson's correlation analysis of oxidative stress biomarkers with dietary antioxidants intakes. Lower levels of Ln-MnSOD were associated with lower levels of zinc,  $r = .10, p < .05$ , and higher levels of carotenoids,  $r = -.10, p < .05$ . Higher levels of 8OHdG were associated with lower levels of Vitamin D,  $r = -.14, p < .01$ , and carotenoids,  $r = -.09, p < .05$ .

Table 12 presents Pearson's correlation analysis of glycemic control with socio-demographic variables and dietary antioxidant intakes for study participants with T2D. Diabetic participants with higher FPG had lower intakes of Vitamin D,  $r = -.14, p < .05$ . Higher A1C levels in T2D participants were associated with being Haitian,  $r = -.19, p < .01$ , and having less education,  $r = -.14, p < .05$ .

In addition, for Haitian Americans with T2D, higher FPG levels were associated with lower BMI,  $r = -.25, p < .01$ , and lower Vitamin C intakes,  $r = -.19, p < .05$ . For African Americans with T2D, higher FPG levels were associated with higher Vitamin E intakes,  $r = -.25, p < .01$ . Higher A1C levels were associated with lower carotenoids intakes,  $r = -.19, p < .05$ , for this group.

Table 11  
*Pearson's Correlations of Oxidative Stress Biomarkers with Study Variables*

<b>Participants (n = 433)</b>			
<b>Variables</b>	<b>MnSOD</b>	<b>LnMnSOD</b>	<b>8OHdG</b>
Energy Intake (kcal/day)	.04	.02	-.05
Vitamin E / 1000 kcal/day	-.00	-.01	.01
Vitamin D / 1000 kcal/day	.08	.07	-.02
Vitamin C / 1000 kcal/day	.06	.07	-.14**
Manganese / 1000 kcal/day	-.06	-.03	.00
Carotenoids / 1000 kcal/day	-.11*	-.10*	-.09*
Zinc / 1000 kcal/day	.10*	.10*	.00

\*  $p < .05$ , \*\*  $p < .01$

BMI = body mass index; MnSOD = Manganese Superoxide Dismutase; 8OHdG = 8-hydroxy-2'-deoxyguanosine. Ln-MnSOD = Natural logarithm of Manganese Superoxide Dismutase.

Table 12  
*Pearson's Correlations of Glycemic Control with Study Variables in Individuals with T2D*

Variables	Glycemic Control (n = 433)	
	FPG	A1C
Ethnicity (African American)	-.12	-.19**
Age (years)	-.04	-.10
Gender (male)	.07	.06
BMI (kg/m <sup>2</sup> )	-.12	-.07
Smoke (yes)	-.04	.01
Energy Intake(kcal/day)	-.06	-.09
Education	-.10	-.14*
Less than high school	.09	.13
high school grad/GED	-.01	-.04
some college/technical school	-.03	-.04
graduate school	-.08	-.08
Vitamin E / 1000 kcal	.11	-.01
Vitamin D / 1000 kcal	-.14*	-.02
Vitamin C / 1000 kcal	-.07	-.05
Manganese / 1000 kcal	.01	.04
Carotenoids / 1000 kcal	.04	.02
Zinc/1000 kcal	-.04	-.05

\*  $p < .05$ , \*\*  $p < .01$

A1C = glycosylated hemoglobin; FPG = fasting plasma glucose; BMI = body mass index.

### **Section 3: Hypotheses Testing**

Hypothesis testing was conducted with Analysis of Covariance (ANCOVA), and multiple linear regression analysis. We compared the levels of MnSOD and 8OHdG by ethnicity and diabetes status using ANCOVAs. Post hoc test using Fisher's LSD procedure were carried out on the adjusted ethnic and diabetes status means for significant tests of interaction.

Relationships of MnSOD and 8OHdG with dietary antioxidants by ethnicity and diabetes status were analyzed by multiple linear regression analyses. The relationships between glycemic controls (A1C) and fasting plasma glucose levels (FPG) with dietary antioxidants by ethnicity and diabetes status were determined with multiple linear regression analyses. The covariates for all analyses were age, gender, smoking status, education, BMI, and energy intake.

**Aim 1. To determine the differences in serum MnSOD and 8OHdG by diabetes status and ethnicity.**

**Hypothesis 1a: Serum levels of MnSOD will be lower in participants with T2D as compared to those without T2D, independent of ethnicity**

#### **ANCOVA on Manganese Superoxide Dismutase (MnSOD)**

In a two way ANCOVA on Ln-MnSOD by ethnicity (Haitian, African American) and diabetes status (yes/no), both main effects were significant,

ethnicity,  $F(1,433) = 55.46, p < .001, \eta^2 = .11$ , diabetes status,  $F(1,433) = 108.57, p < .001, \eta^2 = .20$ . However, the main effects were moderated by significant interaction of ethnicity by diabetes status,  $F(1,433) = 293.43, p < .001, \eta^2 = .40$ . By convention, a “small” effect is  $\eta^2 = .01$ , a “medium” effect is  $\eta^2 = .06$ , and a “large” effect is  $\eta^2 = .16$ . These effects were all very large. The adjusted mean Ln-MnSOD for African Americans without diabetes ( $M = 8.16$ ) was significantly larger than for African Americans with diabetes ( $M = 7.40$ ) and for Haitian Americans with and without diabetes ( $M = 7.63; M = 7.46$ , respectively).

Hypothesis one was not supported. Although African Americans with diabetes had lower MnSOD levels than African Americans without diabetes, this was not the case for Haitian Americans, so lower serum levels of MnSOD in T2D participants was not independent of ethnicity.

**Hypothesis 1b: Serum levels of 8OHdG will be higher in participants with T2D when compared to without T2D, independent of ethnicity.**

#### **ANCOVA on mtDNA 8-hydroxy-2'-deoxyguanosine (8OHdG)**

In a two way ANCOVA on 8OHdG by ethnicity and diabetes status, both main effects were significant, ethnicity,  $F(1, 433) = 6.44, p = .012, \eta^2 = .02$ , diabetes status  $F(1,433) = 126.38, p < .001, \eta^2 = .23$ . There was not a significant interaction effect,  $F(1,433) = .05, p = .826, \eta^2 < .01$ .

In support of Hypothesis 1b, the adjusted 8OHdG mean ( $M = 1761.36$ ) for individuals with diabetes was significantly higher than those without diabetes ( $M = 1544.11$ ), independent of ethnicity. Additionally, the adjusted 8OHdG mean for African Americans ( $M = 1680.47$ ) was significantly higher than for Haitian Americans ( $M = 1625.00$ ).

**Hypothesis 1c: There will be an inverse relationship between serum levels of MnSOD and 8OHdG in participants with T2D, independent of ethnicity.**

#### **Multiple Linear Regression of MnSOD with 8OHdG**

The multiple regression analysis of 8OHdG on MnSOD with control variables of ethnicity, diabetes status, age, gender, smoking status, education, BMI, and energy intake was significant,  $R^2 = 29.6\%$ ,  $F(10,433) = 18.15$ ,  $p < .001$ . However, MnSOD did not explain significant additional variability of 8OHdG,  $R^2 \text{ change} = 0.3\%$ ,  $F(1,432) = 2.14$ ,  $\beta = -.09$ ,  $p = .145$ . In the final model, significant covariates were: having T2D,  $\beta = .51$ ,  $p < .001$ , being male,  $\beta = .14$ ,  $p = .002$ , and being African American,  $\beta = .22$ ,  $p = .011$ .

Hypothesis 1c was not supported in that the data did not show an inverse relationship between the serum levels of MnSOD and 8OHdG in African Americans and Haitian Americans with T2D.

**Aim 2: To determine the relationships of serum MnSOD and 8OHdG with various dietary antioxidants by diabetes status and ethnicity.**

**Hypothesis 2a: Serum 8OHdG levels will be negatively associated with dietary intake of antioxidants, independent of diabetes status and ethnicity.**

**Multiple Linear Regression of 8OHdG on dietary intake of antioxidants**

Multiple linear regression analysis showed that vitamin C intake per 1000 kcal explained significant additional variability of 8OHdG,  $R^2$  change = 0.8%,  $F(1,432) = 5.25$ ,  $\beta = -.10$ ,  $p = .022$ . In this model, lower levels of 8OHdG were associated with higher vitamin C levels after controlling for age, gender, smoking status, education, BMI, energy intake, ethnicity, diabetes status and the interaction between ethnicity and diabetes status. Significant covariates were: having type 2 diabetes,  $\beta = .48$ ,  $p < .001$ ; being African American,  $\beta = .13$ ,  $p = .034$ ; the interaction between having type 2 diabetes and African American,  $\beta = -.14$ ,  $p < .001$ ; and being male,  $\beta = .12$ ,  $p < .005$ .

Vitamin D intake per 1000 kcal did not explain significant additional variability of 8OHdG,  $R^2$  change = 0.0%,  $F(1,432) = 0.10$ ,  $\beta = .01$ ,  $p = .922$ . Significant covariates were: having type 2 diabetes,  $\beta = .49$ ,  $p < .001$ ; being male,  $\beta = .13$ ,  $p = .002$ ; and being African American,  $\beta = .13$ ,  $p = .037$ .

Vitamin E intake per 1000 kcal did not explain significant additional variability of 8OHdG,  $R^2$  change = 0.0%,  $F(1,432) = 0.80$ ,  $\beta = .01$ ,  $p = .927$ . Significant covariates were: having type 2 diabetes,  $\beta = .49$ ,  $p < .001$ ; being male,  $\beta = .13$ ,  $p = .003$ ; and being African American,  $\beta = .13$ ,  $p = .035$ .



Carotenoids intake per 1000 kcal did not explain significant variability of 8OHdG,  $R^2$  change = 0.2%,  $F(1,432) = .975$ ,  $\beta = -.04$ ,  $p = .324$ . Significant covariates were: having type 2 diabetes,  $\beta = .49$ ,  $p < .001$ ; and being male,  $\beta = .13$ ,  $p = .003$ .

Hypothesis 2a was supported for vitamin C, but not for vitamin D, E, or carotenoids.

**Hypothesis 2b: MnSOD levels will be negatively associated with dietary intake of antioxidants, independent of diabetes status and ethnicity.**

**Multiple linear regression analysis on MnSOD on dietary intake of antioxidants**

Vitamin C intake per 1000 kcal did not explain significant additional variability of ln-MnSOD,  $R^2$  change = 0.2%,  $F(1, 432) = 1.90$ ,  $p = .169$ . Significant covariates were being African American,  $\beta = .878$ ,  $p < .001$ , having diabetes,  $\beta = .22$ ,  $p < .001$ , and interaction between ethnicity and diabetes status,  $\beta = -1.01$ ,  $p < .001$ .

Vitamin D intake per 1000 kcal did not explain significant additional variability of ln-MnSOD,  $R^2$  change = 0.0%,  $F(1, 432) = .294$ ,  $p = .588$ . Significant covariates were being African American,  $\beta = .872$ ,  $p < .001$ , having diabetes,  $\beta = .215$ ,  $p < .001$ , and interaction between ethnicity and diabetes status,  $\beta = -1.007$ ,  $p < .001$ .

Vitamin E intake per 1000 kcal did not explain significant additional variability of ln-MnSOD,  $R^2$  change = 0.1%,  $F(1,432) = .879$ ,  $p = 0.349$ . Significant covariates were being African American,  $\beta = .88$ ,  $p < .001$ , having diabetes,  $\beta = .21$ ,  $p < .001$ , and the interaction between African American and diabetes status,  $\beta = -1.01$ ,  $p < .001$ .

Carotenoids intake per 1000 kcal did not explain significant additional variability of ln-MnSOD,  $R^2$  change = 0.1%,  $F(1, 432) = 1.268$ ,  $p = .261$ . Significant covariates were being African American,  $\beta = .863$ ,  $p < .001$ , having diabetes,  $\beta = .215$ ,  $p < .001$ , and interaction between ethnicity and diabetes status,  $\beta = -1.009$ ,  $p < .001$ .

Hypothesis 2b was not supported for any of the antioxidants, vitamin C, D, E or carotenoids.

**Aim 3: To examine the relationships of glycemic control (A1C) and fasting plasma glucose level with dietary antioxidants in T2D by ethnicity.**

Control variables for the multiple regression analyses were: ethnicity, age, gender, education, energy intake, BMI, and smoking status. Only diabetic participants were included in these analyses.

Haitian Americans with T2D had significantly higher fasting plasma glucose (mg/dl) ( $M = 158$ ) than African Americans with T2D ( $M = 143$ ), and similarly, Haitian Americans with T2D had significantly higher A1C levels (%) ( $M = 8.4$ ) than African Americans with T2D ( $M = 7.5$ ), (Table 6).

**Hypothesis 3a: There will be no relationship between serum A1C and any dietary antioxidants in participants with T2D independent of ethnicity.**

### **Multiple Linear Regression of Hemoglobin A1C (A1C)**

Vitamin C intake per 1000 kcal did not explain significant additional variability of A1C,  $R^2$  change = 0.0%,  $F(1,432) = .27$ ,  $\beta = .04$ ,  $p = .601$ . The significant covariates was being African American,  $\beta = -.19$ ,  $p = .023$ .

The multiple regression analysis of A1C on vitamin D was not significant,  $R^2 = 6.9\%$ ,  $F(8, 224) = 2.09$ ,  $p = .995$ . Vitamin D did not explain significant additional variability in the model,  $R^2$  change = 0.0%,  $\beta = -.01$ ,  $p = .905$ . The significant covariate was being African American,  $\beta = -.20$ ,  $p = .020$ .

The multiple regression analysis of A1C on vitamin E, was not significant,  $R^2 = 6.9\%$ ,  $F(8, 224) = 2.09$ ,  $p = .943$ . Vitamin E did not explain significant additional variability in the model,  $R^2$  change = 0.0%,  $\beta = .01$ ,  $p = .943$ . The significant covariate was being African American,  $\beta = -.20$ ,  $p = .020$ .

The multiple regression analysis of A1C on carotenoids, was not significant,  $R^2 = 6.9\%$ ,  $F(8, 224) = 2.09$ ,  $p = .685$ . Carotenoids did not explain significant additional variability in the model,  $R^2$  change = 0.0%,  $\beta = .04$ ,  $p = .604$ . The significant covariate was being African American,  $\beta = -.12$ ,  $p = .045$ .

Hypothesis 3a was supported since A1C was not related to any of the antioxidants, vitamin C, D, E or carotenoids, for T2D participants.

**Hypothesis 3b: There will be no relationship between fasting plasma glucose level and any of the dietary antioxidant intakes in T2D independent of ethnicity.**

**Multiple regression analysis of fasting plasma glucose (FPG)**

The multiple regression analysis of FPG on vitamin C per 1000 kcal was not significant,  $R^2 = 4.1\%$ ,  $F(8,224) = 1.20$ ,  $p = .302$ . Vitamin C intake did not explain significant additional variability of FPG,  $R^2 \text{ change} = 0.1\%$ ,  $F(1,432) = 1.17$ ,  $\beta = -.07$ ,  $p = .280$ . The significant covariate was being African American,  $\beta = -.19$ ,  $p = .023$ .

The multiple regression analysis of FPG on vitamin D per 1000 kcal was not significant,  $R^2 = 5.3\%$ ,  $F(8,224) = 1.57$ ,  $p = .135$ . Vitamin D intake per 1000 kcal explained significant additional variability of FPG,  $R^2 \text{ change} = 1.7\%$ ,  $F(1,432) = 4.05$ ,  $\beta = -.13$ ,  $p = .045$ . The significant covariate was being African American,  $\beta = -.20$ ,  $p = .020$ .

The multiple regression analysis of FPG on vitamin E intake per 1000 kcal was not significant,  $R^2 = 4.9\%$ ,  $F(8,224) = 1.44$ ,  $p = .183$ . Vitamin E intake did not explain significant additional variability of FPG,  $R^2 \text{ change} = 1.3\%$ ,  $F(1,432) = 3.11$ ,  $\beta = .11$ ,  $p = .084$ . The significant covariate was being African American,  $\beta = -.19$ ,  $p = .023$ .

The multiple regression analysis of FPG on carotenoids intake per 1000 kcal was not significant,  $R^2 = 3.7\%$ ,  $F(8,224) = 1.07$ ,  $p = .388$ . Carotenoids did not

explained significant additional variability of FPG,  $R^2$  change = 1.9%,  $F(1,432)$   
= 2.09,  $\beta = -.14$ ,  $p = .083$ .

Hypothesis 3b was supported since fasting plasma glucose was not significantly related to any of the antioxidants, vitamins C, D, E, or carotenoids for T2D participants.

Table 13  
*Results of Hypothesis Testing*

HYPOTHESIS	RESULTS
<p><b>H<sub>1a</sub>:</b> Serum levels of MnSOD will be lower in participants with T2D as compared to those without T2D, independent of ethnicity.</p>	<p><b>Hypothesis 1a</b> was not supported. Although African Americans with diabetes had lower MnSOD levels than African Americans without diabetes, this was not the case for Haitian Americans, so lower serum levels of MnSOD in T2D participants was not independent of ethnicity.</p>
<p><b>H<sub>1b</sub>:</b> Serum levels of 8OHdG will be higher in participants with T2D when compared to those without T2D, independent of ethnicity.</p>	<p><b>Hypothesis 1b</b> was supported since the adjusted serum levels of 8OHdG mean for individuals with diabetes was significantly higher than for those without diabetes, independent of ethnicity. Also, adjusted 8OHdG mean for African Americans was significantly higher than for Haitian Americans.</p>
<p><b>H<sub>1c</sub>:</b> There will be an inverse relationship between serum levels of MnSOD and 8OHdG in participants with T2D, independent of ethnicity.</p>	<p><b>Hypothesis 1c</b> was not supported by the findings in this study.</p>
<p><b>H<sub>2a</sub>:</b> Serum 8OHdG levels will be negatively associated with dietary intake of antioxidants, independent of diabetes status and ethnicity.</p>	<p><b>Hypothesis 2a</b> was not supported for vitamin C since multiple linear regression analysis showed that vitamin C intake per 1000 kcal explained significant additional variability of 8OHdG, <math>R^2</math> change = 0.8%, <math>\beta</math> = -0.10, <math>p</math> = .022</p>
<p><b>H<sub>2b</sub>:</b> Serum MnSOD levels will be negatively associated with dietary intake of antioxidants, independent of diabetes status and ethnicity.</p>	<p><b>Hypothesis 2b</b> was not supported since multiple regression analysis showed that none of the antioxidants, vitamins C, D, E or</p>

carotenoids, were significant in explaining the variability of Ln-MnSOD.

**H<sub>3a</sub>:** There will be no relationship between serum A1C and dietary antioxidants in participants with T2D independent of ethnicity.

**Hypothesis 3a** was supported since serum A1C was not related to any of the antioxidants in the multiple regression analyses on T2D participants.

**H<sub>3b</sub>:** There will be no relationship between fasting serum glucose level and any of the dietary antioxidant intakes in T2D independent of ethnicity.

**Hypothesis 3b** was supported since fasting plasma glucose was not related to any of the antioxidants in the multiple regression analyses on T2D participants.

## **CHAPTER V**

### **DISCUSSION**

This chapter presents the discussion of the results. It is organized as follows: First, the descriptive statistics of the participants' general characteristics and socio-demographic status; Secondly the interpretation and qualitative analysis are discussed in the order which the aims and hypothesis were presented in this study. Finally, the study strengths and limitations, conclusions, and recommendations for future studies are provided.

Researchers and healthcare practitioners recognize that there are ethnic differences and disparities in many health disorders. It has been reported that blacks have a higher incidence of diabetes and diabetes related complications (Huffman et al., 2013) than whites, and there is an increasing awareness of ethnic group differences among subgroups normally grouped together as blacks. Two such subgroups are African Americans and Haitian Americans, both of whom were examined in this research study.

#### **General Characteristics of Participants**

African Americans are affected by diabetes disproportionately as compared to the general population. They are 1.8 times more likely to have diabetes and also more likely to develop diabetes complications such as kidney disease, blindness and cardiovascular disease when compared with whites (ADA, 2013). The prevalence of having diabetes in African Americans was determined to be 18.7 percent (ADA, 2013). Often time poor dietary patterns correlate with



poor health, and the traditional diet of African Americans called “soul food” has been reported as being a poor diet, consisting of southern style foods which include pork chops and fried fatty foods (Anderson-Loftin et al., 2005).

The culture of Haitian Americans may explain the differences in study variables when compared with African Americans (“Background on Haiti”, 2010). Haitian Americans resistance to healthcare screening may relate to their mistrust of healthcare providers. This under-utilization of health care resources may result in undiagnosed or untreated cardiovascular disease and T2D. According to a report by Huffman et al. (2013), although the diet of Haitian Americans is healthier than African Americans, it is not necessarily a healthy diet. The researchers reported that African American diet consisted of high fat content as compared with Haitian Americans whose diet consisted of fish, chicken, fruits and vegetables. African Americans scored lower than Haitian Americans using the Health Eating Index, indicating that Haitian Americans had a healthier diet than African Americans. The components of a high fat diet include hydrogenated oils, animal fats, free fatty acids, which are found in African Americans and may contribute to an increase risk of T2D and this type of dietary pattern may lead to increased oxidative stress (Watters, et al., 2007).

The information on the general characteristics of the respective diets for the study participants were obtained from a FFQ completed by the participants and from physiologic biometrics recorded by trained research assistants. In this study, African American participants were generally younger, had higher BMI,

higher energy intakes, were more educated, and had a greater percentage of smokers than Haitian Americans (Table 1). There were similar numbers of male and female participants for both ethnicities. The data obtained from the FFQ show higher energy intakes observed in African Americans which explains the higher BMI compared with Haitian Americans.

The characteristics of participants by diabetes status are shown in Table 2. Participants with T2D had higher BMI ( $32.1 \text{ kg/m}^2 \pm 6.5$ ) compared with participants without T2D ( $29.7 \text{ kg/m}^2 \pm 5.7$ ). The average BMI of participants without T2D were within the range classified as overweight and those with T2D were classified as obese. Since the participants without T2D were classified as overweight, they also have an increased risk for diabetes (Sanada et al., 2012). These findings complement those reported by other researchers (Wee et al., 2008) who used data obtained from the 1999-2004 National Health and Nutrition Examination Survey (NHANES).

The participants with T2D had lower energy intake when compared to participants without T2D. The lower energy intake in participants with T2D may be explained by low calorie diets which are normally prescribed by healthcare practitioner as part of a treatment program. It is well documented that there is a strong positive association between energy intake with insulin resistance (Donin et al., 2013) and that weight loss is central to glycemic control improvement (Looker et al., 2001). Additionally, the low energy intake may be a result of under-reporting or due to false perception of food portion sizes and

misrepresentation of actual intake (Samuel-Hodge et al. 2004). Olendzki et al. (2014) reported similar findings about under-reporting and they observed that the prevalence of under-reporting in a Caribbean Latino population studied was related to BMI, gender, and educational level. In this study, if the total energy intake calculated from the FFQ was <500 kcal per day or >5000 kcal per day, then the data was not included in the analysis. Similar cutoffs were reported by Hebert et al. (2002) as a common means to exclude reporting errors and extreme values.

### **Biomarkers**

There are many assays developed to quantify oxidative stress, including the measure of oxidation of proteins, lipids, DNA, and antioxidant enzymes. The focus of this study is blood antioxidant enzyme manganese superoxide dismutase (MnSOD) and the byproduct of mtDNA damage known as 8-hydroxy-2'-deguanosine (8OHdG). These variables were studied because of their localization and interaction in the mitochondria, and also because of their participation in the T2D associated progressive disorders (Kirk et al., 2006; Fairheller et al., 2011). The relationship between oxidative stress and diabetes status was examined because the literature review has shown that reactive oxygen species also influences the glycemic control (Kirk et al., 2006; Fairheller et al., 2011). In addition to elevated reactive oxygen species, the literature presented evidence that there is a direct correlation with elevated levels of oxidative stress biomarkers.

Glycemic control can be determined with the blood biomarkers FPG and A1C (ADA, 2013). This study examined serum levels of oxidative stress biomarkers and glycemic control indicators and provided data on macro and micronutrients intakes obtained from food frequency questionnaire. The relationship of serum levels of manganese superoxide dismutase and mtDNA 8-hydroxy-2'-deoxyguanosine were examined. In addition, the relationship when compared with dietary antioxidants intake in T2D in African Americans and Haitian Americans, two different ethnic groups, were determined.

An intensive literature search showed limited amount of data on the differences within minority groups. This study provided information of differences on serum levels of MnSOD and 8OHdG among African Americans and Haitian Americans. In addition, this report is the first cross sectional study that examined the relationship of oxidative stress biomarkers among African Americans and Haitians with and without T2D.

The aim of this study was to examine the serum levels of 8OHdG, the surrogate biochemical marker for mtDNA damage, and MnSOD which is the body's primary antioxidant enzyme that protects the DNA in the mitochondria. We also investigated their relationship to dietary antioxidant intakes and glycemic control. Previous studies (Arab et al., 2011; Kirk et al., 2006; Fairheller et al., 2011) reported differences between African Americans and whites for glycemic control, oxidative stress biomarkers, and dietary antioxidants. Kirk et al. found ethnic disparities in glycemic control in African

Americans and Non-Hispanic White adults with diabetes and reported that the cause of disparity may be related to the access to medical care and the amount of dietary antioxidants consumed. In this study, differences were found in glycemic control and dietary antioxidants intakes between African Americans and Haitian Americans. While access to medical care and attendance of doctor's visits was not a part of this project, these variables may have played a role. The findings of this study show significantly higher levels of 8OHdG and lower levels of MnSOD found in African Americans with T2D than in Haitian Americans with T2D, indicating higher oxidative stress among African Americans.

The mitochondria produce superoxide ions, the most abundant ROS produced, that may participate in the damage of cellular macromolecules. There is evidence that superoxide has an association with the development of diabetes complications and that MnSOD is the first line of defense in neutralizing superoxide in the mitochondria (Du et al., 2003; Brownlee, 2005). This study showed that the serum levels of MnSOD were higher in African Americans than Haitian Americans. Upon closer examination, the serum MnSOD levels of African Americans were lower for those with diabetes compared to without diabetes. These finding supported previous reports of decreased MnSOD activity in white blood cells of participants with diabetes compared to those without diabetes (Wegner, et al., 2014; Kazi et al., 2008). These findings may be interpreted that the mtDNA is not being protected efficiently due to the reduce MnSOD level and could lead to development diseases associated with T2D. Additionally, it was observed that dietary manganese intake level was lower in

African Americans compared with Haitian Americans, and since manganese is a cofactor for the production of MnSOD, then may indicate a need for an improved quality in their diet. Currently there is no information available in the literature on serum levels of MnSOD in African American versus Haitian Americans.

The significant differences in serum levels of MnSOD and 8OHdG among African Americans and Haitian Americans provide evidence of ethnic difference within the black population. African Americans group had greater levels of both MnSOD and 8OHdG when compared with Haitian Americans. These observations also suggest that there appears to be ethnic differences in T2D, a major risk factor for CVD, therefore therapeutic interventions need to be managed according to ethnicity. To the best of our knowledge, this is the first time that these differences were determined.

The method that is used to quantify the serum levels of 8OHdG in this study was based on the ELISA principle, and has been validated and critically reviewed by Helliwell et al. (1996). The ELISA method is believed to be advantageous over analytical methods such as HPLC and gas chromatography/mass spectrometry. This is due to the elimination of artificial 8OHdG which may be introduced during the isolation of DNA, especially in phenol-based DNA purification procedures (Claycamp, 1992). The fact that we were able to identify significant association between 8OHdG and MnSOD suggest that cross-reactivity was not likely to interfere with the validity of the

assay. In addition, the intra-assay coefficient of variation, 8.5%, indicates that the ELISA assay had repeatability.

A two way ANOVA showed that ethnicity and diabetes status had a significant relationship with 8OHdG. Higher levels of serum 8OHdG were found in T2D group compared to those participants without T2D. In addition, lower serum 8OHdG levels were found in Haitian Americans with T2D compared with African Americans with T2D. The role of MnSOD is to protect mtDNA from oxidative stress, and the data showed that MnSOD was higher while 8OHdG was lower in Haitian Americans than in African Americans. The strength of this observation was considered to be large since the effect size was large for both main effects. These findings indicate that there was more mtDNA damage in the T2D groups, of which African Americans may have a greater risk of T2D associated complications when compared with Haitian Americans with T2D.

The positive correlation of 8OHdG and BMI in the diabetic group suggests that obesity may have an additive effect with increased fasting plasma glucose in oxidative mtDNA damage. The covariates were age, gender, smoking status, education, BMI, and energy intake. Similar results were reported by Al-Aubaidy et al. (2011) in their clinical study on oxidative DNA damage and obesity in T2D mellitus. They also suggested that serum 8OHdG levels were already increasing in prediabetes.

One of the risk factors for diabetes is smoking, which may contribute to elevated levels of ROS. Isik et al. 2007 showed that smoking may contribute to ROS through the weakening of the primary antioxidant defense system and production of free radicals. The literature provides conflicting evidence of the relationship of 8OHdG in smokers and non-smokers. In this study, we did not find any significant correlation of either 8OHdG or MnSOD with smoking, but this may be attributed to the low sample size of participants who were identified as smokers, thus the comparison may have lacked the power to detect a significant difference.

There were significant differences found with 8OHdG and gender. Gender, in addition to smoking and BMI, was also reported in the literature as significant predictor of increased 8OHdG levels (Loft, et al., 1992).

Although there was a weak relationship in the overall correlation between Ln-MnSOD and 8OHdG, there is evidence that higher serum 8OHdG levels were associated with lower serum MnSOD levels. The regression analysis of 8OHdG on MnSOD was significant, with covariates of ethnicities, diabetes status, age, gender, education, energy intake, BMI, and smoking status. However, after controlling for all covariates, MnSOD did not explain the significance and additional variability of 8OHdG. In the final model, significant covariates were being male, African American, and having with T2D.

We examined the relationship between dietary antioxidants intakes and found that serum 8OHdG levels negatively correlated with vitamin C intakes.



That is, lower dietary intake of vitamin C was found to be associated with higher levels of 8OHdG. Similar results were reported by Moller et al. (2002) in a dietary antioxidant intervention study. This observation may be due to the possible protection of the mtDNA from oxidative stress. Also, we observed a negative correlation between dietary carotenoids intakes with MnSOD and 8OHdG. There were no relationship observed between vitamin E and vitamin D with either MnSOD or 8OHdG.

In T2D, uncontrolled blood glucose levels may participate in disease pathophysiology which is associated with DNA damage. In this study, the findings were similar to the studies reported by Salem et al. (2012) in that subjects with T2D had greater DNA damage, higher levels of inflammation and oxidative stress, and were positively associated with higher levels of blood glucose levels. Since high blood glucose levels may interfere with cell replication and adversely influence the death rate of cells, there is a need to study ways in which to maintain DNA integrity and also to reduce the abnormal levels of ROS.

This study used A1C and FPG as indices glycemic control. The data showed that there were ethnic differences in A1C where African Americans had lower A1C than Haitian Americans. These findings were similar to Vimalananda et al. (2011) study that compared diabetes control among Haitians, African Americans, and Non-Hispanic Whites. Although Haitian Americans appear to consume less carbohydrate than the African Americans, the Haitian Americans

had worse glycemic control. These findings may suggest that MnSOD may contribute to glycemic control, but proper medication use may be a major factor and this study was not designed to address this variable. Although findings of a negative relationship with glycemic control and serum MnSOD levels were not found in the scientific literature for Haitian Americans, a similar relationship was observed in Type 1 diabetes patients by Wegner et al. (2014). The report did not identify the ethnicity of the type 1 diabetes patients.

There was a marginal association of fasting plasma glucose with vitamin E, and vitamin D. Vitamin E intakes were not significant with FPG, but it explained some variance and it was marginally significant. In addition, dietary intake of vitamin D was found to be associated with lower fasting plasma glucose. Dietary intakes of vitamin D were not significantly associated with FPG, but it explained a small but significant variance in FPG. Saedisomeolia et al. (2013) had different findings in their cross-sectional study. They observed a positive relationship between serum vitamin D levels with glycemic control in Iranians, where 82% of the participants with T2D and 75% of the participants without T2D were either vitamin D deficient or insufficient. The researchers interpreted these findings that vitamin D had beneficial effect on glycemic control.

### **Strengths of the Study**

This study is the first to report on the serum levels of MnSOD and 8OHdG in Haitian Americans with and without T2D, and it also provided data

on the relationship between these oxidative stress biomarkers with dietary and glycemic control indicators. This study provides evidence that there are ethnic difference in African American and Haitian American in dietary intakes, glycemic control indicators and oxidative stress levels components. This implies that educators and clinicians should be cognizant that treatment modalities should be ethnically based.

The instruments used in this study for data collection from the subjects were validated and standardized. The research personnel were trained to properly and accurately use the instruments and also correctly complete and score the questionnaires used to gather information from the participants.

The participants of this study were provided a copy of the results of their cardiovascular risk analysis, blood glucose levels, A1C, and lipid profile as determined from the blood collected and, in some cases, they were alerted to cardiovascular risk that they were not aware or would have identified if it was not for this study.

### **Limitations of the Study**

A limitation of this study was that it was cross-sectional design and provided a snapshot relationship. In addition, although a validated nutrition assessment questionnaire was used to assess the dietary intake of antioxidants, it relies heavily on the subjects recall biases and estimate of portion size (Samuel-Hodge et al., 2004; Olendzki et al., 2014). The results of this study should be interpreted with caution and indeed, the lack of association between 8OHdG and

dietary antioxidants could have a more favorable outcome if antioxidant levels were determined from serum or plasma. The study design was observational and the results may not be interpreted to have causality effect.

### **Conclusion and Recommendations**

This study found inverse relationship between serum MnSOD and 8OHdG; suggesting that serum MnSOD and 8OHdG are useful biomarkers of oxidative stress in subjects with T2D. We found that there were decreased serum levels of MnSOD in participants with T2D when compared to participants without T2D, and that there were elevated levels of 8OHdG present in participants with T2D indicating higher oxidative stress in persons with T2D.

Additionally, we observed ethnic differences between African Americans and Haitian Americans with T2D, showing lower oxidative stress among diabetic Haitian Americans associated with higher intake of dietary antioxidants. The dietary antioxidants zinc and vitamin C were inversely correlated with 8OHdG suggesting that dietary intakes of antioxidant may provide health benefits by reducing mtDNA damage.

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## APPENDICES

- Appendix A: Recruitment Flyer (English version)
- Appendix B: Recruitment Flyer (Creole version)
- Appendix C: Florida International University IRB Approval
- Appendix D: Form A- For Initial Submission for IRB Approval
- Appendix E: IRB Exemption Memorandum
- Appendix F: Harvard Food Frequency Questionnaire
- Appendix G: Socio-demographic Questionnaire
- Appendix H: Document to collect measured parameters
- Appendix I Summary of study method

## **APPENDIX A**

# **Cardiovascular Disease Risk Study in Haitian & African-American**

**You are invited to participate in a study  
conducted at Florida International  
University  
by Dr. Fatma G. Huffman**

## **Criteria to enroll:**

- You must be Haitian or African-American
- You must be 35 years old or older
- You must agree to give three tablespoons of blood to test glucose levels and other biochemical tests
- You must agree to give a urine sample

You will receive information on your diet, physical activity level, body mass index, blood pressure and laboratory blood analysis. The whole process generally takes 3 hours.

**You will receive \$ 75.00 upon completion of the study**

## **For information, please contact:**

Dr. Fatma G. Huffman: 305-348-6427 or [huffmanf@fiu.edu](mailto:huffmanf@fiu.edu)

## **APPENDIX B**

# **Étid sou maladi Kadiovaskilè Lakay Ayisyen ak Afriken-Amériken**

Nou invité ou pou ou kapab patisipé nan yon  
étid Ké Dr. Fatma G. Huffman ap fè Nan  
Florida International Université

## **Kondisyon pou kapab patisipé nan étid sa-a:**

- Ou sipozé Ayisyen ou byen Afriken-Amériken
- Ou sipozé genyen 35 ans ou plis
- Aksepté ké yo pran kèk gout san sou ou min-m pou yo kapab tchéké sik ou avèk lòt analiz nan san ou.
- Aksepté pou ou bay yon ti échantiyon pipi

Konsiltasyon a ap dire 3 zè de tan. Nan moman sa a, wap  
résévwa enfomasyon sou dayèt ou, enfomasyon sou aktivité  
fisik ou, enfomasyon sou tensyon ou, plis lòt résilta  
laboratwa.

**Kòm rékompans wap résévwa \$75 pou patisipasyon ou**

**Pou plis enfomasyon sou étid la, ou kapab kontakté:**

Dr. Fatma G. Huffman: 305-348-6427 or [huffmanf@fiu.edu](mailto:huffmanf@fiu.edu)

Gustavo Zarini: 305-348-6427 or [gzarini@hotmail.com](mailto:gzarini@hotmail.com)

Erskine Clerjeune: 786-355-4589 or [eclerjeune@yahoo.com](mailto:eclerjeune@yahoo.com)

E. Nelson: 954-479-1150 or [Enels002@fiu.edu](mailto:Enels002@fiu.edu)

## **APPENDIX C**

## MEMORANDUM

**To:** Dr. Patma Hoffman  
**CC:** File  
**From:** Chris Grayson, CIM, Associate Director of Research Compliance *CGS*  
**Date:** 1/14/10  
**Proposal Title:** "Cardiovascular Disease Risk in Minority Populations with and without Type 2 Diabetes: Haitian & African-American."  
**Approval #** 011210-00

---

The Institutional Review Board of Florida International University has approved your study for the use of human subjects. Your IRB approval date is **January 12, 2010** and this approval will expire on **January 12, 2011**. As a requirement of IRB approval you are required to:

- 1) Provide immediate written notification to the IRB of:
  - Any additions to, or changes in the procedures involving human subjects,
  - Every serious or unusual or unanticipated adverse event as well as problems with the rights or welfare of the human subjects. Confirmation of receipt of serious AE reports must be made with the IRB office.
- 2) Utilize copies of the date stamped consent document(s) for the recruitment of subjects and receive annual renewal of consent documents.
- 3) **Receive annual review and re-approval prior to your expiration date.**

**Special Conditions:** *N/A*

Please note your approval number is indicated above. For further information, you may visit the ORI – Human Subjects website at <http://ori.fiu.edu/IRB.html>.



## **APPENDIX D**

APPLICATION FOR APPROVAL OF RESEARCH INVOLVING HUMAN SUBJECTS  
**FORM A - FOR INITIAL SUBMISSION**

1. **PROJECT TITLE:** Oxidative Stress Biomarkers In African And Haitian Americans With And Without Type 2 Diabetes: The Relationship Between Serum Levels Of Manganese Superoxide Dismutase And Mdma 8-Hydroxy-2'-Deoxyguanosine, And Antioxidants

2. **PRINCIPAL INVESTIGATOR INFORMATION** *(Click to choose from pull down list)*  
**PI Name:** MICHAEL A. MCLEAN **PI Position:** Graduate Student  
**PI Email Address:** MMCLEAN612@AOL.COM **PI Panther ID:** 1005527  
**PI Department:** DIETETICS AND NUTRITION *If PI is a Student, Provide Campus Phone/Fax For Faculty Supervisor*  
**Campus Phone #:** - - **Fax #:** - - **Other Phone #:** 954 - 616 - 5958  
**\*FACULTY SUPERVISOR (If PI is a Student or Non-FIU):** FATMA G. HUFFMAN

3. **CO-INVESTIGATORS / PROJECT PERSONNEL:** *(Click to choose from pull down list)*

	Univ. Affiliation	Panther ID
N/A		

4. **PROJECT OVERVIEW**

a. **Funding Agency:** N/A **Funding Status:** Not Seeking Funding

b. **Project Start Date (MM/DD/YY):** 08/01/2012 **Duration of Project:** 12 MONTHS

c. **Is this a Clinical Trial and/or Interventional Research Project?**  
 No  Yes, include a Data and Safety Monitoring Plan in research protocol (see manual for description)

d. **What is the risk classification of this study?**  
 **No Known or Minimal Risks.** *"The probability and magnitude of harm or discomfort anticipated in the research are not greater than those encountered in daily life or during the performance of routine physical or psychological examinations or tests."*  
 **More than Minimal Risks.** Include a Data and Safety Monitoring plan in research protocol, and familiarize all research staff with Adverse Event procedures (see manual for description)

e. **Is there any real or apparent conflict of interest on the part of any study personnel (e.g. stock or stock options, interest in technology, consultant to sponsor)?**  
 No  Yes, provide disclosure of conflict of interest with application

5. **BRIEF DESCRIPTION OF SUBJECTS**

a. **Anticipated Number of subjects (if data sets are being used please indicate # of data sets)** 501

b. **Duration of subject participation (Indicate hours/days/weeks/months):** N/A


c. **Is there subject compensation? (If yes, please specify):** No

## **APPENDIX E**

## MEMORANDUM

**To:** Michael McLean

**CC:** Dr. Fatma Huffman  
File

**From:** Jada Dixon, MJ, MPH, IRB Coordinator 

**Date:** September 12, 2012

**Proposal Title:** "Oxidative Stress Biomarkers in African and Haitian Americans with and without Type 2 Diabetes: The Relationship between Serum Levels of Manganese Superoxide Dismutase and mtDNA 8-hydroxy-2'-deoxyguanosine, and Antioxidants"

**IRB Exemption #** 073112-01

---

The Health Sciences Institutional Review Board of Florida International University has reviewed your study for the use of human subjects via the Exempt Review process. Your study was deemed Exempt by the Institutional Review Board on **July 31, 2012**.

As a requirement of IRB approval you are required to:

- 1) **Submit a completion report** (Form B-2) upon completion of your project in order for the file to be closed.

## **APPENDIX F**



# DIETARY ASSESSMENT

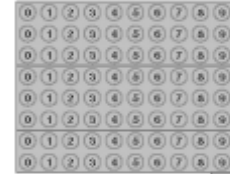


ID NUMBER: \_\_\_\_\_



• Darken one circle per question that corresponds to your answer

• Follow arrows



## VITAMINS

1. Do you currently take **multi-vitamins**? (Please report other individual vitamins in question 2.)

- No
- Yes

a) How many do you take per week?

- 2 or less
- 3-5
- 6-9
- 10 or more

b) For how many years have you been taking them?

- 1 year or less
- 2-4 years
- 5-9 years
- 10 or more years

c) What specific brand (or equivalency) do you usually take?

- Centrum Silver
- Centrum
- Other
- Theragran M
- One-A-Day Essential

e.g., AARP Alphabet II Formula 643 Multivitamins and Minerals

2. **Not counting multi-vitamins**, do you currently take any of the following specific vitamins or minerals? **DO NOT** report content of multi-vitamins mentioned above!

### Vitamin A

- No
- Yes, seasonal only
- Yes, currently take it most months

### Dose per day?

- Less than 10,000 IU
- 10,000 to 15,000 IU
- 16,000 to 22,000 IU
- 23,000 IU or more
- Don't know

### How long?

- 0-1 year
- 2-4 years
- 5-9 years
- 10 years or more

### Beta Carotene

- No
- Yes, seasonal only
- Yes, currently take it most months

### Dose per day?

- Less than 10,000 IU
- 10,000 to 15,000 IU
- 16,000 to 22,000 IU
- 23,000 IU or more
- Don't know

### How long?

- 0-1 year
- 2-4 years
- 5-9 years
- 10 years or more

PLEASE DO NOT WRITE IN THIS AREA



SERIAL #

309-9196  
pub

2. (Continued) **Not counting multi-vitamins**, do you currently take any of the following specific vitamins or minerals? DO NOT report content of multi-vitamin question.

**Vitamin B<sub>6</sub>**

- No  
 Yes, currently take it

**Dose per day?**

- Less than 50 mg  
 50 to 99 mg  
 100 to 149 mg  
 150 mg or more  
 Don't know

**How long?**

- 0-1 year  
 2-4 years  
 5-9 years  
 10 years or more

**Vitamin C**

- No  
 Yes, seasonal only  
 Yes, currently take it most months

**Dose per day?**

- Less than 400 mg  
 400 to 700 mg  
 750 to 1,250 mg  
 1,300 mg or more  
 Don't know

**How long?**

- 0-1 year  
 2-4 years  
 5-9 years  
 10 years or more

**Vitamin D**

(In calcium supplements or separately)

- No  
 Yes, seasonal only  
 Yes, currently take it most months

**Dose per day?**

- Less than 300 IU  
 300 to 500 IU  
 600 to 900 IU  
 1,000 IU or more  
 Don't know

**How long?**

- 0-1 year  
 2-4 years  
 5-9 years  
 10 years or more

**Vitamin E**

- No  
 Yes, currently take it

**Dose per day?**

- Less than 100 IU  
 100 to 250 IU  
 300 to 500 IU  
 600 IU or more  
 Don't know

**How long?**

- 0-1 year  
 2-4 years  
 5-9 years  
 10 years or more

**Type:**

- Natural  
 Regular (dl)  
 Unknown

**Selenium**

- No  
 Yes, currently take it

**Dose per day?**

- Less than 80 mcg  
 80 to 130 mcg  
 140 to 250 mcg  
 260 mcg or more  
 Don't know

**How long?**

- 0-1 year  
 2-4 years  
 5-9 years  
 10 years or more

**Iron**

- No  
 Yes, currently take it

**Dose per day?**

- mg of elemental iron (325 mg Ferrous Sulfate = 65 mg elemental iron)  
 Less than 20 mg  
 20 to 39 mg  
 40 to 49 mg  
 50 mg or more  
 Don't know

**How long?**

- 0-1 year  
 2-4 years  
 5-9 years  
 10 years or more

**Zinc**

- No  
 Yes, currently take it

**Dose per day?**

- Less than 25 mg  
 25 to 74 mg  
 75 to 100 mg  
 101 mg or more  
 Don't know

**How long?**

- 0-1 year  
 2-4 years  
 5-9 years  
 10 years or more

2. (Continued) **Not counting multi-vitamins**, do you currently take any of the following specific vitamins or minerals? DO NOT report content of multi-vitamin question.

**Calcium or Dolomite  
(Include Tums)**

- No
- Yes, currently take it

**Dose per day?**

- (Include elemental Calcium in Tums)
- Less than 600 mg
  - 600 to 900 mg
  - 901 to 1,500 mg
  - 1,501 mg or more
  - Don't know

**How long?**

- 0-1 year
- 2-4 years
- 5-9 years
- 10 years or more

**Fish Oil  
(Omega 3 fatty acids)**

- No
- Yes, currently take it

**Dose per day?**

- Less than 800 mg
- 800 to 1499 mg
- 1500 to 2499 mg
- 2500 mg or more
- Don't know

**How long?**

- 0-1 year
- 2-4 years
- 5-9 years
- 10 years or more

**Potassium**

- No
- Yes, currently take it

**Dose per day?**

- Less than 2.5 mEq (100 mg)
- 3 to 10 mEq
- 11 to 20 mEq
- 21 mEq or more
- Don't know

**How long?**

- 0-1 year
- 2-4 years
- 5-9 years
- 10 years or more

**Which other supplements are you taking currently on a regular basis (at least once per week)?**

- |  |   |   |
|--|---|---|
| <input type="radio"/> None                                   | <input type="radio"/> Vitamin B <sub>12</sub> | <input type="radio"/> CoEnzyme Q <sub>10</sub>          |
| <input type="radio"/> Metamucil                              | <input type="radio"/> Flaxseed oil            | <input type="radio"/> Choline                           |
| <input type="radio"/> Cod liver oil                          | <input type="radio"/> Flaxseed                | <input type="radio"/> Evening primrose                  |
| <input type="radio"/> Brewer's yeast                         | <input type="radio"/> B-complex               | <input type="radio"/> Ginkgo biloba                     |
| <input type="radio"/> Folic acid or folate (B <sub>9</sub> ) | <input type="radio"/> Melatonin               | <input type="radio"/> Lycopene                          |
| <input type="radio"/> Magnesium                              | <input type="radio"/> Chromium                | <input type="radio"/> DHEA                              |
| <input type="radio"/> Niacin                                 | <input type="radio"/> Lecithin                | <input type="radio"/> Glucosamine/Chondroitin           |
|  |   | <input type="radio"/> Other Supplements (specify) _____ |

**DAIRY FOODS**

In the following section, please describe how often on average you have used the amount specified in the past year. Please indicate your average total use, taking the portion size into account. For example, if you use 1/2 a glass of milk twice a week, mark 1 glass per week to represent your average total intake.

3. For each food listed, fill in the circle indicating your average total use of the amount specified during the past year.

**Skim milk (8 oz. glass)**

- Never
- Less than once per month
- 1-3 glasses per month
- 1 glass per week
- 2-4 glasses per week
- 5-6 glasses per week
- 1 glass per day
- 2-3 glasses per day
- 4 or more glasses per day

**1% or 2% milk (8 oz. glass)**

- Never
- Less than once per month
- 1-3 glasses per month
- 1 glass per week
- 2-4 glasses per week
- 5-6 glasses per week
- 1 glass per day
- 2-3 glasses per day
- 4 or more glasses per day

**Whole milk (8 oz. glass)**

- Never
- Less than once per month
- 1-3 glasses per month
- 1 glass per week
- 2-4 glasses per week
- 5-6 glasses per week
- 1 glass per day
- 2-3 glasses per day
- 4 or more glasses per day



3. (Continued) Please fill in your average total use, during the past year, of each specified food.

**Soy milk (8 oz. glass)**

- Never  
 Less than once per month  
 1-3 glasses per month  
 1 glass per week  
 2-4 glasses per week  
 5-6 glasses per week  
 1 glass per day  
 2-3 glasses per day  
 4 or more glasses per day

**Cream, e.g., in coffee, whipped or sour cream (1 tbs.)**

- Never  
 Less than once per month  
 1-3 tbs. per month  
 1 tbs. per week  
 2-4 tbs. per week  
 5-6 tbs. per week  
 1 tbs. per day  
 2 or more tbs. per day

**Non-dairy coffee whitener (1 tbs.)**

- Never  
 Less than once per month  
 1-3 tbs. per month  
 1 tbs. per week  
 2-4 tbs. per week  
 5-6 tbs. per week  
 1 tbs. per day  
 2 or more tbs. per day

**Frozen yogurt, sherbet or low-fat ice cream (1 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 Once per day  
 2 or more servings per day

**Regular ice cream (1 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 Once per day  
 2 or more servings per day

**Flavored yogurt, sweetened with fruit or other flavoring (1 cup)**

- Never  
 Less than once per month  
 1-3 cups per month  
 1 cup per week  
 2-4 cups per week  
 5-6 cups per week  
 1 cup per day  
 2 or more servings per day

**Yogurt, low carb, artificially sweetened or plain (1 cup)**

- Never  
 Less than once per month  
 1-3 cups per month  
 1 cup per week  
 2-4 cups per week  
 5-6 cups per week  
 1 cup per day  
 2 or more servings per day

**What type of yogurt do you usually eat?**

- None  
 Regular  
 Low fat  
 Nonfat

**Cottage or ricotta cheese (1/2 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 Once per day  
 2 or more servings per day

**Cream cheese (1 oz.)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 Once per day  
 2 or more servings per day

**Other cheese, e.g., American, cheddar, etc., plain or as part of a dish (1 slice or 1 oz. serving)**

- Never  
 Less than once per month  
 1-3 slices per month  
 1 slice per week  
 2-4 slices per week  
 5-6 slices per week  
 1 slice per day  
 2 or more slices per day

**What type of cheese do you usually eat?**

- None  
 Regular  
 Low fat or lite  
 Nonfat

3. (Continued) Please fill in your average total use, during the past year, of each specified food.

**Pure butter (small pat or tsp.), added to food or bread; exclude use in cooking**

- Never
- Less than once per month
- 1-3 pats per month
- 1 pat per week
- 2-4 pats per week
- 5-6 pats per week
- 1 pat per day
- 2-3 pats per day
- 4 or more pats per day

**"Spreadable butter"—butter/oil blend (small pat or tsp.), added to food or bread; exclude use in cooking**

- Never
- Less than once per month
- 1-3 pats per month
- 1 pat per week
- 2-4 pats per week
- 5-6 pats per week
- 1 pat per day
- 2-3 pats per day
- 4 or more pats per day

**Margarine or spread (small pat or tsp.), added to food or bread; exclude use in cooking**

- Never
- Less than once per month
- 1-3 pats per month
- 1 pat per week
- 2-4 pats per week
- 5-6 pats per week
- 1 pat per day
- 2-3 pats per day
- 4 or more pats per day

**What form of margarine or spreadable butter do you usually use? (Exclude pure butter)**

- Form?  None  Stick  Spray  Tub  Squeeze (liquid)
- Type?  Regular  Nonfat  Light spread

What spread brand and type (e.g., Shedd's Spread Country Crook Light Tub)?

PROOF

0	0	0
1	1	1
2	2	2
3	3	3
4	4	4
5	5	5
6	6	6
7	7	7
8	8	8
9	9	9

**FRUITS**

4. Please fill in your average total use, during the past year, of each specified food.

Please try to average your seasonal use of foods over the entire year. For example, if a food such as cantaloupe is eaten 4 times a week during the 3 months that it is in season, then the average total use would be once per week over the year.

**Raisins (1 oz. or small pack) or grapes (1/2 cup)**

- Never
- Less than once per month
- 1-3 times per month
- Once per week
- 2-4 times per week
- 5-6 times per week
- Once per day
- 2 or more servings per day

**Prunes or dried plums (6 prunes or 1/4 cup)**

- Never
- Less than once per month
- 1-3 times per month
- Once per week
- 2-4 times per week
- 5-6 times per week
- Once per day

**Prune Juice (small glass)**

- Never
- Less than once per month
- 1-3 glasses per month
- 1 glass per week
- 2-4 glasses per week
- 5-6 glasses per week
- 1 glass per day
- 2 or more glasses per day

**Bananas (1)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2 or more per day

**Cantaloupe (1/4 melon)**

- Never
- Less than once per month
- 1-3 times per month
- Once per week
- 2-4 times per week
- 5-6 times per week
- Once per day
- 2-3 times per day
- 4 or more servings per day

**Avocado (1/2 fruit or 1/2 cup)**

- Never
- Less than once per month
- 1-3 times per month
- Once per week
- 2-4 times per week
- 5-6 times per week
- One per day
- Two or more per day

307 (cont.)

4. (Continued) Please fill in your average total use, during the past year, of each specified food.

**Applesauce (1/2 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 One or more per day

**Fresh apples or pears (1)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 per day  
 2–3 per day  
 4 or more per day

**Apple juice or cider (small glass)**

- Never  
 Less than once per month  
 1–3 glasses per month  
 1 glass per week  
 2–4 glasses per week  
 5–6 glasses per week  
 1 glass per day  
 2 or more glasses per day

**Oranges (1)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 per day  
 2–3 per day  
 4 or more per day

**Orange juice—calcium fortified (small glass)**

- Never  
 Less than once per month  
 1–3 glasses per month  
 1 glass per week  
 2–4 glasses per week  
 5–6 glasses per week  
 1 glass per day  
 2 or more glasses per day

**Orange juice—regular (not calcium fortified) (small glass)**

- Never  
 Less than once per month  
 1–3 glasses per month  
 1 glass per week  
 2–4 glasses per week  
 5–6 glasses per week  
 1 glass per day  
 2 or more glasses per day

**Grapefruit (1/2)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2–3 times per day  
 4 or more times per day

**Grapefruit juice (small glass)**

- Never  
 Less than once per month  
 1–3 glasses per month  
 1 glass per week  
 2–4 glasses per week  
 5–6 glasses per week  
 1 glass per day  
 2 or more glasses per day

**Other fruit juices (small glass)**

- Never  
 Less than once per month  
 1–3 glasses per month  
 1 glass per week  
 2–4 glasses per week  
 5–6 glasses per week  
 1 glass per day  
 2 or more glasses per day

**Strawberries, fresh, frozen or canned (1/2 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once or more per day

**Blueberries, fresh, frozen or canned (1/2 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5 or more servings per week

**Peaches or plums (1 fresh or 1/2 cup canned)**

- Never  
 Less than once per month  
 1–3 per month  
 Once per week  
 2–4 per week  
 5–6 per week  
 1 or more per day

**Apricots (1 fresh, 1/2 cup canned or 5 dried)**

- Never  
 Less than once per month  
 1–3 per month  
 Once per week  
 2–4 per week  
 5 or more servings per week

**VEGETABLES**

5. Please fill in your average total use, during the past year, of each specified food.

**Tomatoes (2 slices)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 or more per day

**Tomato or V8 juice (small glass)**

- Never  
 Less than once per month  
 1–3 glasses per month  
 1 glass per week  
 2–4 glasses per week  
 5–6 glasses per week  
 1 glass per day  
 2 or more glasses per day

**Tomato sauce (1/2 cup) e.g., spaghetti sauce**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5 or more servings per week

**Salsa, picante or taco sauce (1/4 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2 or more servings per day

**Tofu, soy burgers, soybeans, miso, or other soy protein (3–4 oz.)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2 or more servings per day

**String beans (1/2 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5 or more servings per week

**Broccoli (1/2 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 1 or more servings per day

**Cabbage or cole slaw (1/2 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 1 or more servings per day

**Cauliflower (1/2 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 1 or more servings per day

**Brussels sprouts (1/2 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 1 or more servings per day

**Carrots, raw (1/2 carrot or 2–4 sticks)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2 or more servings per day

**Carrots, cooked (1/2 cup) or carrot juice (2–3 oz.)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2 or more servings per day

**Corn (1 ear or 1/2 cup frozen or canned)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 or more servings per day

**Peas or lima beans (1/2 cup fresh, frozen or canned)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 1 or more servings per day

**Mixed vegetables, stir fry (1/2 cup), vegetable soup (1 cup)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 1 or more servings per day

5. (Continued) Please fill in your average total use, during the past year, of each specified food.

**Beans or lentils, baked, dried or soup (1/2 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**Dark orange (winter) squash (1/2 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**Eggplant, zucchini or other summer squash (1/2 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**Yams or sweet potatoes (1/2 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**Spinach, cooked (1/2 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**Spinach, raw as in salad (1 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**Kale, mustard, or chard greens (1/2 cup)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**Iceberg or head lettuce (serving)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 Once per day  
 2 or more servings per day

**Romaine or leaf lettuce (serving)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 Once per day  
 2 or more servings per day

**Celery (2-3 sticks)**

- Never  
 Less than once per month  
 1-3 per month  
 Once per week  
 2-4 per week  
 5-6 per week  
 Once per day  
 2 or more servings per day

**Peppers: green, yellow or red (3 slices)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**Onions as a garnish or in a salad (1 slice)**

- Never  
 Less than once per month  
 1-3 slices per month  
 1 slice per week  
 2-4 slices per week  
 5-6 slices per week  
 1 or more slices per day

**Onions as a vegetable, rings or soup (1/2 cup)**

- Never  
 Less than once per month  
 1-3 per month  
 1 per week  
 2-4 per week  
 5-6 per week  
 1 or more per day

**EGGS, MEAT & FISH**

6. Please fill in your average total use, during the past year, of each specified food.

**Egg Beaters or egg whites only (1/4 cup or 1 egg)**

- Never  
 Less than once per month  
 1–3 eggs per month  
 1 egg per week  
 2–4 eggs per week  
 5–6 eggs per week  
 1 egg per day  
 2 or more eggs per day

**Omega-3 fortified eggs, including yolk (1 egg)**

- Never  
 Less than once per month  
 1–3 eggs per month  
 1 egg per week  
 2–4 eggs per week  
 5–6 eggs per week  
 1 egg per day  
 2 or more eggs per day

**Regular eggs, with yolk (1)**

- Never  
 Less than once per month  
 1–3 eggs per month  
 1 egg per week  
 2–4 eggs per week  
 5–6 eggs per week  
 1 egg per day  
 2 or more eggs per day

**Bacon (2 slices)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 1 or more servings per day

**Chicken or turkey sandwich or frozen dinner**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5 or more per week

**Other chicken or turkey, with skin (3 oz.)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2 or more servings per day

**Other chicken or turkey, including ground without skin, (3 oz.)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2 or more servings per day

**Beef or pork hot dogs (1)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 per day  
 2 or more per day

**Chicken or turkey hot dogs or sausages (1)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 per day  
 2 or more per day

**Salami, bologna, or other processed meat sandwiches**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5 or more per week

**Other processed meats, e.g., sausage, kielbasa, etc. (2 oz. or 2 small links)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2 or more servings per day

**Hamburger, lean or extra lean (1 patty)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 or more per day

6. (Continued) Please fill in your average total use, during the past year, of each specified food.

**Hamburger, regular  
(1 patty)**

- Never  
 Less than once per month  
 1-3 per month  
 1 per week  
 2-4 per week  
 5-6 per week  
 1 or more per day

**Beef, pork, or lamb as a  
sandwich or mixed dish, e.g.,  
stew, casserole, lasagna,  
frozen dinner, etc.**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more times per day

**Pork as a main dish, e.g.,  
ham or chops (4-6 oz.)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more times per day

**Beef or lamb as a main dish,  
e.g., steak, roast (4-6 oz.)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more times per day

**Liver: beef, calf or pork  
(4 oz.)**

- Never  
 Less than once per month  
 1 time per month  
 2-3 times per month  
 Once per week  
 2 or more servings per week

**Liver: chicken or turkey  
(1 oz.)**

- Never  
 Less than once per month  
 1 time per month  
 2-3 times per month  
 Once per week  
 2 or more servings per week

**Canned tuna fish  
(3-4 oz.)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 Once per day  
 2 or more servings per day

**Breaded fish cakes,  
pieces, or fish sticks  
(1 serving, store bought)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more per day

**Shrimp, lobster,  
scallops, clams as a  
main dish (1 serving)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more times per day

**Dark meat fish, e.g., tuna  
steak, mackerel, salmon,  
sardines, bluefish,  
swordfish (3-5 oz.)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**Other fish, e.g., cod,  
haddock, halibut  
(3-5 oz.)**

- Never  
 Less than once per month  
 1-3 times per month  
 Once per week  
 2-4 times per week  
 5-6 times per week  
 1 or more servings per day

**CEREALS, BREADS & STARCHES**

7. Please fill in your average total use, during the past year, of each specified food.

**Cold breakfast cereal (1 serving)**

- Never
- Less than once per month
- 1-3 cups per month
- 1 cup per week
- 2-4 cups per week
- 5-6 cups per week
- 1 cup per day
- 2-3 cups per day
- 4 or more cups per day

**Cooked oatmeal/cooked oat bran (1 cup)**

- Never
- Less than once per month
- 1-3 cups per month
- 1 cup per week
- 2-4 cups per week
- 5-6 cups per week
- 1 cup per day
- 2-3 cups per day
- 4 or more cups per day

**Other cooked breakfast cereal (1 cup)**

- Never
- Less than once per month
- 1-3 cups per month
- 1 cup per week
- 2-4 cups per week
- 5-6 cups per week
- 1 cup per day
- 2-3 cups per day
- 4 or more cups per day

**What brand and type of cold breakfast cereal do you usually eat?** →

Specify brand & type (e.g., "General Mills Rice Chex")

**White bread (slice), including pita bread**

- Never
- Less than once per month
- 1-3 slices per month
- 1 slice per week
- 2-4 slices per week
- 5-6 slices per week
- 1 slice per day
- 2-3 slices per day
- 4-5 slices per day
- 6+ slices per day

**Rye or Pumpernickel bread (1 slice)**

- Never
- Less than once per month
- 1-3 slices per month
- 1 slice per week
- 2-4 slices per week
- 5-6 slices per week
- 1 slice per day
- 2-3 slices per day
- 4-5 slices per day
- 6+ slices per day

**Whole wheat, oatmeal, other whole grain bread (1 slice)**

- Never
- Less than once per month
- 1-3 slices per month
- 1 slice per week
- 2-4 slices per week
- 5-6 slices per week
- 1 slice per day
- 2-3 slices per day
- 4-5 slices per day
- 6+ slices per day

**Bagels, English muffins, or rolls (1 whole)**

- Never
- Less than once per month
- 1-3 times per month
- Once per week
- 2-4 times per week
- 5-6 times per week
- Once per day
- 2 or more per day

**Muffins or biscuits (1)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2 or more per day

**Brown rice (1 cup)**

- Never
- Less than once per month
- 1-3 cups per month
- 1 cup per week
- 2-4 cups per week
- 5-6 cups per week
- 1 cup per day
- 2 or more cups per day

307 (10/01)

PROOF

0	0	0
1	1	1
2	2	2
3	3	3
4	4	4
5	5	5
6	6	6
7	7	7
8	8	8
9	9	9



7. (Continued) Please fill in your average total use, during the past year, of each specified food.

**White rice (1 cup)**

- Never  
 Less than once per month  
 1–3 cups per month  
 1 cup per week  
 2–4 cups per week  
 5–6 cups per week  
 1 cup per day  
 2 or more cups per day

**Pasta, e.g., spaghetti, noodles, couscous, etc. (1 cup)**

- Never  
 Less than once per month  
 1–3 cups per month  
 1 cup per week  
 2–4 cups per week  
 5–6 cups per week  
 1 cup per day  
 2 or more cups per day

**Tortillas (2)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 per day  
 2–3 per day  
 4 or more per day

**Other grains, e.g., bulgar, kasha, buckwheat, etc. (1 cup)**

- Never  
 Less than once per month  
 1–3 cups per month  
 1 cup per week  
 2–4 cups per week  
 5–6 cups per week  
 1 cup per day  
 2 or more cups per day

**Pancakes or waffles (2 small pieces)**

- Never  
 Less than once per month  
 1–3 servings per month  
 1 serving per week  
 2–4 servings per week  
 5–6 servings per week  
 1 serving per day  
 2 or more servings per day

**French fried potatoes (6 oz. or 1 serving)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 1 or more servings per day

**Potatoes, baked, boiled (1) or mashed (1 cup)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 per day  
 2 or more servings per day

**Potato chips or corn/tortilla chips (small bag or 1 oz.)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 per day  
 2 or more servings per day

**Crackers, regular or low fat, e.g., Triscuits, Ritz (6)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2–3 times per day  
 4 or more servings per day

**Pizza (2 slices)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2 or more servings per day

**BEVERAGES**

**CARBONATED BEVERAGES**—Consider the serving size as one 12 oz. glass, bottle or can for these carbonated beverages.

8. Please fill in your average total use, during the past year, of each specified food.

**LOW-CALORIE (Sugar-free types)**

**Low-calorie beverage with caffeine, e.g., Diet Coke, Diet Mt. Dew (1 glass, bottle or can)**

- Never  
 Less than once per month  
 1–3 cans per month  
 1 can per week  
 2–4 cans per week  
 5–6 cans per week  
 1 can per day  
 2–3 cans per day  
 4 or more cans per day

**Other low-calorie beverage without caffeine, e.g., Diet 7-Up (1 glass, bottle or can)**

- Never  
 Less than once per month  
 1–3 cans per month  
 1 can per week  
 2–4 cans per week  
 5–6 cans per week  
 1 can per day  
 2–3 cans per day  
 4 or more cans per day

**REGULAR TYPES (not sugar-free)**

**Carbonated beverage with caffeine and sugar, e.g., Coke, Pepsi, Mt. Dew, Dr. Pepper (1 glass, bottle or can)**

- Never  
 Less than once per month  
 1–3 cans per month  
 1 can per week  
 2–4 cans per week  
 5–6 cans per week  
 1 can per day  
 2–3 cans per day  
 4 or more cans per day

**Other carbonated beverage with sugar, e.g., 7-Up, Root Beer, Ginger Ale (1 glass, bottle or can)**

- Never  
 Less than once per month  
 1–3 cans per month  
 1 can per week  
 2–4 cans per week  
 5–6 cans per week  
 1 can per day  
 2–3 cans per day  
 4 or more cans per day

**OTHER BEVERAGES**

**Other sugared beverages: Punch, lemonade, sports drinks, or sugared ice tea (1 glass, bottle, can)**

- Never  
 Less than once per month  
 1–3 glasses per month  
 1 glass per week  
 2–4 glasses per week  
 5–6 glasses per week  
 1 glass per day  
 2–3 glasses per day  
 4 or more glasses per day

**Beer, regular (1 glass, bottle, can)**

- Never  
 Less than once per month  
 1–3 cans per month  
 1 can per week  
 2–4 cans per week  
 5–6 cans per week  
 1 can per day  
 2–3 cans per day  
 4–5 cans per day  
 6+ cans per day

**Light beer, e.g., Bud Light (1 glass, bottle, can)**

- Never  
 Less than once per month  
 1–3 cans per month  
 1 can per week  
 2–4 cans per week  
 5–6 cans per week  
 1 can per day  
 2–3 cans per day  
 4–5 cans per day  
 6+ cans per day

8. (Continued) Please fill in your average total use, during the past year, of each specified food.

**Red wine (5 oz. glass)**

- Never  
 Less than once per month  
 1-3 glasses per month  
 1 glass per week  
 2-4 glasses per week  
 5-6 glasses per week  
 1 glass per day  
 2-3 glasses per day  
 4-5 glasses per day  
 6+ glasses per day

**White wine (5 oz. glass)**

- Never  
 Less than once per month  
 1-3 glasses per month  
 1 glass per week  
 2-4 glasses per week  
 5-6 glasses per week  
 1 glass per day  
 2-3 glasses per day  
 4-5 glasses per day  
 6+ glasses per day

**Liquor, e.g., whiskey, gin, etc. (1 drink or shot)**

- Never  
 Less than once per month  
 1-3 drinks per month  
 1 drink per week  
 2-4 drinks per week  
 5-6 drinks per week  
 1 drink per day  
 2-3 drinks per day  
 4-5 drinks per day  
 6+ drinks per day

**Water, bottled, sparkling or tap (8 oz. cup)**

- Never  
 Less than once per month  
 1-3 cups per month  
 1 cup per week  
 2-4 cups per week  
 5-6 cups per week  
 1 cup per day  
 2-3 cups per day  
 4-5 cups per day  
 6+ cups per day

**Herbal tea or decaffeinated tea (8 oz. cup)**

- Never  
 Less than once per month  
 1-3 cups per month  
 1 cup per week  
 2-4 cups per week  
 5-6 cups per week  
 1 cup per day  
 2-3 cups per day  
 4-5 cups per day  
 6+ cups per day

**Tea with caffeine, including green tea (8 oz. cup)**

- Never  
 Less than once per month  
 1-3 cups per month  
 1 cup per week  
 2-4 cups per week  
 5-6 cups per week  
 1 cup per day  
 2-3 cups per day  
 4-5 cups per day  
 6+ cups per day

**Decaffeinated coffee (8 oz. cup)**

- Never  
 Less than once per month  
 1-3 cups per month  
 1 cup per week  
 2-4 cups per week  
 5-6 cups per week  
 1 cup per day  
 2-3 cups per day  
 4-5 cups per day  
 6+ cups per day

**Coffee with caffeine (8 oz. cup)**

- Never  
 Less than once per month  
 1-3 cups per month  
 1 cup per week  
 2-4 cups per week  
 5-6 cups per week  
 1 cup per day  
 2-3 cups per day  
 4-5 cups per day  
 6+ cups per day

**Dairy coffee drink (hot/cold) e.g., cappuccino (16 oz.)**

- Never  
 Less than once per month  
 1-3 cups per month  
 1 cup per week  
 2-4 cups per week  
 5-6 cups per week  
 1 cup per day  
 2-3 cups per day  
 4-5 cups per day  
 6+ cups per day

**SWEETS, BAKED GOODS & MISCELLANEOUS**

9. Please fill in your average total use, during the past year, of each specified food.

**Milk chocolate (bar or packet), (e.g., Hershey's, M&M's)**

- Never  
 Less than once per month  
 1-3 per month  
 1 per week  
 2-4 per week  
 5-6 per week  
 1 per day  
 2-3 per day  
 4 or more per day

**Dark chocolate e.g., Hershey's, Dark or Dove Dark**

- Never  
 Less than once per month  
 1-3 candy bars per month  
 1 candy bar per week  
 2-4 candy bars per week  
 5-6 candy bars per week  
 1 candy bar per day  
 2-3 candy bars per day  
 4 or more candy bars per day

**Candy bars, (e.g., Snickers, Milky Way, Reeses)**

- Never  
 Less than once per month  
 1-3 candy bars per month  
 1 candy bar per week  
 2-4 candy bars per week  
 5-6 candy bars per week  
 1 candy bar per day  
 2-3 candy bars per day  
 4 or more candy bars per day

9. (Continued) Please fill in your average total use, during the past year, of each specified food.

**Candy without chocolate (e.g., 1 pack mints, Lifesavers) (1 oz.)**

- Never  
 Less than once per month  
 1–3 times per month  
 Once per week  
 2–4 times per week  
 5–6 times per week  
 Once per day  
 2–3 times per day  
 4 or more times per day

**Jams, jellies, preserves, syrup, or honey (1 tbs.)**

- Never  
 Less than once per month  
 1–3 tbs. per month  
 1 tbs. per week  
 2–4 tbs. per week  
 5–6 tbs. per week  
 1 tbs. per day  
 2–3 tbs. per day  
 4 or more tbs. per day

**Peanut butter (1 tbs.)**

- Never  
 Less than once per month  
 1–3 tbs. per month  
 1 tbs. per week  
 2–4 tbs. per week  
 5–6 tbs. per week  
 1 tbs. per day  
 2–3 tbs. per day  
 4 or more tbs. per day

**Fat free or light popcorn (3 cups)**

- Never  
 Less than once per month  
 1–3 servings per month  
 1 serving per week  
 2–4 servings per week  
 5–6 servings per week  
 1 serving per day  
 2 or more servings per day

**Regular popcorn (3 cups)**

- Never  
 Less than once per month  
 1–3 servings per month  
 1 serving per week  
 2–4 servings per week  
 5–6 servings per week  
 1 serving per day  
 2 or more servings per day

**Pretzels (1 small bag or serving)**

- Never  
 Less than once per month  
 1–3 servings per month  
 One serving per week  
 2–4 servings per week  
 5–6 servings per week  
 One serving per day  
 2 or more servings per day

**Cookies, fat free or reduced fat (1)**

- Never  
 Less than once per month  
 1–3 cookies per month  
 1 cookie per week  
 2–4 cookies per week  
 5–6 cookies per week  
 1 cookie per day  
 2–3 cookies per day  
 4 or more cookies per day

**Cookies, other ready-made (1)**

- Never  
 Less than once per month  
 1–3 cookies per month  
 1 cookie per week  
 2–4 cookies per week  
 5–6 cookies per week  
 1 cookie per day  
 2–3 cookies per day  
 4 or more cookies per day

**Cookies, home baked (1)**

- Never  
 Less than once per month  
 1–3 cookies per month  
 1 cookie per week  
 2–4 cookies per week  
 5–6 cookies per week  
 1 cookie per day  
 2–3 cookies per day  
 4 or more cookies per day

**Brownies (1)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 per day  
 2 or more per day

**Doughnuts (1)**

- Never  
 Less than once per month  
 1–3 per month  
 1 per week  
 2–4 per week  
 5–6 per week  
 1 per day  
 2–3 per day  
 4 or more per day

**Cake, home baked (slice)**

- Never  
 Less than once per month  
 1–3 slices per month  
 1 slice per week  
 2–4 slices per week  
 5–6 slices per week  
 1 or more slices per day

**Cake, ready-made (slice)**

- Never  
 Less than once per month  
 1–3 slices per month  
 1 slice per week  
 2–4 slices per week  
 5–6 slices per week  
 1 or more slices per day

**Pie, homemade (slice)**

- Never  
 Less than once per month  
 1–3 slices per month  
 1 slice per week  
 2–4 slices per week  
 5–6 slices per week  
 1 or more slices per day

**Pie, ready-made (slice)**

- Never  
 Less than once per month  
 1–3 slices per month  
 1 slice per week  
 2–4 slices per week  
 5–6 slices per week  
 1 or more slices per day

9. (Continued) Please fill in your average total use, during the past year, of each specified food.

**Sweet roll, coffee cake or other pastry, fat free or reduced fat (serving)**

- Never
- Less than once per month
- 1-3 times per month
- Once per week
- 2-4 times per week
- 5-6 times per week
- Once per day
- 2 or more servings per day

**Sweet roll, coffee cake or other ready made pastry (serving)**

- Never
- Less than once per month
- 1-3 times per month
- Once per week
- 2-4 times per week
- 5-6 times per week
- Once per day
- 2 or more servings per day

**Sweet roll, coffee cake or other pastry, home baked (serving)**

- Never
- Less than once per month
- 1-3 times per month
- Once per week
- 2-4 times per week
- 5-6 times per week
- Once per day
- 2 or more servings per day

**Peanuts (small packet or 1 oz.)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2 or more servings per day

**Walnuts (1 oz.)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2 or more servings per day

**Other nuts (small packet or 1 oz.)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2 or more servings per day

**Breakfast bars, e.g., Nutrigrain, granola, Kashi (1)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2 or more bars per day

**Energy bars, e.g., Clif, Luna, Glucerna, Powerbar (1)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2 or more bars per day

**Low carb bars, e.g., Atkins, Zone, South Beach (1)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2 or more bars per day

**Oat bran, added to food (1 tbs.)**

- Never
- Less than once per month
- 1-3 tbs. per month
- 1 tbs. per week
- 2-4 tbs. per week
- 5-6 tbs. per week
- 1 tbs. per day
- 2 or more servings per day

**Other bran (wheat, etc.), added to food (1 tbs.)**

- Never
- Less than once per month
- 1-3 tbs. per month
- 1 tbs. per week
- 2-4 tbs. per week
- 5-6 tbs. per week
- 1 tbs. per day
- 2 or more servings per day

**Wheat germ (1 tbs.)**

- Never
- Less than once per month
- 1-3 tbs. per month
- 1 tbs. per week
- 2-4 tbs. per week
- 5-6 tbs. per week
- 1 tbs. per day
- 2 or more servings per day

**Chowder or cream soup (1 cup)**

- Never
- Less than once per month
- 1-3 cups per month
- 1 cup per week
- 2-4 cups per week
- 5-6 cups per week
- 1 or more cups per day

**Ketchup or red chili sauce (1 tbs.)**

- Never
- Less than once per month
- 1-3 tbs. per month
- 1 tbs. per week
- 2-4 tbs. per week
- 5-6 tbs. per week
- 1 tbs. per day
- 2 or more servings per day

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**DIET CHANGES**

17. Do you currently follow a special diet?

- No
- Yes →  Physician prescribed
- Self prescribed

a) If yes, for how many years?

(Number of years on diet)

b) If yes, what kind of diet do you follow?

(Select more than one if necessary.)

- Weight reduction (low calorie)
- Low cholesterol
- Low sodium
- Diabetic
- Low fat
- Low triglyceride
- Ulcer
- High Potassium

(Specify type of diet) (Exclude weight reduction diets)

Other

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18. How has your use of the following foods and beverages changed over the PAST TEN YEARS?

**Whole milk**

- Use has decreased
- Use about the same
- Use has increased

**Butter**

- Use has decreased
- Use about the same
- Use has increased

**Margarine**

- Use has decreased
- Use about the same
- Use has increased

**Eggs**

- Use has decreased
- Use about the same
- Use has increased

**Fish**

- Use has decreased
- Use about the same
- Use has increased

**Red meat**

- Use has decreased
- Use about the same
- Use has increased

**Fruits**

- Use has decreased
- Use about the same
- Use has increased

**Vegetables**

- Use has decreased
- Use about the same
- Use has increased

**Whole wheat bread**

- Use has decreased
- Use about the same
- Use has increased

**Whole grains**

- Use has decreased
- Use about the same
- Use has increased

**Sugar**

- Use has decreased
- Use about the same
- Use has increased

**Alcohol**

- Use has decreased
- Use about the same
- Use has increased

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17
8
0 0
1 1
2 2
3 3
4 4
5 5
6 6
7 7
8 8
9 9
0 0 0
1 1 1
2 2 2
3 3 3
4 4 4
5 5 5
6 6 6
7 7 7
8 8 8
9 9 9
18

10. What kind of fat is usually used for frying and sautéing at home? (Exclude Pam type spray.)

- Real butter
Margarine
Olive oil
Vegetable oil
Vegetable shortening
Lard/bacon fat

11. What kind of fat is usually used for baking at home? (Exclude Pam type spray.)

- Real butter
Margarine
Olive oil
Vegetable oil
Vegetable shortening
Lard/bacon fat

12. How often do you eat food fried, stir-fried in oil, or sautéed at home?

- Never
Less than once a week
1-3 times per week
4-6 times per week
Daily

13. How often do you eat deep fried food away from home or as take out (e.g., french fries, fried chicken, fish, clams, shrimp, etc.)?

- Never
Less than once a week
1-3 times per week
4-6 times per week
Daily
2 or more times per day

14. How often do you eat toasted breads, bagel or English muffin (e.g., sliced/half bagel)?

- Never
Less than once a week
1-3 times per week
4-6 times per week
Daily
2 or more times per day

15. What type of cooking oil is usually used at home (e.g., Mazola Corn Oil)?

(Specify brand and type)

Text input box for specifying brand and type of cooking oil.

16. Are there any other foods not mentioned above that you usually eat at least once per week?

Include for example: Mushrooms, radish, horseradish, dates, figs, rhubarb, mango, mixed dried fruit, papaya, custard, venison, hot peppers, pickles, olives, SlimFast, Ensure (regular or plus), Glucerna shake.

(Do not include dry spices and do not list something that has been listed in the previous sections.)

Table with 2 columns: Other foods that you usually eat at least once per week, Servings per week. Rows (a), (b), (c).

Vertical column of bubbles for marking answers, numbered 10 through 16.

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9. (Continued) Please fill in your average total use, during the past year, of each specified food.

**Salt added at table (1 shake)**

- Never
- Less than once per month
- 1-3 shakes per month
- 1 shake per week
- 2-4 shakes per week
- 5-6 shakes per week
- 1 shake per day
- 2-3 shakes per day
- 4-5 shakes per day
- 6+ shakes per day

**How many teaspoons of sugar do you add to your beverages or food each day?**

Teaspoons

**Splenda (1 packet)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2-3 per day
- 4-5 per day
- 6+ per day

0	0
1	1
2	2
3	3
4	4
5	5
6	6
7	7
8	8
9	9

**Other artificial sweetener (1 packet)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2-3 per day
- 4-5 per day
- 6+ per day

**Garlic (1 clove or 4 shakes)**

- Never
- Less than once per month
- 1-3 per month
- 1 per week
- 2-4 per week
- 5-6 per week
- 1 per day
- 2-3 per day
- 4-5 per day
- 6+ per day

**Low fat or fat free mayonnaise (1 tbs.)**

- Never
- Less than once per month
- 1-3 tbs. per month
- 1 tbs. per week
- 2-4 tbs. per week
- 5-6 tbs. per week
- 1 tbs. per day
- 2 or more tbs. per day

**Regular mayonnaise (1 tbs.)**

- Never
- Less than once per month
- 1-3 tbs. per month
- 1 tbs. per week
- 2-4 tbs. per week
- 5-6 tbs. per week
- 1 tbs. per day
- 2 or more tbs. per day

**Salad dressing (1-2 tbs.)**

- Never
- Less than once per month
- 1-3 tbs. per month
- 1 tbs. per week
- 2-4 tbs. per week
- 5-6 tbs. per week
- 1 tbs. per day
- 2-3 tbs. per day
- 4 or more tbs. per day

**Type of salad dressing:**

- Nonfat
- Low fat
- Olive oil dressing
- Other vegetable oil dressing

**Olive oil added to food or bread (1 tbs.); exclude use in cooking**

- Never
- Less than once per month
- 1-3 tbs. per month
- 1 tbs. per week
- 2-4 tbs. per week
- 5-6 tbs. per week
- 1 tbs. per day
- 2-3 tbs. per day
- 4-5 tbs. per day
- 6+ tbs. per day

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## **APPENDIX G**

ID #: \_\_\_\_\_

Date \_\_\_\_\_

## **CVD RISK STUDY: HAITIAN & AFRICAN AMERICAN**

## Section I - Demographics

Please answer each of the following questions by filling in the blanks with the correct answers or by choosing the single best answer.

**Note:** For this survey, a Health Care Provider refers to a doctor, nurse practitioner, or physician assistant.

Q1. Age: \_\_\_\_\_ years old

Q2. Birth date: \_\_ \_\_ / \_\_ \_\_ / \_\_ \_\_  
( Month / Day / Year )

Q3. Sex: <sub>1</sub> Male <sub>2</sub> Female

Q4. Height: \_\_\_\_\_ centimeters

Q5. Weight: \_\_\_\_\_ kilograms

Q6. Waist Circumference: \_\_\_\_\_ centimeters

Q7. What year were you first told you had diabetes? (Please enter the year) \_\_\_\_\_

Q8. What is your marital status? (check one box)

<sub>1</sub> Never married

<sub>2</sub> Married

<sub>3</sub> Separated/Divorced

<sub>4</sub> Widowed

Q9. Which country were you born in? (check one box)

- <sub>1</sub> Haiti
- <sub>2</sub> United States of America
- <sub>3</sub> Other \_\_\_\_\_

Q.10 How long have you been in the United States of America? (check one box)

- <sub>1</sub> Less than one year
- <sub>2</sub> One to three years
- <sub>3</sub> Four to six years
- <sub>4</sub> Seven to ten years
- <sub>5</sub> Eleven to fifteen years
- <sub>6</sub> More than fifteen years

Q11. How much schooling have you had? (Years of formal schooling completed)  
(check one box)

- <sub>1</sub> 8 grades or less
- <sub>2</sub> Some high school
- <sub>3</sub> High school graduate or GED
- <sub>4</sub> Some college or technical school
- <sub>5</sub> College graduate (bachelor's degree)
- <sub>6</sub> Graduate degree

Q12. Which of the following best describes your current employment status?

(check one box)

- <sub>1</sub> Working full-time, 35 hours or more a week
- <sub>2</sub> Working part-time, less than 35 hours a week
- <sub>3</sub> Unemployed or laid off and looking for work
- <sub>4</sub> Unemployed and not looking for work
- <sub>5</sub> Homemaker
- <sub>6</sub> In school
- <sub>7</sub> Retired
- <sub>8</sub> Disabled, not able to work
- <sub>9</sub> Something else? (Please specify): \_\_\_\_\_

Q13. How would you describe the insurance plan(s) you have had in the past 12 months?

(check all that apply)

- <sub>1</sub> An individual plan – the member pays for the plan premium
- <sub>2</sub> A group plan through an employer, union, etc. – the employer pays all or part of the plan premium
- <sub>3</sub> U.S. Governmental Health Plan (e.g., Military, CHAMPUS, VA)
- <sub>4</sub> Medicaid
- <sub>5</sub> Medicare
- <sub>6</sub> I have not had an insurance plan in the past 12 months

Q14. Which of the categories best describes your total annual combined household income from all sources? (check one box)

- <sub>1</sub> Less than \$5,000
- <sub>2</sub> \$5,000 to \$9,999
- <sub>3</sub> \$10,000 to \$19,999
- <sub>4</sub> \$20,000 to \$29,999
- <sub>5</sub> \$30,000 to \$39,999
- <sub>6</sub> \$40,000 to \$49,999
- <sub>7</sub> \$50,000 to \$59,999
- <sub>8</sub> \$60,000 to \$69,999
- <sub>9</sub> \$60,000 to \$69,999
- <sub>10</sub> \$70,000 and over
- <sub>11</sub> Don't know

Q15. How many person(s) age 18 years and over live in the same house you live? \_\_\_\_\_

Q16. What language do you prefer to write something? (check one box)

- <sub>1</sub> Only Creole
- <sub>2</sub> More Creole than English
- <sub>3</sub> Both equally

<sub>4</sub> More English than Creole

<sub>5</sub> Only English

Q17. What language do you prefer to speak with someone? (check one box)

<sub>1</sub> Only Creole

<sub>2</sub> More Creole than English

<sub>3</sub> Both equally

<sub>4</sub> More English than Creole

<sub>5</sub> Only English

Q18. What language do you prefer to read with something? (check one box)

<sub>1</sub> Only Creole

<sub>2</sub> More Creole than English

<sub>3</sub> Both equally

<sub>4</sub> More English than Creole

<sub>5</sub> Only English

Q19. Your smoking habit. (check one box)

<sub>1</sub> Never smoked cigarettes, cigars or a pipe

<sub>2</sub> I quit smoking cigarettes/cigars/pipes at least one year ago

<sub>3</sub> I smoke cigarettes: \_\_\_\_\_ cigarettes per day

<sub>4</sub> I smoke cigar: \_\_\_\_\_ cigars per day



<sub>5</sub> I smoke pipe: \_\_\_\_\_ pipes per day

<sub>6</sub> I chew tobacco: \_\_\_\_\_ times per day

Q20. In general, would you say your health is: (check one box)

<sub>1</sub>

<sub>2</sub>

<sub>3</sub>

<sub>4</sub>

<sub>5</sub>

Excellent

Very Good

Good

Fair

Poor

### Section II – Medication History

Q21. Are you currently (in last 6 months) prescribed any medicine for the treatment of diabetes by your physician? (check one box)

<sub>1</sub>

<sub>2</sub>

No

Yes

**If “yes” check all the medication(s) that apply:**

▪ **ORAL DIABETES MEDICATION(S):** <sub>1</sub> No <sub>2</sub> Yes

▪ **If “yes”** How many **oral diabetes medication(s)** you take?

\_\_\_\_\_

▪ **INSULIN:** <sub>1</sub> No <sub>2</sub> Yes

Q22. Are you currently (in last 6 months) prescribed any other medicine prescribed by your physician? (check one box)

<sub>1</sub>

<sub>2</sub>

No

Yes

**If “yes” check all the medication(s) that apply:**

Cholesterol: <sub>1</sub> No

<sub>2</sub> Yes

Hypertension: <sub>1</sub> No

<sub>2</sub> Yes

Diuretics: <sub>1</sub> No

<sub>2</sub> Yes

Depression: <sub>1</sub> No

<sub>2</sub> Yes

Aspirin: <sub>1</sub> No

<sub>2</sub> Yes

Pain Relievers: <sub>1</sub> No

<sub>2</sub> Yes

Estrogen Replacement Therapy:

<sub>1</sub> No

<sub>2</sub> Yes

Other(s): \_\_\_\_\_

\_\_\_\_\_

Q23. Are you currently (in last 6 months) taking any other non-prescription medication (over-the-counter)?

<sub>1</sub><sub>2</sub>

No

Yes

**If “yes” check all the medication(s) that apply:**

Antacids and Acid Reducers: <sub>1</sub> No <sub>2</sub> Yes

Antidiarrheals: <sub>1</sub> No <sub>2</sub> Yes

Antiemetic Medicines: <sub>1</sub> No <sub>2</sub> Yes

Antihistamines: <sub>1</sub> No <sub>2</sub> Yes

Cough Medicines: <sub>1</sub> No <sub>2</sub> Yes

Decongestants: <sub>1</sub> No <sub>2</sub> Yes

Laxatives: <sub>1</sub> No <sub>2</sub> Yes

Pain Relievers: <sub>1</sub> No <sub>2</sub> Yes

If "yes" check all the medication(s) that apply:

Aspirin (Bayer, St. Joseph) <sub>1</sub> No <sub>2</sub> Yes  
<sub>1</sub> No <sub>2</sub> Yes

Ibuprofen (Advil, Motrin)

Ketoprofen (Orudis KT) <sub>1</sub> No <sub>2</sub> Yes  
<sub>1</sub> No <sub>2</sub> Yes

Naproxen (Aleve)

Other(s): \_\_\_\_\_  
\_\_\_\_\_

### Section III – Family History

Q24. Family history of diabetes (check all that apply)

- <sub>1</sub> Your mother has diabetes
- <sub>2</sub> Your father has diabetes
- <sub>3</sub> Your son has diabetes
- <sub>4</sub> Your daughter has diabetes
- <sub>5</sub> You have no family history of diabetes
- <sub>6</sub> You don't know your family history of diabetes

Q25. Family history of premature coronary heart disease (check all that apply)

- <sub>1</sub> Your mother had coronary heart disease before age 65 years old
- <sub>2</sub> Your sister had coronary heart disease before age 65 years old
- <sub>3</sub> Your father had coronary heart disease before age 55 years old
- <sub>4</sub> Your brother had coronary heart disease before age 55 years old
- <sub>5</sub> You have no family history of coronary heart disease
- <sub>6</sub> You don't know your family history of coronary heart disease

**Section IV – Support**

Q1. I **want** a lot of help and support from my family or friends in:

(circle one answer for each line)

	<b>Strongly Disagree</b>	<b>Somewhat Disagree</b>	<b>Neutral</b>	<b>Somewhat Agree</b>	<b>Strongly Agree</b>	<b>Does Not Apply</b>
following my meal plan.	1	2	3	4	5	N/A
taking my medicine.	1	2	3	4	5	N/A
taking care of my feet.	1	2	3	4	5	N/A
getting enough physical activity.	1	2	3	4	5	N/A
testing my sugar.	1	2	3	4	5	N/A
handling my feelings about diabetes.	1	2	3	4	5	N/A

Q2. My family or friends help and support me a lot to:

(circle one answer for each line)

	<b>Strongly Disagree</b>	<b>Somewhat Disagree</b>	<b>Neutral</b>	<b>Somewhat Agree</b>	<b>Strongly Agree</b>	<b>Does Not Apply</b>
a) follow my meal plan.	1	2	3	4	5	N/A
b) take my medicine.	1	2	3	4	5	N/A
c) take care of my feet.	1	2	3	4	5	N/A
d) get enough physical activity.	1	2	3	4	5	N/A
e) test my sugar.	1	2	3	4	5	N/A
f) handle my feelings about diabetes.	1	2	3	4	5	N/A

Q3. My family or friends: (circle one answer for each line)

	<b>Strongly Disagree</b>	<b>Somewhat Disagree</b>	<b>Neutral</b>	<b>Somewhat <u>Ag</u></b>	<b>Strongly Agree</b>
a) accept me and my diabetes.	1	2	3	4	5
b) feel uncomfortable about me because of my diabetes.	1	2	3	4	5
c) encourage or reassure me about my diabetes.	1	2	3	4	5
d) discourage or upset me about my diabetes.	1	2	3	4	5
e) listen to me when I want to talk about my diabetes.	1	2	3	4	5
f) nag me about diabetes.	1	2	3	4	5

Q4. Who helps you the **most** in caring for your diabetes? (check only one box)

- <sub>1</sub> Spouse
- <sub>2</sub> Other family members
- <sub>3</sub> Friends
- <sub>4</sub> Paid helper



<sub>5</sub> Doctor

<sub>6</sub> Nurse

<sub>7</sub> Case manager

<sub>8</sub> Other health care professional

<sub>9</sub> No one

**Section V - Diet Adherence Scale**

Q1. Has any health care provider or nurse <sub>1</sub> No <sub>2</sub> Yes <sub>3</sub> Not sure told you to follow a meal plan or diet?

	Never		Sometimes		Always
Q2. How often do you follow a meal plan or diet?	1	2	3	4	5

Q3. Have you been told to follow a schedule for your meals and snacks? <sub>1</sub> No <sub>2</sub> Yes

Q4. Have you been told to weigh or measure your food? <sub>1</sub> No <sub>2</sub> Yes

Q5. Have you been told to use exchange lists or food group lists to plan your meals? <sub>1</sub> No <sub>2</sub> Yes

	Never		Sometimes		Always
Q6. How often do you follow the schedule for your meals and snacks?	1	2	3	4	5
Q7. How often do you weigh or measure your food?	1	2	3	4	5
Q8. How often do you (or the person who cooks your food) use the exchange lists or food group lists to plan your meals?	1	2	3	4	5

**Section VI - Exercise Barriers Scale**

For the following questions, please circle the appropriate response.

(circle one answer for each line)

Q1. How often do you have trouble getting enough exercise because:	Rarely		Sometimes		Often
a) it takes too much effort?	1	2	3	4	5
b) you don't believe it is useful?	1	2	3	4	5
c) you don't like to do it?	1	2	3	4	5
d) you have a health problem?	1	2	3	4	5
e) it makes your diabetes more difficult to control?	1	2	3	4	5

### Section VII – Education / Advice Received

Q1. Has your health care provider or nurse ever told you to take special care of your feet?

(check one box)

<sub>1</sub> No    <sub>2</sub> Yes    <sub>3</sub> Not Sure

Q2. Has your health care provider or nurse ever told you to follow an exercise program?

(check one box)

<sub>1</sub> No    <sub>2</sub> Yes    <sub>3</sub> Not Sure

**Q3. Has your health care provider or nurse ever told you to follow a meal plan or diet?**

(check one box)

<sub>1</sub> No    <sub>2</sub> Yes    <sub>3</sub> Not Sure

**Q4. Have you ever received diabetes education? (for example: attended a series of classes or**

series of meetings with a diabetes educator) (check one box)

<sub>1</sub> No    <sub>2</sub> Yes    <sub>3</sub> Not Sure

### Section VIII - Long-Term Care Benefits Scale

For the following questions, please circle the appropriate response.

(circle one answer for each line)

Q1. Taking the best possible care of diabetes will delay or prevent:	<b>Strongly Disagree</b>	<b>Disagree</b>	<b>Neutral</b>	<b>Agree</b>	<b>Strongly Agree</b>
a) eye problems	1	2	3	4	5
b) kidney problems	1	2	3	4	5
c) foot problems	1	2	3	4	5
d) hardening of the arteries	1	2	3	4	5
e) heart disease	1	2	3	4	5

**Section IX - Understanding**

Q1. How do you rate your understanding of: (circle one answer for each line)	<b>Poor</b>	<b>Good</b>	<b>Excellent</b>		
a) overall diabetes care	1	2	3	4	5
b) coping with stress	1	2	3	4	5
c) diet for blood sugar control	1	2	3	4	5
d) the role of exercise in diabetes	1	2	3	4	5
e) medications you are taking	1	2	3	4	5
f) how to use the results of blood sugar monitoring	1	2	3	4	5
g) how diet, exercise, and medicines affect blood sugar levels	1	2	3	4	5
h) prevention and treatment of high blood sugar	1	2	3	4	5
i) prevention and treatment of low blood sugar	1	2	3	4	5
j) prevention of long-term complications of diabetes	1	2	3	4	5
k) foot care	1	2	3	4	5
l) benefits of improving blood sugar control	1	2	3	4	5
m) pregnancy and diabetes	1	2	3	4	5

**Section X - Self-Care Adherence:**

For the following questions, please circle the appropriate response.

(circle one answer for each line)

	Never		Sometimes		Always
Q1. I keep my blood sugar in good control.	1	2	3	4	5
Q2. I keep my glycated hemoglobin (HbA <sub>1c</sub> ) in good control.	1	2	3	4	5
Q3. I keep my weight under control.	1	2	3	4	5
Q4. I do the things I need to do for my diabetes (diet, medicine, exercise).	1	2	3	4	5

## **APPENDIX H**



ID # \_\_\_\_\_

**CVD RISK STUDY:  
HAITIAN & AFRICAN AMERICAN**

Weight: \_\_\_\_\_ lb

Weight: \_\_\_\_\_ kg

Height: \_\_\_\_\_ in

Height: \_\_\_\_\_ cm

BMI: \_\_\_\_\_

Waist circumference: \_\_\_\_\_ in

Waist circumference: \_\_\_\_\_ cm

**Blood Pressure: 1**

Systolic: \_\_\_\_\_ mm Hg

Diastolic: \_\_\_\_\_ mm Hg

**Blood Pressure: 2**

Systolic: \_\_\_\_\_ mm Hg

Diastolic: \_\_\_\_\_ mm Hg

**Average Blood Pressures**

Average Systolic: \_\_\_\_\_ mm Hg

Average Diastolic \_\_\_\_\_ mm Hg

## **APPENDIX I**

Aim	Hypotheses	Variables	Test
<p>1. To determine differences in Serum MnSOD and 8OHdG by diabetes status and ethnicity.</p>	<p>1a: Serum levels of MnSOD will be lower in participants with T2D as compared with those without T2D, independent of ethnicity.</p> <p>1b: Serum levels of 8OHdG will be higher in participants with T2D when compared to those without T2D, independent of ethnicity.</p> <p>1c: There will be an inverse relationship between serum levels of MnSOD and 8OHdG in participants with T2D, independent of ethnicity.</p>	<p><u>Dependent Variables</u></p> <p>1a: MnSOD 1b: 8OHdG</p> <p><u>Independent Variables</u></p> <p>Diabetes status, ethnicity</p> <p><u>Covariates</u></p> <p>Age, gender, smoking, education, BMI, energy intakes</p>	<p>1a: ANCOVA</p> <p>1b: ANCOVA</p> <p>1c: Pearson's correlation and multiple linear regression</p>

<p>2. To examine the relationships of serum MnSOD and 8OHdG with various dietary antioxidants by diabetes status and ethnicity.</p>	<p>2a: Serum 8OHdG levels will be negatively associated with dietary intake of antioxidants, independent of diabetes status and ethnicity.</p> <p>2b: MnSOD levels will be negatively associated with dietary intake of antioxidants, independent of diabetes status and ethnicity</p>	<p><u>Dependent Variables</u></p> <p>2a: 8OHdG 2b: MnSOD</p> <p><u>Independent Variables</u></p> <p>Dietary intake of antioxidants (Vit E, Vit C, Vit D, carotenoids) Diabetes status, ethnicity</p> <p><u>Covariates</u></p> <p>Age, gender, smoking, education, BMI, energy Intakes</p>	<p>2a: Pearson's correlation and multiple linear regression.</p> <p>2b: Pearson's correlation and multiple linear regression.</p>
<p>3. To examine the relationships of glycemic control (A1C and FPG) with various dietary antioxidants in T2D by ethnicity.</p>	<p>3a: There will be no relationship between serum A1C and dietary antioxidants in participants with T2D independent of ethnicity.</p> <p>3b: There will be no relationship between fasting plasma glucose level and any of the dietary antioxidant intakes in T2D independent of ethnicity.</p>	<p><u>Dependent Variables</u></p> <p>3a: A1C 3b: FPG</p> <p><u>Independent Variables</u></p> <p>Dietary intake of antioxidants (Vit E, Vit C, Vit D, carotenoids) ethnicity</p> <p><u>Covariates</u></p> <p>Age, gender, smoking, education, BMI, energy intakes</p>	<p>3a: Pearson's correlation and multiple linear regression</p> <p>3b: Pearson's correlation and multiple linear regression</p>

VITA

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- |              |  |
|--------------|--|
| 1984-1986    | Pre-Medicine<br>Broward College<br>Hollywood, Florida  |
| 1986-1989    | B.Sc., Biology<br>Florida International University<br>Miami, Florida                               |
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#### PUBLICATIONS AND PRESENTATIONS

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