2003

Factors Associated with Metabolic Syndrome

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DOCTORAL PROGRAM IN HEATLH RELATED SCIENCES
SCHOOL OF ALLIED HEALTH PROFESSIONS
VIRGINIA COMMONWEALTH UNIVERSITY

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Factors Associated with Metabolic Syndrome

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for the degree of Doctor of Philosophy at
Virginia Commonwealth University

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Acknowledgement

- My husband, David - " Some succeed because they are destined to, most succeed because they are determined to." Thank you for always believing in me.

- My children, Jordan and Leah - You keep me grounded. Thank you for your love and sense of humor.

- Dr. Dolores Clement - My academic advisor, dissertation chair, teacher, and mentor. I am immensely grateful to have had this opportunity to learn from her on so many levels.

- My dissertation committee- Dr. Dolores Clement, Dr. Janet Lynch, Dr. John Nestler and Dr. Ken White – I am most appreciative to all of you, for your expert advice and encouragement throughout the dissertation process.

- Eleanor Campbell – Thank you for your patience and statistical expertise.

- In Memoriam - Donna Campanella and Conny Frisch - Dear friends whose spirit, strength and determination will always be an inspiration to me.

- To my many friends and family – Thank you for your love and support.

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Abstract

FACTORS ASSOCIATED WITH METABOLIC SYNDROME

By Patricia M. Selig, Ph.D.

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

Virginia Commonwealth University, 2003

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The metabolic syndrome, a clinical condition linked to diabetes and cardiovascular disease is a powerful predictor for overall mortality, and is present in more than 20% of the U.S. population (Ford, Giles, & Dietz, 2002). This study examines gender differences as well as other factors associated with metabolic syndrome as defined by the Adult Treatment Panel III of the National Cholesterol Education Program.

A sample of 10,134 adults between 20-64 years of age was selected from the Third National Health and Nutrition Survey. Metabolic syndrome was present in 19.6 % of this sample. An ecological model of health services was used to analyze metabolic syndrome. The four model domains include population characteristics, environmental factors, health behaviors, and utilization of health care services.

The descriptive results showed statistically significant differences in individuals with

metabolic syndrome and without metabolic syndrome. Those with metabolic syndrome were proportionately more older, reported a past medical history of cardiovascular disease and family history of diabetes, had lower levels of education and a lower annual household income. There were no differences between men and women in age, geographic residence, education or health insurance coverage. However, there were higher proportions of women with metabolic syndrome in all race categories when compared to men with metabolic syndrome with the exception of Caucasians. A family history of diabetes, a family history of cardiovascular disease, a past personal history of cardiovascular disease, level of income, habitual activity and having a usual source of health care were found to be statistically significant between men and women with metabolic syndrome.

Results of the logistic regression analysis revealed that overall, women were 30% less likely to have metabolic syndrome, yet African American women and Hispanic American women were nearly twice as likely to have metabolic syndrome than Caucasian women. Further research on gender differences for shared medical conditions is needed.

CHAPTER 1: INTRODUCTION

Introduction to the Problem

Chronic illness is one of the most predominant health care problems in the United States. It is projected that by the year 2020, a total of 134 million people will have a chronic illness (Hoffman & Rice, 1996). Chronic health conditions can span half a lifetime or more. Often, an individual has several coexisting chronic diseases. While advancements in the detection and treatment of chronic illness are evident, there has been less success in reducing secondary complications of many chronic diseases.

Chronic illness presents a particular challenge to our health care system. Rising healthcare costs are demanding a tight rein on the management of resources. Almost eighty-percent of the health care dollar is spent on long-term illness and its associated complications (Etzweiler, 1997). Health care needs are expected to increase in scope and complexity given the expanding aging population. In an effort to efficiently utilize available resources, evolving health care systems are challenging contemporary practice. As we move into the twenty-first century, health service research must focus more on identifying and developing optimal health care delivery models that better meet chronic health care needs.

Disease management is a strategy for comprehensive health care delivery. Disease management programs prioritize primary and secondary prevention through risk

reduction. While all persons should be counseled on risk reduction, targeting high-risk populations for disease prevention may be a more efficient strategy.

Diabetes is a common, chronic disease affecting approximately 16 million people in the United States (Centers for Disease Control and Prevention [CDC], 1997). The estimated cost of diabetes in the United States exceeds $132 billion per year (American Diabetes Association, 2002). While people with diabetes make up approximately 8% of the population, their health care costs represent 15% of the total U.S. health care expenditures (Rubin, Altman, & Mendelson, 1992).

There are two types of diabetes. Type 1 diabetes is an autoimmune disease that is usually diagnosed before the age of 40 years. Type 2 diabetes is a metabolic disorder that is generally diagnosed in older adults. More than 90% of people with diabetes have type 2 diabetes. Diabetes is a chronic condition that persists throughout one's lifetime.

Type 2 diabetes develops over several years before a clinical diagnosis is confirmed. Up to 50% of people with type 2 diabetes have complications associated with the disease at the time of diagnosis (United Kingdom Prospective Diabetes Study Group, 1991). It is the leading cause of new cases of adult blindness, end stage renal disease, and non-traumatic lower extremity amputations (Reiber, Boyko, & Smith, 1995).

Cardiovascular disease is the leading cause of death in the United States. Cardiovascular disease is the most common complication associated with diabetes. People with diabetes are 2-4 times more likely to experience a cardiac event than people without diabetes (Wingard, Barrett-Connor, & Harris, 1995). Cardiovascular disease

coupled with type 2 diabetes account for more than 77,000 deaths annually. There is no doubt that cardiovascular disease and diabetes are a deadly combination.

Type 2 diabetes and cardiovascular disease share antecedent conditions that comprise a syndrome known as metabolic syndrome. Metabolic syndrome is characterized by high blood pressure, abdominal obesity, high blood glucose levels, and abnormal blood lipid levels. While metabolic syndrome is a recognized syndrome by the American Diabetes Association, the American Heart Association and the World Health Organization, there is no consensus on the management of metabolic syndrome. Identification of high-risk groups for primary and secondary prevention appears to be the most sensible approach to reducing potential complications associated with this syndrome.

Although many medical conditions are shared by men and women, women's health issues have largely been limited to reproductive health (Gully, 2000).Yet men and women differ in their risk and response to the treatment of certain disease states. The most noted gender dicrepancies are found in women with diabetes and cardiovascular disease (Hennekens, 1998; Vaccarino, Parsons, Every, Barron, Krummholz, 1999). More women than men exhibit risk factors for cardiovascular disease at the time their diabetes is diagnosed. Women with diabetes are six times more likely to develop cardiovascular disease as compared to women without diabetes (Barrett-Connor, Cohn, Wingard, & Edelstein, 1991; Manson, Colditz, et al., 1991). Diabetes is a stronger predictor for cardiovascular disease in women when compared to men (Abbott, Donahue, Kannel, & Wilson, 1988; Hypertension in Diabetes Study Group, 1993).

Until recently, research studies were primarily based on men and their response to disease. Women of reproductive age were excluded from clinical trials because of the potential risk to the fetus or to themselves. Once research results on new therapies are made available, treatments are extended to females, regardless of whether there is sufficient female representation in the study. As a result, the National Institutes of Health advocate equal representation of women in scientific studies to better understand gender differences (Office of Research on Women's Health, National Institutes of Health, 1992).

Disease management within high-risk, gender-specific populations may be a more efficient approach to address discrepancies in women's health. Examining diabetes and cardiovascular disease within the context of the metabolic syndrome may provide insight as to why women with diabetes are more vulnerable to cardiovascular disease. If women are more predisposed than men to develop metabolic syndrome, aggressive risk reduction strategies specifically tailored to women are warranted to reduce gender disparities. The Office of Research on Women's Health at the National Institutes of Health has identified diabetes risk assessment and the diagnosis of cardiovascular disease in high risk women as a priority for women's health research in the 21st century (Pinn, 1999). Retrospective analysis may provide some clues and direction for future prospective research.

Diabetes

Type 2 diabetes is a metabolic disease characterized by hyperglycemia. The pathogenesis of diabetes is multi-factorial. Risk factors for type 2 diabetes are listed in

Table 1. References to diabetes throughout the manuscript are addressing type 2 diabetes unless otherwise noted.

Prevalence

Diabetes is a growing and serious health problem. The World Health Organization and the International Diabetes Institute predict that diabetes will double by the year 2010. This would increase the total number of people with diabetes from 123 million to over 220 million people worldwide (King, & Rewers, 1993, Amos, McCarty, & Zimmet 1997). Diabetes is a global problem that could potentially reach epidemic proportions. Type 2 diabetes affects 1 in 17 Americans. It is the seventh leading cause of death in the United States (CDC, 1999). The prevalence of type 2 diabetes has grown over the past four decades. This phenomenon parallels a population that continues to grow older, be less active, and more obese (Harris, 1995). The incidence of diabetes is expected to increase given the re-established diagnostic criteria for diabetes set forth by the American Diabetes Association in 1997 (ADA, 1997). While the incidence of type 1 diabetes is distributed equally in men and women, type 2 diabetes is more prevalent in women (Kenny, Aubert, & Geiss, 1995). Whether this discrepancy will continue to be true in the future is unknown.

Diabetes is more prevalent in ethnic minorities (See Figure 1). It is more common in African Americans, Hispanic Americans, Native Americans, Asian Americans, and Pacific Islanders.

Table 1.

Risk Factors for Type 2 Diabetes

Age $\geq$ 45
Family history of diabetes (parents or siblings with diabetes)
Obesity (20% over desired body weight or a body mass index (BMI) $\geq$27 kg/m^2)
Habitual physical inactivity
Hypertension ($\geq$ 140/90 mm Hg)
Dyslipidemia (triglyceride level $\geq$ 250mg/dl, high-density lipoprotein $\leq$ 35 mg/dl)
Women with a history of polycystic ovary syndrome
Women with a history of gestational diabetes
Women who have delivered a baby $\geq$ 9 pounds
Ethnic minorities (African Americans, Hispanic Americans, Native Americans, Asian Americans, and Pacific Islanders)
Impaired fasting glucose (fasting blood glucose 110-126)
Impaired glucose tolerance (random blood glucose 140-200)

Note. Adapted from "Screening for Diabetes, " by American Diabetes Association. 2001, Diabetes Care, 24, (S1), p. 22.

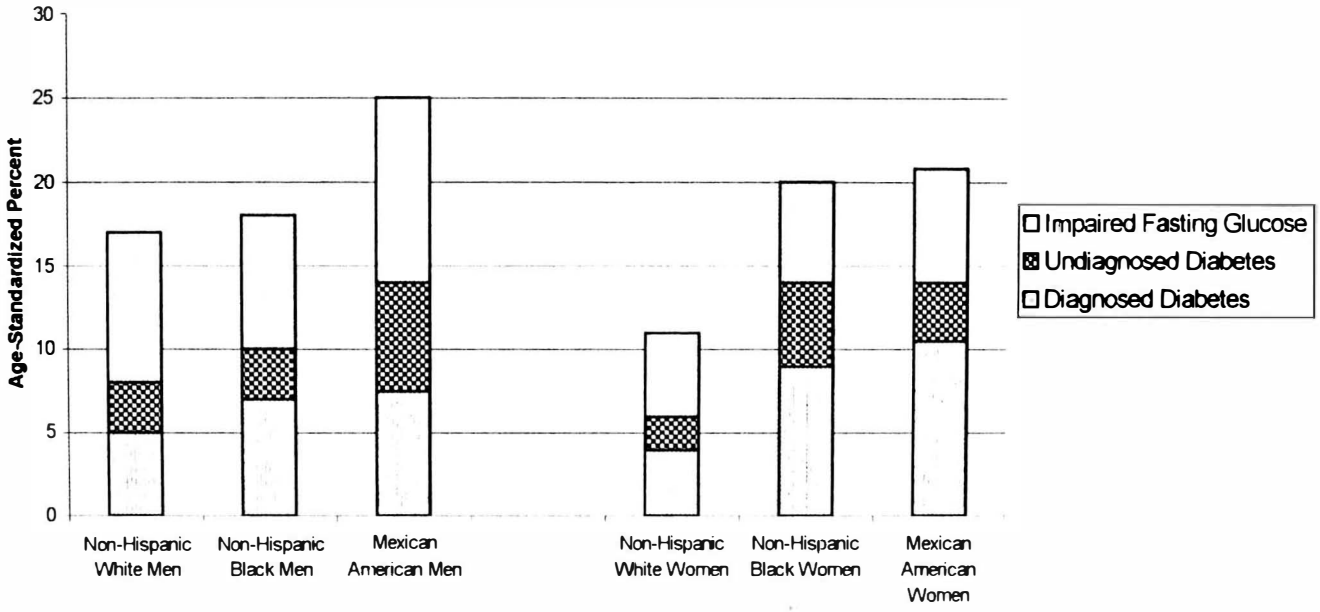

Figure 1, Age-Standardized Prevalence of Undiagnosed Diabetes and Impaired Fasting Glucose in the United States, Based on NHANES III, 1988 – 1994.

From "Prevalence and DM, IFG, and IGT in U.S. Adults," by K.M. Flegal and C.C. Cowie, 1998, Diabetes Care, p. 518, Adapted with permission of the Author.

Over the past 20 years there has been a 10 % increase in diabetes among ethnic minorities and a 7% increase among non – Hispanic whites (CDC, 1997; Diabetes, Petit, Jome & Arslanian, 1999). Ethnic minorities experience a disproportionate degree of morbidity and mortality associated with diabetes (American Diabetes Association [ADA], 2000). The incidence and prevalence of diabetes rises sharply across all populations with respect to age. One in five Americans over the age of 65 has diabetes (CDC, 1998).

Pathophysiology

Diabetes develops when insulin secretion (insulin deficiency) and/or insulin action (insulin resistance) are impaired. Adequate insulin production and appropriate insulin performance are necessary to maintain glucose homeostasis. Insulin production and its subsequent release from the pancreas are a response to the influx of glucose from energy sources or food intake. This occurs in two phases. There is an immediate release that occurs within minutes and a second more gradual release that persists as long as glucose levels remain elevated. Persistent hyperglycemia is associated with end-organ damage. The eyes, kidneys, nerves, heart, and blood vessels are particularly vulnerable. Complications associated with diabetes are often life threatening. Intensive management of diabetes can ameliorate or significantly reduce complications (Diabetes Control and Complications Trial Research Group, 1993). The greatest challenge is to prevent the development of diabetes.

Diabetes that develops during pregnancy is called gestational diabetes. Women with gestational diabetes produce an adequate amount of insulin but are unable to properly utilize insulin. Gestational diabetes usually resolves after delivery. However, women who have had gestational diabetes are at an increased risk for the development of type 2 diabetes in the future.

Insulin action takes place in the peripheral tissue or target cells. Insulin facilitates the uptake of glucose within the cell when it binds to an insulin receptor. This activates a cascade of intracellular events that stimulate protein carrier molecules to bind with glucose and transport it into the cell. Glucose cannot be utilized as an energy source unless it is transported across and into the cell. When this cycle is disturbed, glucose levels rise (See Figure 2).

Insulin action is impaired in obese individuals. Once obesity is present, the body attempts to preserve this altered state. Obesity or excess adiposity disrupts autophosphorylation, which facilitates glucose transport, oxidation and storage within the cell (Caro, Dohm, Pories, & Sinha, 1989; Evans, Hoffman, Kalkhoff, & Kissebah, 1983). The degree of insulin resistance at the peripheral tissue level is inversely proportional to the impairment of autophosphorylation. When glucose is less available, the body reverts to compensatory mechanisms. The liver converts stores of glycogen to glucose, which results in more hyperglycemia. Fat cells further contribute to this aberrant cycle by mobilizing free fatty acids. At the peripheral level free fatty acids compete with glucose for energy. Because free fatty acids are a preferred fuel, glucose is underutilized and

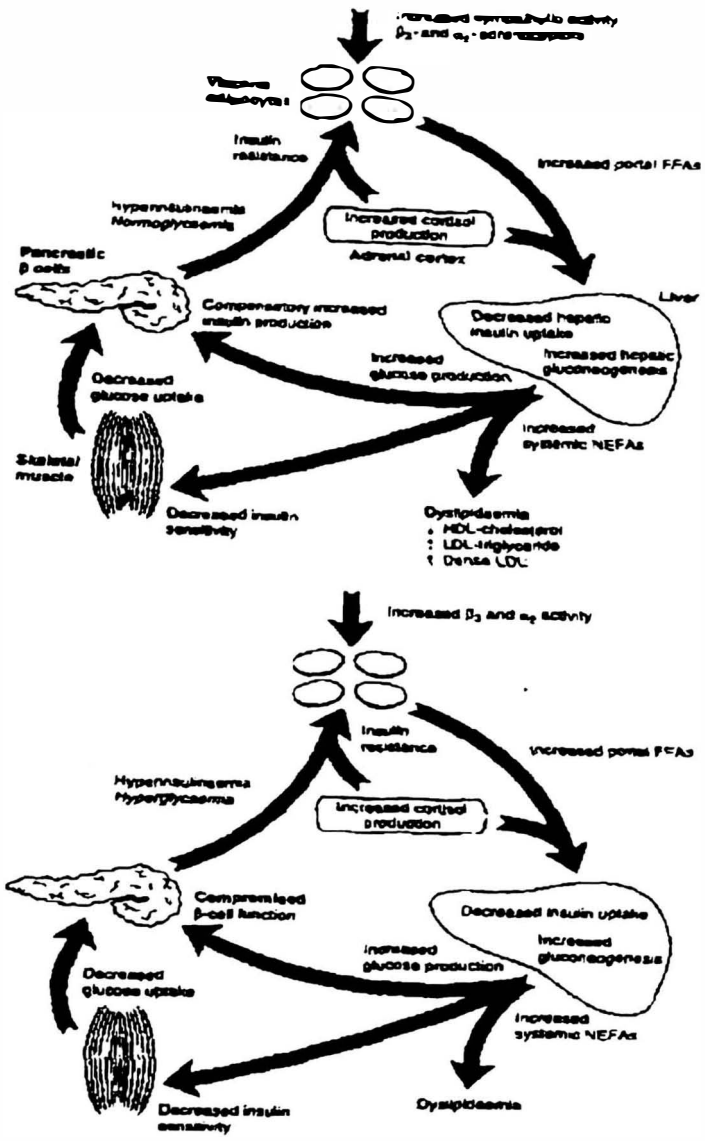

Figure 2, The Relationship of Obesity to Type 2 Diabetes

From P.G. Kopelman, "Obesity", Type 2 Diabetes; Prediction and Prevention. (Ed.) John Wiley and Sons, Sussex, England. Reprinted with permission.

serum glucose levels rise. Hyperglycemia stimulates the pancreas to produce more insulin. This demand eventually leads to pancreatic exhaustion. With diminished or no insulin production, glucose levels remain elevated and diabetes is inevitable. Obesity and insulin resistance are critical precursors to the development of diabetes (DeFronzo, 1997).

Diagnosis

Diabetes develops in stages. Criteria for the stages and diagnosis of diabetes can be found in Table 2. Stage one is normal glucose regulation, stage two is impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), and stage three is diabetes mellitus. The degree of hyperglycemia may vary in the early developmental stages of diabetes. Individuals may not experience clinical symptoms in the early stages as compensatory mechanisms mobilize to maintain glucose homeostasis. Therefore, diabetes may be present for a long time before the criteria for diagnosis is met. All of the biochemical reactions that occur in the development of diabetes are not completely understood. Until there is a way to identify cellular dysfunction earlier in the disease, primary prevention is focused on risk reduction of clinical factors.

Insulin Resistance

Insulin resistance is an impaired biological response to exogenous (delivered to the body from an external source) or endogenous (produced within the body) insulin (ADA, 1998).

Table 2.

Criteria for the Diagnosis of Impaired Fasting Glucose (IFG).

Impaired Glucose Tolerance (IGT), and Diabetes Mellitus

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*Impaired Fasting Plasma Glucose (IFG)

Glucose ≥ 110 mg/dl and < 126 mg/dl.

**Impaired Glucose Tolerance (IGT)

Glucose ≥ 140 and < 200 mg/dl

***Diabetes Mellitus

Fasting glucose ≥ 126 mg/dl or

2 hour post load glucose ≥ 200 mg/dl or

*** Symptoms of diabetes and a *random glucose of ≥ 200 mg/dl

Testing must be confirmed on a subsequent day to confirm diagnosis of diabetes

---

* Fasting is defined as no caloric intake for at least 8 hours
** Impaired is defined after a 2 hour post-load glucose of 75 g anhydrous glucose dissolved in water
*** Symptoms of diabetes include thirst, frequent urination, and weight loss.

Note. Adapted from "Clinical Practice Recommendations 2001," American Diabetes Association, 2001, Diabetes Care, 24, (S1), 22s.

Insulin resistance refers to the disruption in glucose uptake and transfer of glucose across the cell membrane. The pancreas compensates by releasing more insulin to assist with glucose transport resulting in high insulin levels. Hyperinsulinemia is the hallmark

characteristic of insulin resistance in individuals who have not yet developed diabetes. Insulin is responsible for the metabolism of carbohydrates, proteins, and fats. Insulin promotes fat storage, suppresses protein breakdown, assists in protein synthesis and vascular endothelial function (ADA 1998; Guyton, 1986). Insulin promotes glucose uptake and processes excess glucose into fat. When insulin is impaired, free fatty acids and triglyceride levels rise. Free fatty acids are the preferred energy source of muscle tissue. When free fatty acids increase, storage deposits become distended and body fats increase (Hjermann, 1992).

Hyperinsulinemia is associated with hypertension, endothelial dysfunction, elevated uric acid levels, increased triglyceride levels, sodium retention, inappropriate membrane ion transportation, proliferation of vascular smooth muscle and coagulopathies. High insulin levels stimulate the sympathetic nervous system, which activates compensatory processes in the body during times of physiologic or emotional stress. The sympathetic nervous system stimulates the cardiovascular system by increasing heart rate and arterial blood pressure. Hyperinsulinemia stimulates the production of plasminogen activator inhibitor-1 (PAI-1). High levels of PAI-1 interfere with the coagulation pathway. Impairment of fibrinolytic activity contributes to cell aggregation, endothelial inflammation and clot formation. Hyperinsulinemia promotes a shift in low-density lipoproteins (LDL) from a large particle mass to dense particles while simultaneously reducing high-density lipoproteins (HDL). With the shift in higher numbers of dense LDL particles and less available HDL particles, more particles are left to accumulate

within the vessel. This contributes to a narrowing of vessel passageways and diminished blood flow to vital organs. All of these biochemical and physiological changes are associated with cardiovascular disease.

Insulin resistance was originally referred to as insulin insensitivity (Himsworth & Kerr, 1939). One of the most important elements of insulin resistance is the body's overwhelming drive to maintain blood glucose homeostasis. Hyperinsulinemia coupled with euglycemia indicates the presence of insulin resistance. Insulin resistance is likely a result of genetic and behavioral factors. Genetic defects of cellular proteins, biological impairments, and the behavioral influences of obesity and inactivity contribute to the development of insulin resistance. The ability to identify insulin resistance would strengthen risk profiling for diabetes and cardiovascular disease.

Metabolic Syndrome

Metabolic syndrome is a metabolic condition associated with diabetes and cardiovascular disease. Metabolic syndrome manifests clinical characteristics of both disease states. Characteristics of metabolic syndrome include hypertension, central obesity, hyperinsulinemia (insulin resistance), high blood glucose levels, and dyslipidemia (O'Keefe, Lavie, & McCallister, 1995).

Hyperglycemia, hypertension, obesity, and dyslipidemia are risk factors for diabetes and cardiovascular disease. While each component confers a unique risk for diabetes or cardiovascular disease, the combination of these risk factors, namely metabolic syndrome, is a more powerful predictor for either disease. Identifying metabolic

syndrome is a critical first step toward reducing the devastating consequences of this deadly syndrome.

There is no international consensus on the name or definition of this syndrome. This has lead to confusion and a blunting of research efforts to analyze its impact. Metabolic syndrome is also referred to as insulin resistance syndrome, metabolic syndrome X, syndrome X and cardiovascular dysmetabolic syndrome. Reavan (1988) originally coined the term "insulin resistance syndrome". While insulin resistance syndrome implies the innate disorder of this syndrome, the term metabolic syndrome was adopted for the purpose of this study, as it is the term more universally accepted in the literature.

The Western Working Group (1998) named the syndrome the cardiovascular dysmetabolic syndrome (CDS) (Fagan & Deedwania, 1998). The group contends that cardiovascular dysmetabolic syndrome more accurately reflects the cardiovascular events associated with the syndrome. The group uses the acronym D-R-O-P to identify its clinical characteristics. D-R-O-P stands for Dyslipidemia, insulin Resistance, Obesity, and high blood Pressure. See Table 3 for the criteria for cardiovascular dysmetabolic syndrome as defined by the Western Working Group.

The World Health Organization (WHO) proposes a different definition of this syndrome. They call it the metabolic syndrome. According to the WHO, the metabolic syndrome is defined by the presence of hypertension, dyslipidemia, obesity and microalbuminuria (Alberti & Zimmet, 1998) Table 4 lists the specific criteria of the metabolic syndrome according to the World Health Organization.

Table 3.

Western Working Group Criteria for the Cardiovascular Dysmetabolic Syndrome (CDS)

D Dyslipidemia*

- Fasting triglycerides > 140 mg/dl or
- HDL cholesterol < 40 mg/dl or
- LDL particle size < 260A

R Insulin Resistance*

- Fasting plasma glucose ≥ 110 mg/dL or
- Type 2 diabetes

O Obesity*

- Body mass index > 25 kg/m^2 or
- Waist/hip ratio > 0.85 or
- Waist > 100 cm

P High Blood Pressure

- Systolic blood pressure ≥ 140 mm Hg or
- Diastolic blood pressure ≥ 90 mm Hg

* Note, CDS is defined by having at least 2 of the first three components (dyslipidemia, insulin resistance, and obesity). Adapted from "The Cardiovascular Dysmetabolic Syndrome (CDS)," by T. C. Fagan & P. C. Deedwania, 1998, American Journal of Medicine, 105, 77s – 82s.

Table 4.

World Health Organization (WHO) Criteria for Metabolic Syndrome

1. Hypertension - systolic blood pressure of $\geq$ 140 mm Hg, a diastolic blood pressure of $\geq$ 90 mm Hg or taking antihypertensive medication.
2. Dyslipidemia - an elevated plasma triglycerides $\geq$ 1.7 mmol/l and/or an HDL cholesterol < 0.9 mmol/l in men and < 1.0 mmol/l in women.
3. Obesity - a body mass index (BMI) of $\geq$ 30kg/m^2 and/or a waist to hip ratio (WHR) of >.90 in men and > .85 in women.
4. Microalbuminuria - a urinary AER greater than or equal to 20 µg/min

The metabolic syndrome is defined according to the following conditions:

1. A person has * type 2 diabetes, impaired fasting glucose, or impaired glucose tolerance and has at least two of the above mentioned components.
2. A person has normal glucose tolerance, has at least two of the above mentioned components and is insulin resistant. Insulin resistance is defined as the highest quartile of the HOMA $_{IR}$ index.

* Type 2 diabetes, IFG, and IGT as defined by the ADA clinical practice guidelines.

Note. Adapted from "Definition, diagnosis, and classification of diabetes mellitus and its complications. A provisional report of a WHO consultation," by K. M. Alberti & P.Z. Zimmet, 1998, Diabetes Medicine, 15, 539 – 553.

The Expert panel of the National Cholesterol Education Program (NCEP) on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel or ATP III) also chose the name metabolic syndrome to identify this syndrome.

NCEP is a division of the National Heart, Lung, and Blood Institute (NHLBI). This expert panel publishes clinical practice guidelines on the prevention and management of high cholesterol. The newest recommendations released in May of 2001 included the definition of metabolic syndrome. Their diagnostic criteria are listed in Table 5. The criteria for metabolic syndrome are easily obtained in the clinical setting. The ATP III criteria provide the operational definition of metabolic syndrome for this study.

The American Association of Clinical Endocrinologists prefer the name dysmetabolic syndrome. The Centers for Disease Control approved their request for a clinical diagnostic code marker. The International Classification of Diseases, Ninth Revision diagnostic code, 277.7 allows for identification and reimbursement for the treatment of dysmetabolic syndrome in clinical practice. The CDC does not specify which or how many clinical characteristics must be present in order for the code to be used. The use of this code is at the professional discretion of the health care provider.

The dysmetabolic syndrome as defined by the CDC is a group of metabolic abnormalities that include an alteration in serum or plasma insulin levels, lipoproteins (triglycerides, LDL cholesterol subtypes and/or HDL cholesterol), uric acid levels, coagulation factors and vascular physiology. The major criteria are insulin resistance (hyperinulinemia coupled with euglycemia), acanthosis nigricans, central obesity

Table 5.

Adult Treatment Panel (ATP III) of the National Cholesterol Education Program (NCEP) Criteria for the Metabolic Syndrome

Risk Factor	Defining level
• Abdominal obesity (waist circumference)	
Men	> 102 cm (>40 in)
Women	> 88 cm (>35 in)
• Triglycerides	≥ 150 mg/dl
• High-density lipoprotein (HDL)	
Men	< 40 mg/dl
Women	< 50 mg/dl
• Blood pressure	≥ 130 / ≥ 85 mm Hg
• Fasting glucose	≥ 110 mg/dl

Metabolic syndrome is diagnosed when 3 or more of the risk factors are present.

Note. Adapted from "Executive summary of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III)", Journal of the American Medical Association, 285, (19), 2486-2509.

(waist circumference > 102 cm for men and > 88 cm for women), dyslipidemia (HDL <.45mg/dL for women and < 35 for men, or triglycerides >150 mg/dL), hypertension, impaired fasting glucose or type 2 diabetes and hyperuricemia. Minor criteria are hypercoaguability, polycystic ovary syndrome, vascular endothelial dysfunction, microalbuminuria, and coronary heart disease.

The prevalence of the metabolic syndrome may vary when different definitions are employed in research. Definitions for metabolic syndrome are listed in Table 6. Ford, Giles, and Dietz (2002) used the definition of metabolic syndrome proposed by the ATP III to identify the prevalence of this syndrome in a representative sample of the US population from the Third National Health and Nutrition Examination Survey. The results from this study showed an overall unadjusted prevalence of 21.8% among participants aged 20 years or older. Another study using the same database found similar prevalence rates in that 22.8% and 22.6% of U.S. men and women respectively had metabolic syndrome (Park, Zhu, Palaniappan, Heshka, Carnathon & Heymsfield, 2003). A more in depth analysis of women with this syndrome using the ATP III definition and the NHANES population is the focus of this study.

Significance of the Problem

Diabetes and cardiovascular disease are two of the most common chronic diseases in the United States. Women with diabetes are at a greater risk for the morbidity and mortality associated with cardiovascular disease. Prevention of cardiovascular disease in women must incorporate strategies that address diabetes as a significant risk factor.

Table 6.

Comparison of definitions of Metabolic Syndrome

Western Working Group "Cardiovascular Dysmetabolic Syndrome" (1998)	World Health Organization "Metabolic Syndrome" (1998)	National Cholesterol Education Program ATP III "Metabolic Syndrome" (2001)
Type 2 DM or Fasting Glucose >110	**Type 2 DM, IFG, IGT, or IR	Fasting glucose ≥ 110
Triglycerides > 140 HDL < 40 LDL size < 260A	Triglycerides > 1.7 HDL < .9 men < 1.0 women	Triglycerides ≥ 150 Or HDL < 40 men < 50 women
BMI > 25 WHR > .85 Waist > 100	BMI > 30 WHR > .9 men > .85 women	Waist >102 men > 88 women
** HTN ≥ 140/90	HTN ≥ 140/90	HTN ≥ 130/85
	Microalbuminuria	
Must have HTN and At least 2/3 remaining Components	Must have Type 2 DM, IFG, IGT, or IR and At least 2/4 remaining components	Must have 3/5 of the components

Several studies have demonstrated that women are victims of health disparities and suffer disadvantages within the health care system (Mark, 2000; Roger, et al., 2000, Schulman, et al., 1999). While women utilize health care services more frequently than men, they receive less counseling on preventive health care practices (Bertakis, Azari, Helms, Callahan, & Robbins, 2000). Responses to the National Ambulatory Medical Care Survey reported that women were counseled less often than men about modifiable risk factors such as exercise, nutrition and weight reduction (CDC, 1998).

Limiting women's health to their reproductive status effectively eliminates exploration of a gender specific response to shared medical conditions. Cardiovascular disease kills more women than cancer, accidents, pneumonia or influenza combined (O'Keefe, et al., 1995). One in nine women between the ages of 45 and 64 years has heart disease. Research indicates that cardiovascular disease affects men and women differently (Mark, 2000; Vaccarino et al., 1999, Williams, Choudri, Morales, Helman, & Oz, 2000). More women than men die from cardiovascular disease (American Heart Association, 1999). Women with diabetes are 3-7 times more likely to develop cardiovascular disease as compared to women who do not have diabetes. In contrast, men with diabetes are only 2-4 times more likely to develop cardiovascular disease as compared to men without diabetes (Wingard, Barrett-Connor E., & Harris, 1995). While diabetes confers a higher risk for cardiovascular disease in women than in men, women do not consider themselves at risk for cardiovascular disease despite having risk factors.

Diabetes is a strong predictor for cardiovascular disease. Diabetes is a stronger predictor of cardiovascular disease in women than in men (Manson, Colditz, et al., 1991). Metabolic syndrome is a strong predictor for diabetes and cardiovascular disease. Reavan, Chen, Jeppesin, Maheux, and Krauss (1993) estimate the prevalence of insulin resistance to be approximately twenty-five percent in people without diabetes. Whether female status or other factors lend more or less risk for the development of the metabolic syndrome is unknown.

If the metabolic syndrome is more common in women, primary prevention strategies that aggressively address the clinical characteristics of metabolic syndrome unique to women are a sensible and responsible approach to reducing the morbidity and mortality experienced by all women. Certain populations experience less favorable outcomes in terms of morbidity and mortality due to specific diseases, as compared to the population as a whole and deserve priority for health service research.

Purpose of the Study

The purpose of this study is to address the following:

1. Whether female status confers a greater risk for metabolic syndrome.
2. Determine what factors contribute to the development of metabolic syndrome.

Research Questions

The primary research interest explores the association of gender to metabolic syndrome. Given the significance of the problem and the purpose of the study, the following research questions are addressed:

1. What is the prevalence of metabolic syndrome in women compared to men?
2. How does the prevalence of metabolic syndrome in women compared to men differ in the presence or absence of cardiovascular disease?
3. Are there factors associated with the population, the environment, an individual's health behaviors, or health care services that influence the development of metabolic syndrome?

Scope of Data and Analysis

The Third National Health and Nutrition Examination Survey (NHANES III) is the seventh in a series of surveys conducted by the National Center for Health Statistics. It was conducted between September 1988 and October 1994. NHANES III is a stratified probability sample of non-institutionalized civilians in the United States. The population surveyed in NHANES III is used to analyze the impact of gender and other factors on metabolic syndrome.

The goal of NHANES III was to assess the health and nutritional status of the population. The survey included an interview, a physical examination, and laboratory measurements. A total of 33,994 participants, 2 months and older, took part in the study. NHANES III is unique from previous surveys in that it produced the largest available sampling of ethnic minorities in the United States.

The proposed study is a non-experimental correlational (ex post facto) design using data from NHANES III. Descriptive statistics are used to identify the prevalence of metabolic syndrome as defined by the ATP III. Women and men between the ages of

20-64 were extrapolated from the NHANES study population. Postmenopausal women are excluded from this study, as prevalence of disease is more gender neutral after 65 years of age. Descriptive, correlational, and multivariate analyses of gender differences are generated using the Statistical Package for the Social Sciences (SPSS). SUDAAN is the statistical software used to adjust for sampling variance.

Discussion

Women's health has received a great deal of political and social support over the past ten years. In 1993 the National Institutes of Health established the Office of Research on Women's Health as a result of the National Institutes of Health Revitalization Act. The U.S. Department of Health and Human Services (HHS), the Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), and the Health Resources and Services Administration (HRSA) have all established women's health divisions (Hamburg, 2001). These restructuring strategies are expected to impact research and health care services for women.

The Lewin Group and the National Women's Center on Health and Leadership at the University of Pennsylvania School of Medicine released their millennium report on the status of women's health in the United States. This report highlights the gains in life expectancy over the last century. Unfortunately, additional life years brought a corresponding increase in chronic disease and disability. This suggests that while women are living longer, they are not necessarily living healthier lives (Haapanen, Milunpalo, Vuori, Oja, & Pasanen, 1997). Almost half of all premature deaths are related to

unhealthy lifestyles such as high fat diets and physical inactivity (McGinnis, 1993). Behavioral modification would save lives and improve the quality of life for many women.

Heart disease, arthritis and cancer were the three medical problems noted by keynote speaker, Margaret Hamburg M.D., at a symposium for quality heath care for women (Hamburg, 2001). Dr. Hamburg presented two startling facts. Women are more likely to die from a heart attack than men, and, women are treated less aggressively during the acute phase of their heart attack (Abbott et al., 1988; Barrett-Connor, Cohn, Wingard, Edelstein, 1991; Gan et al., 2000). The explanation for these facts is not known. It is interesting that in noting the health care issues facing women, Dr. Hamburg did not mention the growing prevalence of diabetes and its impact on cardiovascular risk in women.

There is a dissonance between vulnerability to disease and the appropriate actions on the part of women and health care professionals that care for them. Women continue to be more concerned about developing breast cancer than cardiovascular disease (Legato, 1997). It will be important to link heart disease with diabetes for appropriate screening and intervention in women. What is reasonable and medically necessary in terms of preventive screenings and treatment offered to women, as defined by community standards and within courts of law may change with new information derived from women's health research. More research on women's vulnerability to disease is needed (Gully, 2000).

The literature review in the following chapter will provide more evidence of the peculiarities of gender in relation to diabetes and cardiovascular disease. Metabolic syndrome will be further explored as a clinical entity. Diabetes and cardiovascular disease are often discussed as separate health care conditions. Current research suggests that diabetes and cardiovascular disease are inextricably linked (Amos et al., 1997; Duncan et al., 1994; Edelman, Kahn, Marcus, & Sobel, 2000; Haffner, Valdez, et al., 1992; Isomaa, et al., 2001). Efforts to reduce the morbidity and mortality of these two chronic diseases could be more organized by public awareness campaigns highlighting women's vulnerability, coordination of women's health care services, and more women's health research.

CHAPTER 2: LITERATURE REVIEW

Introduction

This chapter further defines metabolic syndrome and its relationship to diabetes and cardiovascular disease through a critical analysis of the literature. Retrospective and prospective studies are examined for gender bias. Prior research studies are analyzed with respect to whether they are sufficiently powered to reach similar conclusions for men and women. The defining clinical characteristics of the metabolic syndrome are supported in the literature.

Risk Factors for Diabetes

The American Diabetes Association's criteria for testing individuals who have not yet experienced symptoms of diabetes can be found in Table 7. Identifying individuals at risk for diabetes allows for earlier identification and intervention for diabetes in the approximately 8 million people who have not yet been diagnosed.

Obesity

Obesity predisposes individuals to the development of a variety of chronic illnesses. Obesity is a risk factor for diabetes, hypertension, cardiovascular disease, degenerative arthritis, and dyslipidemia (Pi-Sunyer, 1993). Up to fifty-five percent of adults, twenty years of age or older, are overweight or obese (National Heart, Lung, and Blood Institutes Obesity Initiative Task Force Members [NHLBI], 1998).

Prospective analysis of data from 1960 to 1991 from the National Health and Examination Surveys showed an increase in the prevalence of being overweight in the United States

Table 7.

Recommendations for Testing for Diabetes in Asymptomatic Individuals

1. Testing for diabetes should be considered in all individuals age 45 years and older. If glucose is within the acceptable range, testing should be repeated at 3-year intervals.
2. Testing should be considered at a younger age or be carried out more frequently in individuals who:
   - Are obese ($\geq$ 20 % desirable body weight or a BMI $\geq$ 27 kg/m^2)
   - Have a first degree relative with diabetes
   - Are members of a high-risk ethnic population (African American, Hispanic American, Native American, Asian American, and Pacific Islander)
   - Women who have delivered a baby weighing > 9 pounds or have been diagnosed with gestational diabetes or polycystic ovary syndrome
   - Have high blood pressure ($\geq$ 140/90 mm/hg)
   - Have an HDL (high-density lipoprotein) cholesterol level $\leq$ 35 mg/dl and/or a triglyceride level $\geq$ 250 mg/dl
   - Have impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)

Note, Adapted from "Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus," American Diabetes Association, 2001, Diabetes Care, 24, (S1), 15s.

(Kuczmarski, Flegal, Campbell & Johnson, 1994). Overweight is defined as a body mass index of $\geq$ 27. 3 cm. for women and $\geq$ 27. 8 cm. for men. The prevalence of being overweight is 31% of adult men and 35% of adult women. While the prevalence is similar for Caucasian men and women, African American women and Mexican American women are twice as likely to be overweight than their male counterparts. The prevalence of being overweight is similar for Caucasian men and African American men. The prevalence of being overweight is delineated to 33 % of Caucasian women, 47 % of Mexican American women and 49 % of African American women (Kuczmarski, Flegal, Campbell, & Johnson, 1994). There is no cohort analysis of individuals with chronic disease in the Kuczmarski et al.(1994) study.

Women with diabetes are more likely to be obese when compared to men with diabetes (Cowie & Harris, 1995). The Nurses Health Study revealed that the risk of developing diabetes correlated with weight gain in women (Colditz, Willett, Rotnitzky, & Manson, 1995). The Nurses Health Study included 84,941 female nurses who had no reported cardiovascular disease or diabetes. This prospective study showed that being overweight or obese was the single most important predictor for the development of diabetes in women when compared to inactivity, a high-fat, low-fiber diet, tobacco use or abstinence of alcohol. (Hu, et al., 2001).

The best method for determining obesity is to calculate a body mass index (BMI). The BMI is calculated by dividing weight in kilograms by height in meters squared. Overweight is defined as a BMI $\geq$ 27 kg/m^2 and obesity as a BMI $\geq$ 30 kg/m^2 (NHLBI, 1998). Insulin sensitivity was adversely affected at a BMI $\geq$ 27 in a study involving 49

subjects (Campbell & Gerich, 1990). Thirty-five percent of participants were women. While the sample size is small, this clinical trial utilized the gold standard, the euglycemic clamp, to assess insulin response. These results are consistent with other studies demonstrating a linear relationship between obesity and diabetes (Modan et al., 1985, Sjostrom, 1992).

Central obesity is a primary abdominal distribution of fat. Retrospective and prospective studies have demonstrated that central distribution of fat is associated with a higher risk of diabetes and cardiovascular morbidity than a diffuse or peripheral distribution in men and women (Bjorntop, 1990; Despres, 1993; Folsom, et al., 1993). Central obesity is defined as a waist circumference (WC) > 102 cm for men and > 88 cm for women (NHLBI, 1998). The waist to hip ratio (WHR) is another frequently used measurement in clinical studies. A WHR > 0.85 is associated with an increased incidence of metabolic disease. The higher the BMI and WHR, the higher the risk for diabetes and cardiovascular disease (Chan, Rimm, Colditz, Stampfer, & Willett, 1994; Ohlson, et al., 1985).

Central obesity is a stronger predictor for diabetes in women than in men (Haffner, Mitchell, Hazuda, & Stern, 1991; Jenson, Haymond, Rizza, Cryer, & Miles, 1989). Haffner et al. (1991) looked at the incidence of diabetes in 1, 288 Mexican – American and 929 Caucasian men and women in the 8 year prospective San Antonio Heart Study. After controlling for overall obesity, central obesity was more strongly associated with the incidence of diabetes in women than in men. The Iowa Women's Health Study found

the WHR to be the best anthropometric predictor of overall mortality when compared to BMI and waist circumference (Folsom et al., 2000). This prospective study followed 41,837 women over five years. Ninety-eight percent were Caucasians between the age of 55-69 years. However, body mass index, waist to hip ratio and waist circumference were all positively correlated with the development of diabetes. Similar findings were substantiated in a study of 32,662 Caucasian women in the United States and Canada who were members of the organization Take Pounds Off Sensibly (TOPS) organization (Morris, Rimm, Hartz, Kalkhoff, & Rimm, 1989).

While distribution of subcutaneous fat is an established independent risk factor for diabetes and cardiovascular disease, visceral adiposity is also a sensitive marker (Depres, et al., 1990). Visceral adiposity is determined by abdominal computed tomography scans that can delineate visceral from subcutaneous fat. This method allows for quantitative analysis of individuals who appear lean. One study compared visceral fat to subcutaneous fat in 50 women, and found notable adverse metabolic changes in Caucasian females when compared to African American females (Albu, Murphy, Frager, Johnson, & Pi-Sunyer, 1997). This study is too small to be conclusive and a diagnostic scan is not clinically feasible to perform on all persons as a screening tool. A waist circumference or WHR are reliable measurements with broader clinical application.

Physical Activity

Habitual moderate physical activity enhances quality of life and reduces the possibility of developing many chronic diseases. Regular physical activity improves

insulin sensitivity and lowers the risk for diabetes and cardiovascular disease (ADA, 1991; Despres & Lamarche, 1993, Diabetes Prevention Program Research Group, 2002, Tuomilehto et al., 2001). The National Institutes of Health sponsored the prospective study, Diabetes Prevention Program (DPP), to identify what interventions were most effective in delaying or halting the development of diabetes. Ethnic minorities made up more than half of the 4000 study participants. Women of ethnic minorities are more than twice as likely to be physically inactive (Crespo, Keteyian, Heath, & Sempos, 1996; Hahn, Teutsch, Franks, Chang, & Lloyd, 1998). The DPP study demonstrated a 58% risk reduction in the progression to diabetes in individuals with impaired glucose tolerance or impaired fasting glucose who followed a low fat diet and exercised 150 minutes a week (Diabetes Prevention Program Research Group, 2002).

A number of retrospective and prospective studies have shown the more physically active an individual is, regardless of gender, the lower the risk for diabetes and cardiovascular disease (Haapanen, et al., 1997; Manson, Colditz, Stampfer, Willett, Krowlewski, et al., 1991). In the Third National Health and Nutrition Survey, 59% of woman exercised infrequently or not at all (Crespo, Keteyian, Heath, & Sempos, 1996). Monitoring physical activity is important because of its influence on obesity, diabetes and cardiovascular disease.

Hyperinsulinemia

Hyperinsulinemia is a surrogate for insulin resistance. Insulin resistance is a precursor to diabetes and is often present for many years before diabetes is diagnmosed.

Up to twenty-five percent of persons without diabetes have characteristics of insulin resistance (Reaven, 1988). Insulin levels are not routinely measured in the clinical setting. Insulin levels are measured by biological assay and referenced to a laboratory standard. The euglycemic insulin clamp method is considered the gold standard. It requires an infusion of glucose and insulin at varying rates while measuring their levels at specified times. An alternative method, the homeostasis model assessment (HOMA) is done without a continuous infusion, but requires sampling glucose and insulin levels episodically. Neither test is practical in the clinical setting. A measurement of insulin concentration after an overnight fast is the most convenient method to determine insulin sensitivity/resistance. The insulin assay has the potential to measure other antigenic epitopes such as pro-insulin, and insulin derivatives that are produced by degradation, dimerization, or glycosylation. High circulating pro-insulin has also been associated with impaired glucose tolerance and diabetes (Davies, Rayman, Gray, Day, & Hales, 1993; Kahn, et al., 1995).

The American Diabetes Association's task force on the standardization of the insulin assay report that there is no 100% accurate procedure available to determine insulin concentrations in a given biological sample (ADA, 1996). The potential lack of reliability is due to cross reactivity to other components in the sample, lack of uniformity in establishing a dependable linearity performance, and the utilization of several types of assays simultaneously for comparison. Enzyme linked immunosorbent assays (ELISA) and/or radioimmunoassays (RIA) are the most commonly used assays. McAuley et al.,

(2001) looked at what variables would best predict insulin sensitivity. Family history of diabetes, BMI, blood pressure, waist circumference, fasting lipids, the HOMA model, insulin to glucose ratio, fasting insulin levels were compared to the gold standard of the euglycemic insulin clamp method in 178 normoglycemic men and women, ages 25–68 years of age. The variables that correlated the strongest were fasting insulin levels, elevated triglyceride levels, waist circumference and body mass index (McAuley et al., 2001).

Reliability is most threatened when several different assays within the same laboratory are used for comparison. The ADA task force recommends that each laboratory develop and meet a minimum standard to ensure accuracy within their domain. All laboratories must assess their internal performance, external comparability, and complete a certification process at regular intervals (ADA, 1996). Fasting insulin levels are a reliable method for identifying insulin resistance when in compliance with ADA recommendations. The ability to measure insulin levels reliably will be an important step toward identifying insulin resistance as a risk factor within the clinical practice setting.

Cardiovascular Disease and Diabetes

More than seventy percent of adults with diabetes die from cardiovascular disease (Geiss, Herman, & Smith, 1995). Forty-four percent of patients with diabetes die within ten years of their diagnosis of diabetes from cardiovascular complications (Panzam, 1987). The United Kingdom Prospective Diabetes Study (UKPDS) was a 20 year

multicenter randomized study that enrolled over 4000 newly diagnosed diabetics. Almost fifty percent of those with diabetes already had complications of cardiovascular disease at the time of their diagnosis (UKPDSG, 1998). The UKPDS study demonstrated that when hypertension was controlled in individuals with diabetes, deaths related to diabetes and all cause mortality decreased.

Diabetes is the risk equivalent to having a previous history of cardiovascular disease (National Cholesterol Education Program [NCEP], 2001). A Finnish study involving 2432 men and women were followed over seven years to determine the incidence of myocardial infarctions. There was an equal distribution of men and women. Cardiovascular risk factors such as smoking, hypertension and elevated cholesterol were controlled. The risk of a cardiovascular event was found to be as high in a person with diabetes as it was in a person who had known cardiac disease after adjusting for age and gender (Haffner, Lehto, Ronnemaa, Pyorala, & Laakso, 1998).

Several studies have demonstrated that the risk for cardiovascular disease is increased even before diabetes is diagnosed. In the 8-year follow up of the San Antonio Heart Study, those who developed type 2 diabetes, were more likely to have risk factors for cardiovascular disease. Out of the 1734 male and female participants, one-half were Mexican-American and one-half were Caucasian. The indicators of risk were a higher incidence of obesity, greater waist circumference, hypertension, higher triglyceride levels, and lower HDL levels (Haffner, Mykkanen, Festa, Burke & Stern, 2000). Another longitudinal study confirmed these findings in a large cohort of females. The Nurses

Health Study recruited 117, 629 female nurses ages 30–55 years with no history of cardiovascular disease in 1976. After a 20 year follow up, there was a substantially increased risk for cardiovascular disease prior to the diagnosis of diabetes (Hu, Stampfer, Haffner, Solomon, Willett and Manson, 2002).

Risk Factors for Cardiovascular Disease

Risk factors for cardiovascular disease include a family history of heart disease, advanced age, tobacco use, sedentary lifestyle, hypertension, diabetes, hyperlipidemia and/or dyslipidemia (NCEP, 2001). Advanced age is defined as $\geq$ 45 years for a man and $\geq$ 55 years for a woman. Winkleby, Kraemer, Ahn, & Varady (1998) used NHANES III data to identify ethnic and socioeconomic differences associated with cardiovascular risk factors. In that study, 5,266 women ages 25-64 years completed the interview and medical examination. Of that sample, there were 1,762 African American, 1,481 Mexican American, and 2,023 Caucasian females. The most significant association to age was found in African American women who showed a steeper incremental increase in hypertension with age than their Caucasian counterparts.

While younger women are less likely to develop cardiovascular disease, they experience higher mortality rates than men when they do develop cardiovascular disease. Data from the National Registry of Myocardial Infarction included 384,878 patients. This study showed that women younger than 50 years of age who were hospitalized for a myocardial infarction had a mortality rate twice that of men the same age (Vaccarino, et al., 1999).

Women generally develop cardiovascular disease approximately ten years later than men (Charney, 1999). This phenomenon has been attributed to the beneficial effect of endogenous estrogen on lipoprotein metabolism. Exogenous hormone replacement was thought to offer a bridge of estrogenic advantage and protection for women in the postmenopausal years. However, hormone replacement therapy (HRT) as an intervention remains controversial.

The Postmenopausal Estrogen/Progestin Intervention Trial was a randomized controlled trial involving 875 women between the ages of 45 and 64 years. Women on estrogen and cyclical progestin were less likely to experience a primary cardiovascular event (Postmenopausal Estrogen/Progestin Interventions Trial Writing Group [PEPI], 1995). This was thought to be due to the favorable effect on lipoproteins and fibrinogen levels. A significant limitation to this study is that there were few ethnic minorities included in the analysis. Those with diabetes were also excluded. The Heart and Estrogen/Progestin Replacement Study (HERS) did not find any appreciable benefit in 2763 women with existing cardiovascular disease on hormone replacement therapy in reducing secondary subsequent cardiovascular events (Hulley, et al., 1998). Further analysis (HERS II) continued to show no additional benefit from hormone replacement therapy (Grady, et al., 2002). In the Estrogen Replacement and Athersclerosis (ERA) trial, those on short term HRT had a more favorable lipid profile but this did not alter the effect on cardiovascular endpoints or existing coronary lesions (Herrington, Reboussin, Brosnihan, et al., 2000). However, there are confounding variables to explain these

results. Less than 10% of women who had known cardiovascular disease in the HERS study had baseline LDL cholesterol levels that met the National Cholesterol Education Project guidelines (PEPI, 1995). In addition, women who had "uncontrolled diabetes" were excluded from the study.

The results of the National Women's Health Initiative, an observational study sponsored by the National Heart, Lung, and Blood Institute (NHLBI) a branch of the National Institute of Health (NIH) was developed to provide insight into whether estrogen replacement therapy reduces the risk of developing cardiovascular disease. In addition, the effect of lifestyle on risk reduction of cardiovascular disease, diabetes, cancer and osteoporosis is being monitored (Wehrmacher, & Messmore, 2000). A total of 161, 809 postmenopausal women were enrolled in this study between 1993 and 1998. In 2002 the study was discontinued with regard to the observations of women on hormone therapy and cardiovascular events. Preliminary data revealed that women who were on combination hormone replacement therapy more than 5 years had a higher risk of cardiovascular disease (Writing Group for the Women's Health Initiative Investigators, 2002). Therefore, recommendations from this study conclude that a combination hormone therapy should not be prescribed for the primary prevention of cardiovascular disease.

Hypertension.

Twenty-five percent of the population in the United States has high blood pressure (Burt, Whelton, & Rocella, 1995). Recommendations for systolic blood pressure (SBP)

and diastolic blood pressure (DBP) is < 120 mm Hg and < 80 mm Hg. respectively. Hypertension (high blood pressure) is defined as a SBP > 140 mm Hg and/or a DBP > 90 mm Hg (Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure [JNC VI], 1997). See Table 8 for classification of blood pressure by JNC VI.

The National Kidney Foundation recommends a SBP < 130 mm Hg and a DBP < 80 mm Hg in persons with diabetes. Retrospective and prospective studies have proven that lowering blood pressure reduces the risk of cardiovascular events by up to 51% in men and women with diabetes (Hansson, Zanchetti, & Caruthers, 1998; Langer, Barrett-Connor, & Wingard, 1990; Sowers & Lester, 1999; UKPDSG, 1998).

Dyslipidemia.

Dyslipidemia is a modifiable risk factor for cardiovascular disease. Each lipoprotein is evaluated in terms of its contribution to overall cardiac risk. The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III or ATP III) released its latest recommendations in 2001. The expert panel recommended a more aggressive management of risk factors for cardiovascular disease than had previously been advocated. The ATP III risk categories are shown in Table 9. This is the first time ATP III defined the metabolic syndrome and recommended aggressive screening and treatment of persons with these multiple risk factors.

Table 8.

Classification of Blood Pressure for Adults Age 18 and Older

Category	Systolic (mm Hg)		Diastolic (mm Hg)
Optimal*	<120	and	<80
Normal	<130	and	<85
High-Normal	130-139	or	85-89
Hypertension			
Stage 1	140-159	or	90-99
Stage 2	160-179	or	100-109
Stage 3	≥ 180	or	≥ 110

Note, * Based on the average of two or more readings taken at each of two or more visits after an initial screen. Adapted from "The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure," NIH Publication No. 98-4080, p. 11.

The dyslipidemia associated with the metabolic syndrome is a combination of a high triglyceride level, a low high-density lipoprotein (HDL) and normal or elevated low-density lipoprotein (LDL) level (Assman, & Schulte, 1992; Depres, et al., 1993). While LDL levels are usually within the normal range, the make-up of the LDL particles are dense and potentially atherogenic in the metabolic syndrome. Low-density lipoprotein

Table 9.

Risk Categories for Cholesterol levels (values in mg/dL).

Lipid	Desirable	Borderline	High Risk
Total Cholesterol	< 200	200-239	≥ 240
HDL Chlolesterol	≥ 60	41 - 59	< 40
LDL Chlolesterol	< 100	130 - 159	≥ 160
Triglycerides	< 150	150-199	200 – 499 high
			≥ 500 very high

Note, Adapted from the "Summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III)," National Cholesterol Education Program (NCEP) Expert Panel, 2001, Journal of the American Medical Association, 269, (23), 3015-3023.

levels represent the amount of cholesterol ester within LDL. If the LDL particles are highly enriched with cholesterol ester, the particles are transported to the liver and not to the arteries where they can form obstructive plaques. High LDL particle concentration is associated with a high risk of cardiovascular disease.

LDL concentration is indirectly measured by apolipoprotein B (apo B). For every LDL particle there is one apo B. A high concentration of apo B is associated with insulin

resistance (Reavan, Chen, Jeppesin, Maheux, & Krauss, 1993). Lipoprotein particles are not only different types, but different sizes. Particle sizes are grouped by phenotype. Pattern A particles are large and buoyant and less atherogenic. Pattern B are small, dense and highly atherogenic. The presence of a high particle concentration (apo B > 120 mg/dL) and a small size conveys the highest risk of cardiovascular disease. Triglyceride levels greater than 150 mg/dL are associated with a high particle dense pattern B, LDL. One of the first large prospective studies to look at cardiovascular disease was the Framingham study, which began in 1948 with continued cohort analyses through 1983. Castelli and investigators analyzed data on 1,600 participants and confirmed that a low HDL level is an independent risk factor for cardiovascular disease in men and women aged 49 years and older (Castelli, et al., 1986). Low HDL levels are a more powerful predictive risk factor for cardiovascular disease in women than in men (Corti, Guralnik, Salive, et al., 1995). The largest study to demonstrate this effect was the NHLBI study, which analyzed data on 86,000 women (Manolio, Pearson, Wenger et al., 1992). Obesity in women is associated with the dyslipidemic profile of metabolic syndrome. Obese women have higher triglyceride levels and lower high-density lipoprotein (HDL) levels when compared to non-obese women (Despres, 1993).

Most of the research on interventions for cholesterol reduction in cardiovascular disease has been limited to men. An exception is the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/Tex CAPS) that included 6, 605 men and 997 women without cardiovascular disease, with average total cholesterol and LDL

cholesterol levels and below average HDL cholesterol levels. Subjects were treated with a cholesterol lowering medication. There was a 40% risk reduction in primary cardiac events with this intervention (Downs, et al., 1998). The women in this study were postmenopausal and over the age of 55 years. Individuals with insulin dependent diabetes, whose diabetes was poorly controlled, as defined by an average blood glucose level greater than 20 % above normal were excluded from the study.

Dyslipidemia is a significant risk factor for diabetes and cardiovascular disease. This profile should alert practitioners to be more aggressive screening for both chronic diseases. This could be a critical step toward reducing cardiovascular deaths when you consider that a primary cardiac event carries a significant mortality risk, particularly for women.

Linking the Metabolic Syndrome, Diabetes and Cardiovascular Disease

Hyperinsulinemia is a risk factor for diabetes (Bergstrom, et al., 1990; Charles, et al., 1991; Haffner, Stern, et al., 1990; Saad, et al., 1989). Hyperinsulinemia is associated with the dyslipidemic profile of hypertriglyceridemia and low HDL (Haffner, Valdez et al., 1992). The clinical quartet of hypertension, hyperinsulinemia, central obesity and dyslipidemia are inextricably linked with metabolic syndrome.

Many studies have demonstrated a coexisting relationship between glucose, insulin, lipoprotein metabolism, and high blood pressure. The association with hyperinsulinemia and high blood pressure was the first to be connected (Welborn, Breckenridge, Rubenstein, Dollery, & Fraser, 1966). Decades passed before others would substantiate

the association of hyperinsulinemia and hypertension (Ferrannini, Buzzigoli, & Bonadona, 1987; Lucas, Estigarribia, Darga, & Reavan, 1985; Manicardi, Camellini, Bellodi, Coscelli, & Ferrannini, 1986; Modan, et al., 1985; Os & Nordby, 1992; Swislocki, Hoffman, & Reavan, 1989). Lowering blood pressure did not lower insulin levels in one small prospective study involving 24 Chinese men (Shen, Shieh, Fuh, Chen, & Reavan, 1988). More research is needed in this area. Clearly, insulin resistance appears to be a key component in the development of metabolic syndrome.

There are no longitudinal studies to suggest that treating insulin resistance alone would delay or prevent the progression to diabetes or cardiovascular disease. While each component of the metabolic syndrome has been analyzed independently for an increased risk of cardiovascular disease, there are no prospective studies that demonstrate treating all components of the metabolic syndrome collectively decrease mortality. This may be due to a lack of consensus on the definition of the metabolic syndrome. More cooperation and research is needed in this area.

There have been attempts to develop a clinically useful screening tool for the metabolic syndrome. Lemieux, et al. (2000) tested the hypothesis that clinical and biomedical measurements could easily identify men at risk for the metabolic syndrome. Lemieux found that fasting hypertriglyceridemia and a waist circumference $\geq$ 90 cm. were enough to identify metabolic syndrome in more than 80% of men. Further validation of the model using angiographic evaluation revealed that only those men with

these two clinical characteristics were at increased risk for cardiovascular disease. There are no similar studies in women.

The overall unadjusted prevalence of metabolic syndrome in the United States is 21.8 % according to a study using the Third National Health and Nutrition Examination Survey (Ford, et al., 2002). A total of 8,814 men and women ages 20 years and older were analyzed for characteristics of metabolic syndrome as defined by the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III or ATP III). This study showed a steeper incremental increase in hypertension as well as other characteristics consistent with the metabolic syndrome in women of ethnic minorities as compared to their Caucasian counterparts. The age-adjusted prevalence of incremental increase in hypertension was higher among women of ethnic minority status compared to men of similar ethnic background.

One year later another study on metabolic syndrome was published using the same database, NHANES, and diagnostic criteria by the ATP III with similar results (Park, et al., 2003). African American men and women had significantly higher frequency of hypertension than Caucasian men and women. Additional ethnic differences using multiple regression models from the Park et al. study (2003) included a lower overall likelihood of metabolic syndrome among African American men yet a higher likelihood among Mexican American women. This may be attributed to the fact that Mexican American women were shown to have higher triglyceride and low HDL levels. Mexican American women and African American women were more obese, as defined as a higher

BMI, than Mexican American men and African American men. Other variables were analyzed for their potential association with metabolic syndrome. Physical inactivity, advanced age, Mexican American ethnicity, current smoker and a lower household income were all associated with increased odds of metabolic syndrome.

The Botnia study noted that the prevalence of metabolic syndrome in 4,483 Scandanavians was shared equally in men and women with diabetes (Isomaa, et al., 2001). However, it was more common in men with impaired fasting glucose or impaired glucose tolerance than in women with impaired fasting glucose or impaired glucose tolerance. Overall, the distribution of metabolic syndrome was 10% in individuals with normal glucose tolerance, 50% in individuals with impaired fasting glucose or impaired glucose tolerance and 80% in persons with type 2 diabetes.

The Athersoclerosis Risk in Communities Study showed that African Americans had a greater number of the abnormalities that make up the metabolic syndrome than Caucasians (Schmidt, et al., 1996). There were a total number of 14,481 participants in this study. There were 3,524 African Americans and an equal distribution of men and women. Of the 2,873 women in the Framingham Study, metabolic syndrome was more commonly found in post-menopausal women than in pre-menopausal women (Kannel, et al., 1976). This observation has been theoretically attributed to a decline in ovarian function, which likely has a negative affect on lipid profiles. Menopausal status appears to be less of a factor in the incidence of metabolic syndrome in African American women, where cardiovascular disease is three times more common (Gillum, Mussolini, &

Madans, 1997). Falkner, Sherif and Kushner (2000) found no gender difference in insulin resistance in African Americans when obesity was controlled. However, this was a small study of 246 subjects who were considerably younger, ages 27–35 years, than other studies on insulin resistance.

Hyperinsulinemia is associated with cardiovascular disease (Haffner, Valdez et al., 1992; Reaven, 1988). The relationship between lipoprotein metabolism, insulin and glucose has been established (Reavan, Lerner, Stern, & Farquhar, 1967; Tobey, Greenfield, Kraemer, & Reavan, 1981). The common denominator is hyperinsulinemia. Impaired glucose tolerance is associated with a 30% percent higher absolute risk of coronary events when compared to normal fasting glucose levels (Cholesterol and Recurrent Events Trial Subgroup, 1998). Obesity and hyperinsulinemia were found to be independent predictors for cardiovascular related death in men in the 10-year Paris Prospective Study (Fontbonne, & Eschwege, 1991). The Atherosclerosis Risk in Communities Study confirmed an association between hyperinsulinemia, diabetes, hypertension, high LDL cholesterol, and low HDL cholesterol (Duncan, et al., 1994). Metabolic syndrome is associated with an increased risk of cardiovascular death (Lehto, Ronnemaa, Pyorala, & Laakso, 2000). Interventions may delay or prevent the development of cardiovascular disease in individuals with metabolic syndrome.

Women's Health

There has been considerable attention to gender differences in the treatment of cardiovascular disease. The National Ambulatory Medical Care Survey revealed that

women were counseled less often than men about modifiable risk factors such as exercise, nutrition and weight reduction (CDC, 1998). Women with cardiovascular disease are not treated as aggressively as they could be (Ayanian, Epstein, 1991; Schrott, Bittner, Vittinghoff, et al., 1997). A study by Schulman, et al. (1999) found that women were 40% less likely to be referred for coronary catheterization despite identical medical histories for men and women. Adjusting for race-sex interaction, African American women were 60% less likely to be referred for cardiac catheterization than African American men, caucasian men or caucasian women. No study has yet to determine that women have experienced adverse outcomes because of less aggressive therapies.

Vulnerable populations are a national health concern in the prevention of diabetes and heart disease. Women of ethnic minorities are particularly vulnerable to diabetes and cardiovascular disease. Women of ethnic minorities are more likely than caucasian females to have risk factors for diabetes and cardiovascular disease (Winkleby, Kraemer, Ahn, & Varady, 1998). The reason for this phenomenon is not completely understood. A meta-analysis of studies on women with polycystic ovary syndrome, a risk factor for diabetes, showed that these women also had risk factors for cardiovascular disease (Wild, 2002). More randomized clinical trials need to be done in special populations such as these to highlight those at greatest risk.

Gender is a non-modifiable risk factor. A woman with diabetes and no cardiovascular disease is at the same risk for a heart attack as a man who has cardiovascular disease but does not have diabetes. If gender is a determinant for

metabolic syndrome, more aggressive screening and interventions could be directed toward women. If metabolic syndrome is equally shared between the sexes, there should be no distinction in the level of intervention for males and females. It will take a shift in practice to treat high-risk asymptomatic patients with therapies that have traditionally been reserved for secondary prevention.

Conceptual Framework

Over the last century, the primary health concerns of people in the United States have changed from controlling or eliminating infectious diseases to chronic disease management. Scientific advancements, a more diverse demography, cultural norms and environmental hazards influence how health is viewed. Health may be simply defined as the absence of disease or as a more general state of well being.

Healthy People is a national health initiative coordinated by the U.S. Department of Health and Human Services (HHS). This report identifies health objectives for the United States after careful statistical analysis of disease prevalence and distribution patterns. Healthy People 2010 is the third report HHS has published on health care goals for United States residents. Healthy People 2010 delineates two broad goals to improve the health of our nation. The first goal is to expand and improve quality of life and the second is to eliminate health disparities among populations.

Chronic illness is a predominant health care issue. Diabetes and cardiovascular disease are two of the most common chronic conditions in the United States. They incur high morbidity, mortality and health care costs. Women and their vulnerability to

diabetes and cardiovascular disease are the focus of this research. Diabetes and cardiovascular disease share antecedent conditions that are encapsulated as the metabolic syndrome. What impact gender has on the prevalence and development of metabolic syndrome is explored through population characteristics, socioeconomic factors, health behaviors and the health care system within an ecological model of health.

An Ecological Model of Health

General systems theory is based on the premise that a system is a culmination of its component parts. There is a dynamic interchange and interdependence between the sub systems. A system may be a single entity or a larger social structure. Systems may be open or closed. A closed system has little or no exchange with the environment. In an open system the environment plays a key role. How systems adapt to outside forces determines the growth and survival of the system.

The well-being paradigm of health constructed by Henrik Blum (1983) is an ecological model of health (See Figure 3). Ecological models are open systems. In Blum's model, health is the central purpose or goal of the system. The forces that interact to shape health or well being are the genetic predisposition of the population, the environment, health behaviors and health care services. The magnitude of the effect of these forces on health is reflected in the width of the four input arrows. This model will provide the operational framework to examine gender and other factors in the development of the metabolic syndrome.

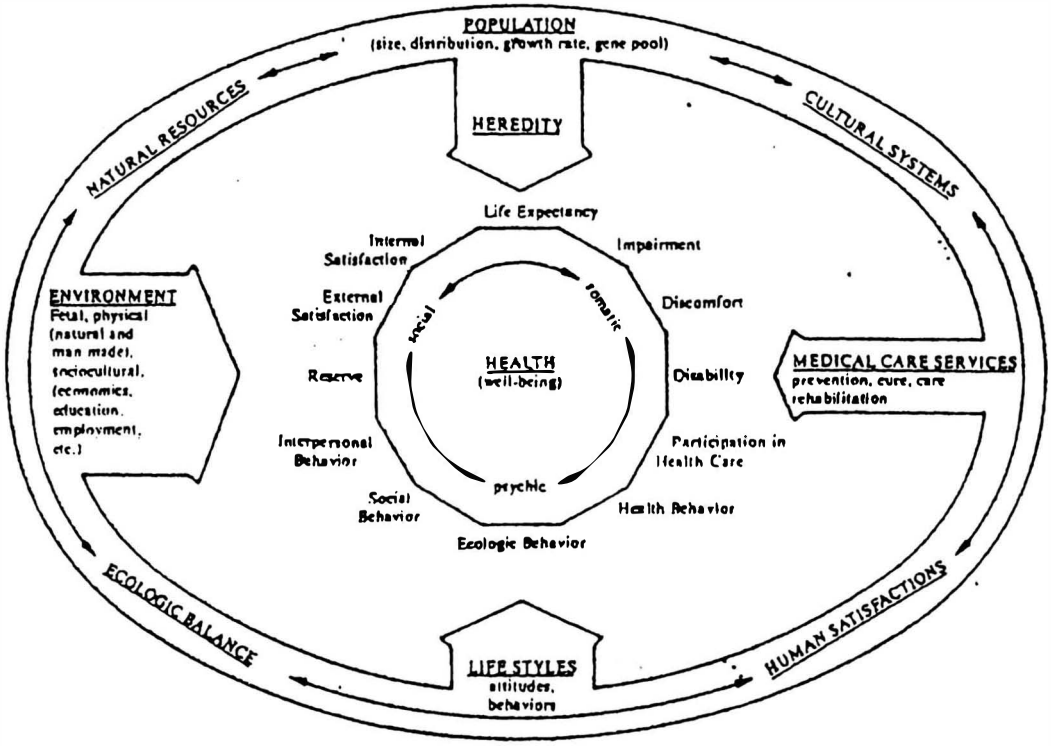

Figure 3, The Force-Field and Well-Being Paradigms of Health; An Ecologic Model of Health.

From Henrik L. Blum's Expanding Health Care Horizons; From A General Systems Concept of Health To A National Policy, 2nd Edition, p. 37, 1983. Reprinted with permission of Third Party Publishing Company.

The demographic characteristics that can affect the development of a disease process include gender, age, and ethnicity. Demographic characteristics are descriptive of an individual or population and are generally non-modifiable. However, demographics factors, like age, may be modified by the passage of time. Risk factors are characteristic of a disease. While risk factors are not directly causal, they can predispose one to the development of disease but may be modified with appropriate interventions to effect the outcome. Demographic characteristics may also act as risk factors. While demographic characteristics may not be modified, they indicate a particular susceptibility to certain disease states. Treating modifiable risk factors should be pursued more aggressively in populations that possess high-risk demographic characteristics.

Health

Health and well being are terms that are used interchangeably by Blum (1983). Health is a result of interactions between the forces within the system. Health is more specifically analyzed within somatic, psychic and social fields. Within these three domains are twelve facets of health. They are life expectancy, impairment, discomfort, participation in health care, health behavior, ecological behavior, social behavior, interpersonal behavior, reserve, external and internal satisfaction.

For the purpose of this study, health is defined as the absence of the metabolic syndrome (See Figure 4). The presence of metabolic syndrome is largely defined within the somatic health domain. Somatic health failure is defined as any disruption of physiologic function or anatomic integrity (Blum, 1983). Furthermore, this analysis will

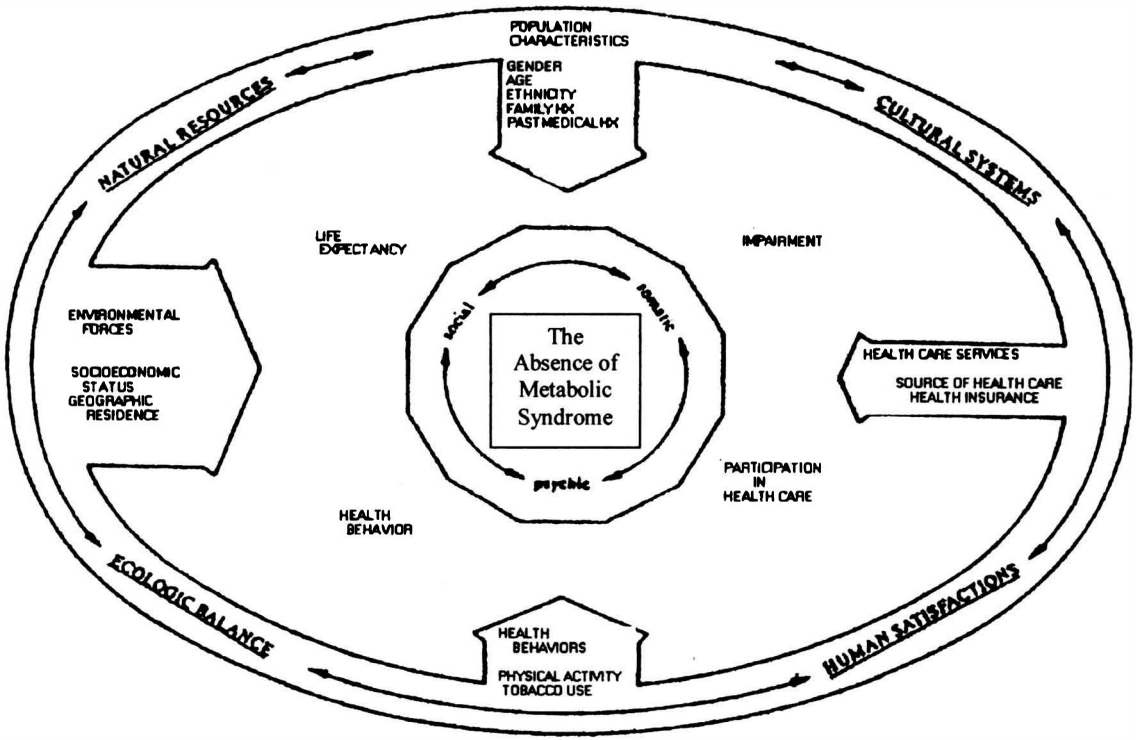

Figure 4, An Ecological Model of the Metabolic Syndrome.

Adapted from Henrik L. Blum's Expanding Health Care Horizons; From A General Systems Concept of Health To A National Policy, 2nd Edition, p. 37, 1983. Reprinted with permission of Third Party Publishing Company.

determine and compare the prevalence of metabolic syndrome in populations with and without cardiovascular disease.

Population Characteristics

The high prevalence of diabetes in select populations supports a genetic input to the etiology of the disease (McCarthy & Hitman, 1993). The global distribution of diabetes is variable among ethnic groups. Diabetes affects less than 2% of the population in rural Tanzania and up to 50% of Pima Indians in the United States (Amos, McCarty, & Zimmet, 1997). Familial aggregation of diabetes suggests the etiology to be a combination of environmental and genetic factors.

The primary biochemical defect of diabetes is insulin resistance. The mechanism by which this defect develops is not completely understood. Given the number and diversity of inherited diseases that include diabetes in its phenotype, it is likely that diabetes is a heterogenous disease at the genetic level (McCarthy & Hitman, 1993). This assumption is consistent with theories on the etiology of cardiovascular disease. Diabetes may be a single representation of a group of linked conditions called metabolic syndrome. It is unlikely that there is a single gene responsible for metabolic syndrome given the heterogeneity of the metabolic defect (Walker & Alberti, 1993). The familial predisposition is compelling. Features of the metabolic syndrome were more commonly found in non-diabetic relatives of people with diabetes, than in non-diabetic relatives of people without diabetes (Walker, 1999). Therefore, population descriptors such as

ethnicity, family history, past medical history and age will be identified and analyzed as to their contribution to the prevalence of the metabolic syndrome.

H_{1A} The prevalence of metabolic syndrome is similar for men and women when age is controlled.

H_{1B} The prevalence of metabolic syndrome is similar for men and women when ethnicity is controlled.

H_{1C} The prevalence of metabolic syndrome is similar for men and women when family history of diabetes is controlled.

H_{1D} The prevalence of metabolic syndrome is similar for men and women when family history of cardiovascular disease is controlled.

H_{1E} The prevalence of metabolic syndrome is similar for men and women when a past medical history of cardiovascular disease is controlled.

Environmental Factors

Deaths due to communicable diseases have been supplanted by chronic disease. Improvements in living conditions such as clean water and food, public education and safer working conditions have helped to reduce deaths related to communicable diseases. Diabetes and cardiovascular disease were an uncommon cause of death at the beginning of this century. Diabetes and cardiovascular disease are a dominant force in morbidity and mortality statistics in the United States (De Courten, McCarty, & Zimmet, 1999).

The growing incidence of people diagnosed with diabetes has been attributed to a corresponding increase in obesity and sedentary lifestyles (Amos, McCarty & Zimmett,

1997). Those living in the most rural or urban areas are more likely to experience chronic disease (Eberhardt, M.S., Ingram, D.D., & Makuc, D.M., 2001). Geographic distribution of individuals with metabolic syndrome may reflect the residence of at risk populations.

In the United States women live longer than men, yet many women have fewer economic assets. Poverty has consistently been associated with poor health status. Wamala et al. (1999) used level of education as a gauge for socioeconomic status and found that women with a lower level of education were at the greatest risk for metabolic syndrome. This study will analyze socioeconomic status by level of education, income and geographic residence for any association with metabolic syndrome.

Environmental factors may alter the genetic impact and expression of metabolic syndrome. The specific pathways of genetic factors interacting with environmental forces in the development of metabolic syndrome are complex. While the precise mechanism of genetic and environmental influence is unknown, the relationship appears to be interdependent.

H_{2A} The prevalence of metabolic syndrome is similar for men and women when geographic residence is controlled.

H_{2B} The prevalence of metabolic syndrome is similar for men and women when income is controlled is controlled.

H_{2C} The prevalence of metabolic syndrome is similar for men and women when education is controlled.

Health Behaviors

Health behavior and lifestyle are major contributors to the development of diabetes and cardiovascular disease. Obesity, physical inactivity, diet, tobacco use and stress are all modifiable risk factors. Physical inactivity is a risk factor for obesity, diabetes, and cardiovascular disease. Manson, et al. (1991) followed 87,253 women in the Nurses Health Study over eight years to determine if there was an association between exercise habits and the incidence of diabetes in the United States. Women who did not exercise were more likely to develop diabetes than women who exercised at least once a week. Participants were between the ages of 34–59 and 98% were Caucasian. This presents a limitation in the degree to which results can be generalized to include ethnic minorities. Increasing daily physical activity can lower the risk of developing disease by maintaining weight and reducing body fat. The association between obesity and diabetes is well established in all populations. Women who are obese are more likely to develop diabetes than men who are obese (Chan et al., 1994, Colditz et al., 1990).

Health beliefs are difficult to measure. This study will use tobacco use and leisure time activity levels as a proxy for health behaviors that have an impact on either the development or the mortality associated with the metabolic syndrome.

H_{3A} The prevalence of metabolic syndrome is similar for men and women when activity level is controlled.

H_{3B} The prevalence of metabolic syndrome is similar for men and women when tobacco use is controlled.

Health Care Services

Health status is influenced by a multitude of factors within the health care delivery system. Access to health care services, having a usual source of health care and health insurance coverage may influence health status. Chronic illness is associated with diminished functional status, pain, and depression. Chronic care requires health care services be available, accessible, and adequate to have a positive influence on outcomes.

Cardiovascular disease is the number one cause of death in women over the age of 50. Diabetes is one of the most predictive risk factors for cardiovascular disease in women. Data from the Cooperative Cardiovascular Project revealed that although there were no statistically significant differences in mortality between men and women, women were not treated as aggressively as men in the management of acute myocardial infarction (Gan, et al., 2000). Even when women have access to health care services, they may not receive the appropriate treatment. The management of these conditions has a critical impact on health status. Intervention by health care professionals is a significant force with regard to the conceptual model.

When individuals acknowledge their vulnerability to disease, they are more likely to utilize health care services. A Gallup Survey by Mosca et al. (2000) revealed that four out of five women and one out of three primary care doctors did not know that cardiovascular disease is the leading cause of death for women. The reality of susceptibility is a shared responsibility between women and their health care provider. Women are more likely to seek advice about their health if they have an established relationship with a health care

provider. When women are aware of their susceptibility to disease, they may be more likely to seek health care services. When professionals are aware of the potential for disease in women they may be more likely to proceed with the necessary diagnostic procedures and treatments.

Financial constraints can negatively impact the decision to treat or accept treatment. Reporting a usual source of health care and/or relationship with a health care provider and a source of insurance will be analyzed within the context of this conceptual framework.

H_{4A} The prevalence of metabolic syndrome is similar for men and women when a source of health care is controlled.

H_{4B} The prevalence of metabolic syndrome is similar for men and women when frequency of health care contacts are controlled.

H_{4C} The prevalence of metabolic syndrome is similar for men and women when a source of health insurance is controlled.

Hypotheses

In summary, the hypotheses that will be tested are as follows:

H_{1A} The prevalence of metabolic syndrome is similar for men and women when age is controlled.

H_{1B} The prevalence of metabolic syndrome is similar for men and women when race-ethnicity is controlled.

H_{1C} The prevalence of metabolic syndrome is similar for men and women when family history of diabetes is controlled.

H_{1D} The prevalence of metabolic syndrome is similar for men and women when family history of cardiovascular disease is controlled.

H_{1E} The prevalence of metabolic syndrome is similar for men and women when a past medical history of cardiovascular disease is controlled.

H_{2A} The prevalence of metabolic syndrome is similar for men and women when geographic residence is controlled.

H_{2B} The prevalence of metabolic syndrome is similar for men and women when income is controlled is controlled.

H_{2C} The prevalence of metabolic syndrome is similar for men and women when education is controlled is controlled.

H_{3A} The prevalence of metabolic syndrome is similar for men and women when activity level is controlled.

H_{3B} The prevalence of metabolic syndrome is similar for men and women when tobacco use is controlled.

H_{4A} The prevalence of metabolic syndrome is similar for men and women when a source of health care is controlled.

H_{4B} The prevalence of metabolic syndrome is similar for men and women when frequency of health care contacts are controlled.

H_{4C} The prevalence of metabolic syndrome is similar for men and women when a source of health insurance is controlled.

H_0 There is no difference in the prevalence of metabolic syndrome between men and women when age, ethnicity, family history, past medical history, socioeconomic status, geographic residence, tobacco use, activity level, source of health care, and a source of health insurance are controlled.

Summary

While diabetes is becoming an epidemic in industrialized countries, many healthcare futurists are not adequately planning for what may be the most challenging chronic disease of the century (Amos, McCarty & Zimmett, 1997). The prevalence of diabetes now outweighs previous projections. Without any change in the identification and treatment of modifiable risk factors, the rates of diabetes are expected to be even higher in the future than previously calculated.

Metabolic syndrome is a significant contributor to the excess cardiovascular morbidity and mortality associated with diabetes. Primary prevention addresses risk factors for disease. Targeting efforts toward reducing two significant risk factors, obesity and inactivity, across populations is a start. Another efficient strategy is to target high-risk populations.

When risk factors for diabetes and cardiovascular disease cluster, as they do in metabolic syndrome, the likelihood of disease increases exponentially. Metabolic syndrome shares common antecedents for diabetes and cardiovascular disease. A more

integrated approach to risk reduction strategies may prevent the development of metabolic syndrome. Unhealthy lifestyles, physical and social environments coupled with a genetic susceptibility can and often do lead to the development of chronic disease. The interactive forces affecting the development of the metabolic syndrome include population characteristics, environmental impacts, health care behaviors and the health care delivery system. While all four areas may affect health, defined as the absence of the metabolic syndrome, this study focus is more heavily weighted on population and behavioral forces.

Populations at risk for metabolic syndrome must be identified. What factors are associated with metabolic syndrome in men and women? Are there factors that are more prevalent in women than in men with metabolic syndrome? This study may begin to answer these questions. The next chapter will address the data and methodology used in this study to determine the presence of metabolic resistance syndrome.

CHAPTER 3: METHODOLOGY

This chapter outlines the research design, methodology and analyses used to examine whether metabolic syndrome is biased with regard to gender. The data source, sample selection and research design schemes are discussed. The dependent and independent variables are defined. Statistical methods used are described and justified. Limitations of the study are clearly stated.

Data Source

The source of data for this study is the Third National Health and Nutrition Examination Survey (NHANES III). NHANES is a periodic survey conducted by the National Center for Health Statistics (NCHS) of the National Centers for Disease Control and Prevention (CDC). The collection and dissemination of this series of surveys began in 1960 with the National Health Examination Survey (NHES). A major strength of these surveys is that they combine interviews with biomedical measurements of participants. NHANES III is the seventh in a series of surveys based on a complex multi-stage sample plan that assessed the health and nutritional status of the non-institutionalized civilian population in the United States from 1988–1994.

The goals of the NHANES series are to:

- Estimate the national prevalence of disease and risk factors.
- Estimate national population reference distributions of selected health parameters.
- Document and investigate secular trends in risk factors and selected diseases.
- Contribute to an understanding of disease etiology.

- Investigate the natural history of selected diseases.

The last two goals are unique to NHANES III. Previous NHANE surveys were designed to be descriptive surveys. NHANES III was intended to serve as both a descriptive survey and an analytical study.

The Second National Health and Nutritional Survey (NHANES II) and the Hispanic Health and Nutrition Examination Survey (Hispanic HANES) preceded NHANES III. NHANES II was conducted between 1976–1980. Both were similar in design with the exception that NHANES II did not include representation from Hispanic communities. The Hispanic HANES followed NHANES II between 1982–1984. This survey included three major Hispanic subgroups, Mexican –Americans in the Southwest, Cubans living in Dade County, Florida, and Puerto Rican residents in the New York City area. The features of both surveys provide the basis for the NHANES III design.

NHANES III is different from previous surveys in several ways. It covers a larger geographic area of the United States. It took place over a longer period of time, 6 years versus 2 - 4 years. It was the first NHANE survey without an upper age limit. NHANES III is particularly distinctive from previous surveys in that it produced the largest available sampling of ethnic minorities in the United States.

NHANES III was conducted in two phases. The first phase took place between October 18, 1988 through October 24, 1991 in 44 locations. The second phase was conducted between September 20, 1991 through October 15, 1994 in 45 locations.

NHANES III used a random sample of individuals from 81 counties across the United States.

Data collection was done by the survey research firm Westat. Data collection began with a household interview in the home. The household interview comprised several questionnaires: the household screener questionnaire, a household adult questionnaire, a household youth questionnaire and a family questionnaire. The household screener questionnaire (HSQ) identified the composition of the household and demographics of sample persons. The household adult questionnaire (HAQ) included questions about select medical conditions and medication usage, lifestyle habits and social supports. The family questionnaire (FQ) was administered to a designated adult in the household. The family questionnaire asked about educational levels, ethnicity, occupation, health insurance coverage, family income, and household characteristics. An additional adult questionnaire supplemented the HAQ, was administered at the Mobile Examination Center (MEC AQ). The MEC adult questionnaire included information on tobacco, drug and alcohol use, diet, vitamin and medication usage, and select medical conditions. All files are linked by a 7 digit sample person identification number (SEQN).

The Mobile Examination Center (MEC) was a specially designed mobile unit that traveled to survey locations around the country. The MEC consisted of 4 trailers, 48 feet long by 8 feet wide. The MEC was formed by parallel parking the 4 trailers. Enclosed passageways connected each trailer. The physical examination and laboratory testing was performed in the home or in the MEC. The survey team included a physician, dentist,

trained medical technicians, and trained health interviewers. There were two examination teams of 16 trained staff. The physicians were licensed and board certified in family medicine, internal medicine or preventive care medicine. They were either a medical doctor (M.D.) or an osteopathic physician (D.O.). Trained bilingual interviewers were available to conduct interviews. All staff attended a month long training program prior to their involvement in the NHANE survey. During the study period, formal retraining programs were offered to assure that staff performed at the appropriate skill level. Data were collected via an advanced computer system, which significantly reduced paper forms and secondary transfer of information.

Most health examinations were performed at the MEC, though a home examination option was employed for very young children and for elderly persons who were unable to come to the MEC. Examinations took approximately 4 hours to complete. The health examinations included a physical examination and laboratory measurement. Measurements included blood and urine analysis, body measurements, vision and hearing tests, and a dental exam. Some blood and urine analyses were performed in the MEC but most were sent to contract laboratories.

Local health and government officials were contacted prior to the survey for consultation and support. Survey participants were transported to and from the MEC and received compensation for their participation. Participants earned $30 for the health examination and were eligible to receive an additional $20 for extraordinary conditions related to their examination, such as fasting prior to laboratory measurements. Those

choosing to drive themselves were compensated for their mileage. All medical and dental reports were shared with each participant. These incentives allowed for a greater level of participation. All information remains confidential. All personal identification information was removed prior to transfer to public data use files.

Sample Selection

The NHANES III sample represents non-institutionalized residents, age 2 months of age or older, that lived in the United States between 1988–1994. NHANES III used a complex, stratified, multi-stage probability cluster sampling design. The first stage of sample selection was to identify 81 primary sampling units (PSU) across the United States. In stage 1 a PSU represented an individual county. In some cases small adjacent counties were combined to maintain a minimum size.

The primary sampling units were then stratified and selected with a probability of proportion to size (PPS). Thirteen large counties or strata were chosen with certainty (probability of one). The thirteen strata or PSUs were then divided into 21 survey locations. Once the thirteen strata were identified, the remaining PSUs were divided into 34 strata. Two PSUs were selected per strata to comprise 68 survey locations. The selection was based on the probability of proportion to size with resultant 81 strata or primary sampling units and 89 survey locations. The 89 locations were randomly assigned, 44 survey sites to Phase 1 (1988–1991) and 45 survey sites to Phase 2 (1991-1994). The geography, weather patterns and the volume of the sample population in the sampling units were considered in scheduling the survey interviews. Survey locations

varied according to their geographic proximity. On average 450 sample persons were interviewed at each location over a period of approximately 4 weeks. The survey locations rotated around the United States each year for the duration of the study.

The second stage of sample selection was to delineate area segments. In phase 1 the area segments were city or suburban blocks. The 1980 census was utilized to identify potential study participants by whether they were residents within the area segment prior to 1980. For the remaining residents, building permits for the year 1980 or later were used to identify households. The second phase of the study did not comprise many new construction sites, as the 1990 census followed shortly after Phase 1 was completed.

The third stage of sample design was to delineate households and those who lived in an eligible group quarter (dormitories). Sub sampling rates were assigned to produce a national approximately equal probability sample with higher rates given to geographic strata with ethnic minorities for the desired sampling population. Sample weights for an individual's probability of selection are provided in the NHANES data files.

The fourth stage allowed for all eligible members of a household to be selected. A sub sample was selected based on sex, age, race and ethnicity. Rates were designed to provide for approximate self-weighting samples within a geographic stratum and to maximize the number of participants per household.

Previous NHANES have shown that ethnic minorities may exhibit distinctly different health characteristics and health status than their Caucasian counterparts. Therefore, NHANES III over sampled African-Americans (12,000) and Hispanic-

Americans (12,000). Each group represented 30% of the sample but 12% and 5% of the population, respectively. The sample group consisted of 39,695 people. Of the 39,695 people, 33,994 persons (86%) aged two months and older were interviewed during the 6 year survey. Adults were defined as any person 20 years of age or older. All interviewed persons were invited to the medical examination center (MEC) for a physical examination and laboratory testing. Of those interviewed, 30,818 persons (78%) were examined in the MEC. A limited examination in the home was given to 493 persons. The home examination was reserved for those individuals who were unable to come to the MEC. There were 10,649 adult females and 9,401 adult males in the survey.

Study Sample

A sample of men and women, between the ages of 20-64 years, was extrapolated from the NHANES III participants. Adults were classified by the survey, as anyone 20 years of age and older. The age range is limited by 64 years because the diagnosis and prevalence of diabetes and cardiovascular disease is more gender neutral in advanced age groups.

This study analyzed data from adults between the ages of 20 and 64 years to determine what factors may influence the prevalence of metabolic syndrome in women as compared to men. A total of 39, 695 individuals participated in NHANES III. Of those participants, 33, 994 ages 2 months and older were interviewed. There are a total of 18,825 adult men and women over the age of 20 years in the NHANES sample. There are 13,573 men and women between the ages of 20 and 64 years of age. After excluding

288 women who were pregnant, 13, 285 remained in the study. Data essential to defining the metabolic syndrome, the dependent variable, is a critical factor in further data reduction. Another 1038 people had to be eliminated because they did not complete the examination. This left 12, 247 people in the sample. Another 311 respondents were eliminated because their fasting time was unknown and 1453 people were eliminated because they had fasted less than 6 hours. Finally, 349 respondents were eliminated because of missing data, such as blood pressure readings, lipid levels or blood sugar readings, which is necessary for the definition of the dependent variable, metabolic syndrome. Missing data and fasting criterion reduced the final sample size to 10,134 study participants.

Research Design

This study is a retrospective non-experimental correlation (ex post facto) cross sectional research design. Two important considerations with respect to the sample design must be appreciated before analysis. One is the complexity of the sample design and the other is the sampling weight. Sample weights are necessary because participants do not have an equal probability of selection. It is imperative that all analyses are done with sample weights or results can be misinterpreted.

The complex design of the sample is a critical consideration in the data analysis. The sampling variance may be underestimated if the complex sample design is not taken into account. The effect of a complex design such as this is represented by the ratio of the variance of a statistic from the complex sample to the variance of the sample of a simple

random sample of the same size. The effect size is a statistical expression of the extent of the relationship between two groups with respect to a characteristic of interest (Polit and Hungler, 1999). A design effect of 1.0 signifies the simple random sample variance to be comparable to the complex sample variance. The average design effect from NHANES III is 1.2 – 1.3. Guidelines for variance estimates are provided by the National Center for Health Statistics (NCHS).

NHANES III sample weights are unique to Phase 1 and Phase 2 of the study. The phase of each sample is designated under the SDPPHASE variable file name. The computer program, SUDAAN, is designed to estimate variances from a complex sample. NCHS recommends using the software program SUDAAN to analyze NHANES data. SUDAAN is used for the statistical analysis of correlated cluster data. SUDAAN accounts for the nonrandom sample design in computing variance estimates. It fits population models using generalized estimating equations. Robust variance estimates are computed to account for intra-cluster correlation, unequal weighting, without replacement samples and stratification methods.

The retrospective design of this study does not allow for manipulation of the dependent variable, metabolic syndrome, yet the ex post facto design allows for variation of the independent variables. Therefore, the cluster of variables designating metabolic syndrome is defined without actual manipulation of its individual components. This study is a non-experimental design because it lacks randomization and manipulation of the independent variables through an intervention.

Plan of Analysis

Prevalence refers to the existing number of cases of a disease present in a specified population at a given time. The objective of this study is to examine the prevalence of metabolic syndrome with respect to identified independent variables within an ecological model of health using both descriptive and mutivariate analyses. In the next section the study variables are identified as dependent or independent variables within the model domains of population, environment, health behaviors and health services. A description of the statistical analysis concludes this chapter. The study results are presented in the next chapter.

Study Variables

Dependent Variable

The dependent variable is the presence of metabolic syndrome. The ATP III definition of metabolic syndrome per the National Cholesterol Education Program Expert Panel is adopted for this study. A minimum of three out of five following criteria must be present to meet the definition of metabolic syndrome.

1) Waist Circumference of >102 cm for men and > 88 cm for women

2) Triglyceride level of $\geq$ 150 mg/dL.

3) HDL cholesterol of < 40 mg/dL in men and < 50 mg/dL in women.

4) High blood pressure $\geq$ 130/85 mm/Hg

5) Fasting Glucose $\geq$ 110 mg/dL or have diabetes

Health is defined as the absence of metabolic syndrome in this analysis. This study conceptualizes the analysis using Blum's Ecology of Health Model to identify what impact population characteristics, the environment, utilization of a health care system or health behaviors have on the development of metabolic syndrome.

Persons older than 20 years were asked to fast for 12 hours if their examination was conducted in the morning. For afternoon examinations all persons older than 12 years were asked to fast for at least 6 hours. Persons of any age who reported using insulin were instructed not to fast. Any person who had not fasted for a minimum of six hours was excluded. Glucose levels were analyzed with a Hitachi 737 from Boehringer-Mannheim Diagnostics. An insulin resistant state is fasting blood glucose $\geq$ 110mg/dL, on oral medications, or on insulin for diabetes are coded as 1. A non-insulin resistant state is defined as a fasting blood glucose < 110mg/dL or not on any medication for diabetes is coded as 0.

Hypertension is coded as 1 if blood pressure measurements met criteria for hypertension or participants report being on medication for high blood pressure. Blood pressure measurements were taken according to a standardized measurement protocol recommended by the American Heart Association. A total of six seated blood pressure measurements were taken on two separate occasions. The first three measurements were taken at the home following administration of the household questionnaire by the interviewer. Participants were asked to refrain from smoking, drinking coffee or using alcohol to prepare for the blood pressure measurements that were obtained at the

conclusion of the interview. The physician took the second set of blood pressure readings at the time of the physical examination. The blood pressure measurement recorded was the average of the last two readings. High blood pressure is coded as 1 if a blood pressure reading was $\geq$ 130/85 mm/Hg or if a subject reported taking medication to treat high blood pressure. Participants whose blood pressure readings are $<$ 130/85 are coded as 0. A waist circumference >102 cm for men and > 88 cm for women are coded as 1 and all others as 0.

Dyslipidemia is defined as the presence of hypertriglyceridemia or a low level of high-density lipoprotein. A total cholesterol (TC), high-density lipoprotein, and triglyceride (TG) level were obtained by venipuncture. Cholesterol levels were performed using a Hitachi 704 from Boehringer-Mannheim Diagnostics. If the HDL $<$ 40 for men and $<$ 50 for women it is coded as 1 and otherwise as 0. If triglycerides are $\geq$ 150 it is coded as 1 and if $<$ 150 it is coded as 0.

The final coding assignment classifies those with metabolic syndrome per the ATP III definition utilizing the statistical software, Statistical Analysis System (SAS). If at least three out of the five criteria are present the participant has metabolic syndrome and is coded as 1. If less than three of the characteristics are present they are coded as 2 and classified as healthy according to Blum's model. In SUDAAN, the variable is re-coded as 1 for metabolic syndrome and otherwise as 0 for analysis.

Independent Variables

The independent variable of particular interest to this study is gender. Gender is a non-modifiable population characteristic. Other independent variables were chosen because they represent risk factors for metabolic syndrome or one of its component characteristics. Variables were grouped in relation to the conceptual model and the construct from which they were extrapolated.

Variables within the population domain.

Gender (HSSEX) is identified in the household screener questionnaire in the household adult data file. This dichotomous variable was coded 1 for males and 2 for females.

Age (HSAGEIR) was obtained at the time of the interview and verified by the reported date of birth. All persons between the ages of 20–64 years were included. Persons were categorized by age within the following decades, 20–29 years, 30–39 years, 40–49 years, 50–59 years, and 60–64 years for descriptive analyses. The age in years was collapsed into two categories, 20-39 years (coded as 1) and 40–64 years (coded as 2) for the purpose of multivariate analyses.

Race-ethnicity (DMARETHN) identified four categories. The categories were Non Hispanic White (coded as 1), Non Hispanic Black (coded as 2), Mexican American (coded as 3) and other which include other Hispanics, Asian Americans or Native Americans (coded as 4).

A family history of cardiovascular disease was reported in the household adult questionnaire. A positive response to the following question indicated a family history of cardiovascular disease and was coded as 1. "Including living and deceased, were any of your blood relatives (grandparents, parents, brothers, sisters, aunts, uncles or cousins) ever told by a doctor that they had a heart attack before the age of 50?"

A family history of diabetes was reported in the household adult questionnaire. A positive response to the following question represents a family history of diabetes and was coded as 1. "Including living and deceased, were any of your blood relatives (grandparents, parents, brothers, sisters, aunts, uncles or cousins) ever been told by a doctor that they had diabetes?"

A past medical history of cardiovascular disease was reported in the household adult questionnaire. A positive response to the following question represents a past history of cardiovascular disease and was coded as 1. "Has a doctor ever told you that you had a heart attack?"

Variables within the environmental domain.

Socioeconomic status is represented by poverty-income ratios (DMPPIR). This is calculated from family income and family size based on US Bureau of Census tables. Family income queries were in the family questionnaire. "Including wages, salaries, self-employment and any other source of income, what was the total combined family income during the last 12 months?" The answers were coded 1 for < $20,000 and 2 for ≥ $20,000.

Educational level was reported in the family questionnaire. "What is the highest grade or year of regular school have you attended?"The response was never attended, kindergarten only, elementary school, high school or college. The response was collapsed into a categorical variable. Anyone with schooling up to but not including high school graduation was coded as 1. A high school graduate or any college education was coded as 2.

Geographic location was differentiated by rural (code =1) or urban (code = 2) areas under the variable name DMPMETRO. Urban classification is based on the USDA rural-urban codes that describe metro and non-metro areas. The USDA codes were collapsed into two categories to prevent identification of counties that were sampled in the survey.

The census region (DMPCREGN) was divided into the Northeast (code =1), Midwest (code = 2), South (code = 3), and West (code = 4). The United States was divided into four broad geographic regions as defined by the Bureau of Census. The South comprised the largest group. Analysis by region did not identify any geographic variation within the study population. However, because all states were not included in the selected sample, regional estimates may not be representative for a given region.

Variables within the health behavior domain.

Leisure time activity was reported in the household adult questionnaire. Participants were asked if their activity level was more active, the same or less active than other men or women their age. Individuals who answered that they were more active than their counterparts were coded as 1 and less active or the same were coded as 2.

Tobacco use is likely to be under-reported and may not be accurate. However, to the extent that it is a significant risk factor for cardiovascular disease and a proxy for health behavior it was retained. Tobacco use is reported in the household adult questionnaire. Data were collected on age of initiation, duration, frequency and amount of tobacco consumed. Tobacco use included cigarettes, cigars, pipes, and smokeless tobacco. Nicotine use was limited to cigarette use for this study. A positive response to the question, "Do you now smoke cigarettes?" confirms tobacco use and was coded as 1. A negative response was coded as 2.

Variables within the health care service domain.

Utilization of health care services, health insurance coverage, participation in public assistance programs, relationships with health care providers, and a history of health care conditions were queried in the survey. The number of contacts made to a health care provider, whether individuals had health insurance and an identified source for health care served as a proxy for health care services.

A usual source of health care was reported in the household adult questionnaire. "Is there a particular clinic, health center, doctor's office, or other place that you usually go to if you are sick, need advice about your health, or for routine care?" If the answer was yes, the person had a usual source of health care and it was coded as 1. If the response was no it was coded as 2.

Questions concerning health insurance coverage were reported in the family questionnaire. "During the last month who was covered by Medicare?" "During the last

month who was covered by Medicaid?" "During the last month who was covered by CHAMPUS, CHAMPVA, the VA or military health care?" "During the last month who was covered by one or more health insurance plans obtained privately or through an employer or union?" A positive answer to any of the aforementioned questions verified the respondent as having health insurance. For descriptive analysis Medicare was coded as 1, Medicaid as 2, CHAMPUS/military as 3 and Private as 4. The categories were then collapsed into a dichotomous variable for multivariate analysis. If an individual had any of the above insurance types they were classified as having insurance and coded as 1. If the response was negative for all four questions, the code was 2 for no health insurance.

Frequency of health visits was reported in the household adult questionnaire. "During the past twelve months about how many times did you see or talk to a medical doctor or assistant (Do not count doctors seen while an overnight patient in a hospital.)?" The response of "none" was coded as 1 and any contact with a doctor or assistant was coded as 2.

Blum's Ecology of Health Model provides the conceptual framework for the statistical analyses in this study. Blum recognized that populations, the environment, health behaviors and health care services impact health. For the purpose of this study, health is defined as the absence of metabolic syndrome. Metabolic syndrome as defined by the ATP III is the dependent variable. Population characteristics are limited to gender, age, race-ethnicity, family history of diabetes, family history of cardiovascular disease, and a past medical history of cardiovascular disease. Household income and geographic

residence are representative of environmental forces. Physical activity and tobacco use are a proxy for health behaviors. Health care service areas of interest were whether individuals had a usual source of health care, the frequency of health care contacts and had health insurance. All variables are listed in Table 10 and are categorized by their respective domains. This study examines what effect population characteristics, environmental factors, health behaviors, and health care services have on the presence of metabolic syndrome.

Statistical Analysis

Descriptive statistical methods and logistic regression were used to analyze the data. A cross tabulation procedure was employed to furnish frequency distributions of the study variables. Correlation procedures were performed to identify associations between variables. Correlation indices describe the magnitude of these relationships. The product –moment correlation coefficient or Pearson's r was computed for all variables in this study. This correlation coefficient ranges from minus one to plus one. A zero indicates no relationship exists between the variables. The Statistical Package for Social Sciences (SPSS) was employed for descriptive and correlation analyses. The correlation indices for the study variables are discussed in the following chapter on study results.

The chi-square statistic (X^2) was provided on all nominal level variables. The chi-square statistic (X^2) is computed by summarizing the differences between the observed and expected frequencies within the cells of the contingency table. This nonparametric

Table 10.

Study Variables

Domain	Variable	Measurement
Health	Metabolic Syndrome (3/5 must be present)	1. Hypertension $\geq$ 130 / 85 mm Hg or on antihypertensive agent 2. Fasting glucose $\geq$ 110 mg/dL. or on medication for diabetes 3. Waist Circumference > 102 cm for men > 88 cm for women 4. Triglycerides $\geq$ 150 mg/dL 5. HDL < 40 in men < 50 in women
Population Characteristics	Gender	Male/Female
	Age	Age in years
	Ethnicity	Non-Hispanic White, Non-Hispanic Black, Mexican American, Other
	Family History	Diabetes, Cardiovascular Disease
	Past Medical History	Cardiovascular Disease
Environmental Factors	Socioeconomic Status	Income levels, Education
	Geographic Residence	Rural/Urban Geographic Region
Health Behaviors	Physical Activity	Level of activity
	Tobacco use	Use of tobacco
Health Care Services	Usual Source of Health Care	Frequency of contacts with a health care provider
	Health Insurance	Source of Health Insurance

test of statistical significance was chosen because the dependent variable is measured on a nominal scale. The chi-square statistic (X^2) is a test of independence of the significance of different proportions among grouped variables. Chi-square testing was performed using SUDAAN, a statistical program recommended by NCHS for analysis of NHANES data. Two chi-square tests of independence were employed. The chi-square statistic (CHISQ) is based on observed minus expected values. The chi-square statistic (CMH) was used to perform chi-square tests of independence on stratified two-way tables. This latter analysis is analogous to the Cochran-Mantel-Haenszel statistic. The chi-square statistic was used to analyze proportional trends in those with and without metabolic syndrome and in women and men with metabolic syndrome for the purpose of hypotheses testing. The results of chi-square statistical (X^2) tests are discussed in the following chapter on study results.

Multivariate analysis measures the impact of independent variables on a dependent variable. Logistic regression is a multivariate statistical method used to analyze relationships between multiple independent variables and a dichotomous dependent variable. Logistic regression provides a model for the relative risk of an event (Hungler and Polit,1999). Relative risk is the probability of an event happening given certain conditions. Relative risk is approximated using an odds ratio. The odds ratio provides an estimate of the strength associated with the independent variable on the dependent variable. For the purpose of this study the odds ratio is the probability of a group having metabolic syndrome as compared to another group having the same outcome. Logistic

regression was used as an analytical technique because the dependent variable is a dichotomous categorical variable. Results show the likelihood of the independent variables being present in an individual with metabolic syndrome.

As noted previously, NHANES III uses a complex multistage probability sample design. Particular methods of statistical analysis are prescribed for the analysis of this complex survey design. Logistic regression was performed using SUDAAN. To compensate for unequal probability of selection, appropriate sampling weights were used to produce the correct population estimates. Sampling weights were used in all analyses. SUDAAN was utilized to compute variance estimates from the NHANES data. SUDAAN accounts for the variable sample weights and is the preferred statistical software program for complex survey designs such as the one used in the NHANE survey.

Variables are differentiated within the domains of the conceptual framework. The dependent variable is whether or not an individual has metabolic syndrome. The independent variables (X) are gender, age, race, family history, past medical history, socioeconomic status, geographic residence, physical activity, tobacco use, frequency and source of health care and health insurance. Logistic regression provides an analytical explanation for the effect each independent variable has on the presence of metabolic syndrome while controlling for the remaining independent variables. The estimated coefficients represent the proportion of the total variance of the dependent variable,

which can be explained by the independent variables. The logistic regression model is expressed as:

$$P / 1 - P = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 \quad + \ldots \beta_k X_k + \epsilon$$

Where:

P is the probability of the dependent variable being present.

$\beta_0, \beta_1, \beta_2 \ldots \beta_k$ are estimations of the coefficients.

$X_1, X_2, X_3 \ldots X_k$ are independent variables.

ϵ is the variance that is due to error or chance.

The study assumes a 95% confidence. Confidence intervals are provided. Model fit is represented by the – 2 Log Likelihood statistic. If the addition of independent variables improves the model the statistic changes. The smaller the value the better the fit. Rejection of the null hypothesis, while maintaining the independent variables, suggests appropriate model fit. Interaction effects are analyzed with logistic regression using the Wald F statistic at the .05 level of significance. The Wald F statistic provides an assessment of the statistical significance of the independent variables. Multicollinearity is assured by analyzing the regression model for changes in the correlation coefficients while including and excluding various independent variables and interaction terms.

Study Limitations

The design of this study limits causal effects of independent variables on the dependent variable because there is no manipulation or intervention of the variables. Error may enter a survey design via sampling error and non-sampling error. Voluntary

participation may incur non-response bias into the study. The potential for non-response bias is greater when there is a low rate of response. Multiple efforts were made to minimize low response rates in NHANES, including reimbursement for participation, providing transportation and childcare on site and locating the MEC in safe, convenient locations. Sample bias due to reliance on self-reported data is another potential limitation as answers are subject to individual recall and may be inaccurate. A retrospective study such as this may be criticized because criteria used to define diagnoses can change over time and may not be as applicable in the future.

A dichotomous dependent variable may limit conclusions drawn from the analysis. The dependent variable, metabolic syndrome, is based on criteria defined by ATP III. The lack of global consensus on the definition of metabolic syndrome is a limitation to this study.

Application of the conceptual model focuses primarily on population characteristics, environmental factors and lifestyles. Specific health beliefs, attitudes and cultural considerations are not available and their exclusion may limit the study. Health care services include access to care and preventive care services. The type of health care service is not a primary focus of this study. Measures of health care service specific to metabolic syndrome are not included in the data available for this analysis. A usual source of care, contacts with health care providers and health insurance provide a proxy for this domain within the conceptual model. Use of proxies as opposed to direct

measures may also limit the ability of the measures to explain the variance in the statistical model.

Summary

Metabolic syndrome and its associated risk factors are explored using the NHANES data. The NHANE surveys have been used in many epidemiological studies and health service research. NHANES allows for estimations of a larger representative population. Data from NHANES indicate that undiagnosed diabetes continues to be a significant health issue. NHANE surveys have contributed to the development of national referenced growth charts, underlined the scope and prevalence of obesity, and exposed areas where more health education is warranted. Limitations of the data available for the study design were discussed.

Blum's ecological model of health provides a framework to explore potential contributors to the prevalence of metabolic syndrome. Logistic regression enlightens our understanding of the impact of multiple variables on the development of metabolic syndrome. Population characteristics, health behaviors, environmental factors and utilization of health care services were analyzed using descriptive and chi-square statistics and logistic regression. The identification of precursors for metabolic syndrome has significant implications for the health of our nation. This chapter details the conceptual model, variables, and statistical analysis that are used in this study. Results are presented in the next chapter followed by the discussion of the analysis.

CHAPTER 4: RESULTS

This chapter presents the results of an analysis of factors that impact the expression of metabolic syndrome. A descriptive analysis of the sample population is provided. The multivariate analysis results are presented within the domains of an ecological model. The conceptual framework is delineated by population characteristics, particularly gender and race, environmental factors, health behaviors, and health care services.

Characteristics of the Study Population

A total of 10,134 men and women comprise the study sample. The sample represents a study population of 1,903,449 men and women given the weighting factors supplied by the National Center for Health Statistics. This analysis was performed on a weighted sample of more than 1.9 million men and women. A subset of 2,231 men and women (19.7 %) of the sample met the criteria for metabolic syndrome. This represents a weighted sample of 802,289 individuals.

A descriptive summary of the population is provided in Table 11. The summaries reflect the frequencies of characteristics within the four conceptual domains of population characteristics, environmental factors, health behaviors and health care services. A test of proportions with chi-square analysis was performed to evaluate if the proportions between groups are equivalent.

Table 11

Characteristics of Study Population (n =10,134)

Characteristics	Sample Number	Weighted Population Prevalence (%)
Metabolic Syndrome	2,231	19.7
Non-Metabolic Syndrome	7,903	80.3
Population Characteristics		
Male	4,765	49.6
Female	5,369	50.4
Age (years)		
20 – 29	2,715	25.6
30 – 39	2,685	28.3
40 – 49	2,152	23.4
50 – 59	1,566	15.5
60 – 64	1,016	7.2
20 – 39	5,400	53.9
40 – 64	4,734	46.1
Race		
Caucasian	3,642	75.8
African American	2,947	10.5
Mexican American	3,109	5.6
Other	436	8.1
Family History of Diabetes		
Yes	4,841	45.2
No	5,293	54.8

Table 11 (continued)

Characteristics of Study Population (n =10,134)

Characteristics	Sample Number	Weighted Population Prevalence (%)
Family History of Cardiovascular Disease		
Yes	1,477	17.9
No	8,657	82.1
Past Medical History of Cardiovascular Disease		
Yes	341	2.8
No	9,793	97.2
Environmental Factors		
Rural	5,259	49.1
Urban	4,875	50.9
Region		
Northeast	1,318	20.5
Midwest	1,878	23.4
South	4,431	35.5
West	2,507	20.6
Household Income		
< 20, 000	4,278	27.9
≥ 20,000	5,856	72.1
Education		
< High school	3,493	20.5
≥ High school	6,641	79.5

Table 11 (continued)

Characteristics of Study Population (n =10,134)

Characteristic	Sample Number	Weighted Population Prevalence (%)
Health Behaviors		
Physical Activity		
Active	2,948	31.6
Less Active	7,186	68.4
Tobacco Use		
Yes	3,003	30.7
No	7,131	69.3
Health Care Services		
Usual Source of Health Care		
Yes	7,422	75.9
No	2,712	24.1
Frequency of Health Care		
No Contacts	2,748	24.0
$\geq$ 1 Contacts	7,386	76.0
Insurance Coverage		
Yes	7,470	82.6
No	2,664	17.4

Population Characteristics

Characteristics within the population domain are gender, race, age, family history of diabetes, family history of cardiovascular disease, and a personal past medical history of cardiovascular disease. All percentages were weighted for population prevalence. The study sample consisted of 4,765 (49.6%) men and 5,369 (50.4%) women. This represents a weighted sample population of greater than 1.4 million men and greater than 1.2 million women.

For the purpose of statistical analysis the age variable was collapsed from four to two categories. The age variable is delineated by both categories in Table 11. The category, 60-64 years of age (7.2%) is the smallest group as it did not comprise a full decade. There were slightly more respondents in the 20-39 age category (53.9%) than in the 40–64 age category (46.1%).

Consistent with expectations given the sampling design of the NHANE survey, the race variable had appropriate population estimates. Sample proportions show 3,642 (75.8%) Caucasians, 2, 947 (10.5%) African Americans, 3,109 (5.6%) Mexican Americans, and 436 (8.1%) representing Native Americans, Asian Americans and other Hispanic groups.

A family history of diabetes was reported in 45.2% of the sample. A family history of cardiovascular disease was reported in 17.9% of the sample. A past medical history of cardiovascular disease was present in just 2.8 % of the sample population.

Environmental Factors

The residence of the study population was distributed to rural (49.1%) and urban (50.9%) areas. The study population was distributed across four geographic regions. The South comprised the largest number of participants (35.5%) within the study population. The remaining study population came from the Northeast (20.5%), the Midwest (23.4%) and the West (20.6%). Close to three-fourths of participants (72.1%) had an annual household income of $20,000 or greater. More than three-fourths of the sample population (79.5%) were high school graduates or had higher levels of education.

Health Behaviors

Physical activity and tobacco use were a proxy for health behaviors in this study. Lifestyles such as habitual inactivity and tobacco use are associated with the development of diabetes, cardiovascular disease and other chronic conditions. More than one-half of the study population (68.4%) reported that they were inactive or less active than their peers. One-third (30.7%) of the study population smoked cigarettes.

Health Care Services

Health insurance coverage included Medicare, Medicaid, military and private insurance. More than three-fourths (82.6 %) of study participants had health insurance. A separate and more detailed examination of health insurance revealed that more than half of respondents had private health insurance (60.2%), followed by Medicaid (8.7 %), Medicare (2.5 %), and the military (2.3 %). Three-fourths (75.9%) of respondents

reported a usual source of health care. Three-fourths of respondents (76%) reported that they made one or more contacts to a health care provider within the previous year.

Comparison of Sample Population with Metabolic and Non-Metabolic Syndrome

Domains within the conceptual framework are used to organize a comparison of study participants with metabolic syndrome from participants without metabolic syndrome. The proportions and chi square statistics are found in Table 12.

Population Characteristics

There were 1,234 females (19.1%) and 997 males (20.3%) with metabolic syndrome. There were no statistically significant findings with regard to metabolic syndrome and gender. There were statistically significant associations for metabolic syndrome and the age variable (X^2 =261.1; $p \leq .001$). The 40–64 year old age group had a higher percentage (30.4%) of individuals with metabolic syndrome than the 20–39 age group (10.6%). The proportion of race across categories was also statistically significant (X^2 = 25.62; $p \leq .01$). The lowest proportion of study participants with metabolic syndrome was found in African Americans (16.6%), with a slightly higher proportion in the other category (18.1 %). Caucasians (20.1%) and Mexican Americans comprised a larger proportion (22.2%) of the sample population with metabolic syndrome.

There were statistically significant differences among the study population with metabolic syndrome who had a family history of diabetes (X^2 = 50.82; $p \leq .001$), a family history of cardiovascular disease (X^2 = 5.96; $p \leq .01$), and a past medical history

Table 12

Characteristics of Study Population with Metabolic and Non- Metabolic Syndrome

	Weighted Sample Prevalence (%)		
Metabolic Syndrome	Yes (N = 2,231)	No (N = 7,903)	X^2
Population Characteristics			
Gender			0.98
Males	20.3	80.7	
Females	19.1	80.9	
Age (years)			261.10***
20–39	10.6	89.4	
40-64	30.4	69.6	
Race			25.62**
Caucasian	20.1	79.9	
African American	16.6	83.4	
Mexican American	22.2	77.8	
Other	18.1	81.9	
Family History of Diabetes			50.82***
Yes	24.4	75.6	
No	15.8	84.2	
Family History of Cardiovascular Disease			5.96**
Yes	23.0	77.0	
No	19.0	81.0	

Table 12 (continued)

Characteristics of Study Population with Metabolic and Non- Metabolic Syndrome

	Weighted Sample Prevalence (%)		
Metabolic Syndrome	Yes (N = 2,231)	No (N = 7,903)	X^2
Past Medical History of Cardiovascular Disease			16.81**
Yes	38.6	61.4	
No	19.1	80.9	
Environmental Factors			
Metro			17.22**
Rural	17.2	82.8	
Urban	22.1	77.9	
Region			6.45
Northeast	17.5	82.5	
Midwest	19.7	80.3	
South	21.4	78.6	
West	18.8	81.2	
Household Income			7.63**
< 20, 000	22.2	77.8	
≥ 20,000	18.7	81.3	
Education			35.71***
< High school	26.6	73.4	
≥ High school	17.9	82.1	

Table 12 (continued)

Characteristics of Study Population with Metabolic and Non- Metabolic Syndrome

	Weighted Sample Prevalence (%)		
Metabolic Syndrome	Yes (N = 2,231)	No (N = 7,903)	X^2
Health Behaviors			
Physical Activity			24.94***
Active	15.4	84.6	
Less Active	21.7	78.3	
Tobacco Use			0.94
Yes	18.8	81.1	
No	20.1	79.9	
Health Care Services			
Usual Source of Health Care			29.83***
Yes	21.4	78.6	
No	14.3	85.7	
Frequency of Health Care			4.78
No Contacts	17.4	82.6	
≥ 1 Contact	20.4	79.6	
Insurance Coverage			0.62
Yes	19.9	80.1	
No	18.8	81.2	

$p = \leq 0.05$ * $p \leq 0.01$ ** $p \leq .001$ ***

of cardiovascular disease ($X^2 = 16.81$; $p \leq .01$). A higher proportion of participants with metabolic syndrome reported a family history of diabetes (24.4%) than those without a family history of diabetes (15.8%). The same was true for a family history of cardiovascular disease. A higher proportion of respondents with metabolic syndrome had a family history of cardiovascular disease (23%) as compared to those with no family history of cardiovascular disease (19%). The proportion of participants with metabolic syndrome who had a personal past medical history of cardiovascular disease were twice (38.6%) the proportion of those without a past medical history of cardiovascular disease (19.1%).

Environmental Factors

There was a significant association between metabolic syndrome and rural and urban residence ($X^2 = 17.22$; $p \leq .01$), household income ($X^2 = 7.63$; $p \leq .05$), and level of education ($X^2 = 35.71$; $p \leq .01$). A higher proportion of participants with metabolic syndrome lived in an urban area (22.1%) as compared to a rural area (17.2%). Participants with metabolic syndrome had proportionately less wealth and less education. Proportionately more participants with metabolic syndrome had less than a high school education (26.6%) as compared to those with a high school or college education (17.9%). Fewer participants with metabolic syndrome reported a household income of $\geq$ 20,000 (18.7%) as compared to those with metabolic syndrome who reported a household income of < 20,000 (22.2%).

Health Behaviors

There were statistically significant findings in those with metabolic syndrome in their reported physical activity ($X^2 = 24.94$; $p < .001$). The proportion of individuals with metabolic syndrome was higher in individuals who were less active (21.7%) than in individuals who reported they were more active (15.4%) than their peers.

Health Care Services

The proportion of respondents who reported a usual source of health care was statistically significant ($X^2 = 29.83$; $p \leq .001$). A higher proportion of individuals with metabolic syndrome had a usual source of health care (21.4%) than those who did not have a usual source of health care (14.3%).

Comparison of Men and Women with Metabolic Syndrome

This researcher was particularly interested in the impact of gender on metabolic syndrome. The following section provides a descriptive analysis of gender and metabolic syndrome within the domains of population, environment, health behaviors and health care services. The comparison of men versus women with metabolic syndrome with weighted sample percents and chi square statistics is located in Table 13.

Population Characteristics

There was a higher proportion of men and women with metabolic syndrome between the ages of 40–64 years ($X^2 = 4.88$; $p = .05$). There was a higher proportion of men with metabolic syndrome between the ages of 20–39 years (31%) than women with metabolic syndrome in that same age group (26.7%).

Table 13

Characteristics of Men and Women with Metabolic Syndrome

	Weighted Sample Prevalence (%)				
Metabolic Syndrome	Yes (N = 2231)		No (N = 7903)		
	Men (N = 997)	Women (N = 1,234)	Men (N = 3,768)	Women (N = 4,135)	X^2
Population Characteristics					
Gender					20.30
	19.1	79.7	80.9	0.98	
Age					4.88*
20–39	31.0	26.7	61.6	58.5	
40–64	68.9	73.2	38.4	41.4	
Race					42.91***
Caucasian	80.9	73.7	75.5	75.2	
African American	6.0	11.7	10.2	11.4	
Mexican American	5.9	6.6	6.1	4.7	
Other	7.0	7.9	7.9	8.6	
Family History Diabetes					60.15***
Yes	52.1	60.2	36.0	48.8	
No	47.8	39.7	63.9	51.1	
Family History Cardiovascular Disease					11.38**
Yes	19.9	21.7	14.7	19.4	
No	80.0	78.2	85.2	80.5	

Table 13 (continued)

Characteristics of Men and Women with Metabolic Syndrome

	Weighted Sample Prevalence (%)				
Metabolic Syndrome	Yes (N = 2231)		No (N = 7903)		
	Men (N = 997)	Women (N = 1,234)	Men (N = 3,768)	Women (N = 4,135)	X^2
Past Medical History of Cardiovascular Disease					
Yes	8.3	2.4	2.7	1.5	16.28**
No	91.6	97.5	97.2	98.4	
Environmental Factors					
Metro					0.25
Rural	44.0	41.4	50.8	50.4	
Urban	55.9	58.5	49.1	49.5	
Region					1.52
Northeast	20.1	16.1	21.2	20.9	
Midwest	23.6	23.3	23.7	23.0	
South	38.8	38.4	34.4	34.9	
West	17.4	22.0	20.5	21.2	
Household Income					8.01*
< 20, 000	25.6	37.6	26.1	27.8	
≥ 20,000	74.3	62.3	73.8	72.1	

Table 13 (continued)

Characteristics of Men and Women with Metabolic Syndrome

	Weighted Sample Prevalence (%)				
Metabolic Syndrome	Yes (N = 2231)		No (N = 7903)		
	Men (N = 997)	Women (N = 1234)	Men (N = 3768)	Women (N = 4135)	X^2
Education					3.67
< High school	24.7	30.9	20.9	16.6	
≥ High school	75.2	69.0	79.0	83.3	
Health Behaviors					
Activity					43.22***
Active	28.2	21.0	38.5	28.1	
Less Active	71.7	78.9	61.4	71.8	
Tobacco Use					25.84***
Yes	31.0	27.5	35.2	27.0	
No	68.9	72.4	64.7	73.0	
Health Care Services					
Usual Source of Health Care					135.8***
Yes	78.1	87.1	65.5	82.9	
No	21.8	12.8	34.5	17.1	
Frequency of Health Care					171.97***
No Contacts	28.3	13.9	34.0	15.7	
≥ 1 Contact	71.6	86.1	65.9	84.2	

Table 13 (continued)

Characteristics of Men and Women with Metabolic Syndrome

	Weighted Sample Prevalence (%)				
Metabolic Syndrome	Yes (N = 2231)		No (N = 7903)		
	Men (N = 997)	Women (N = 1234)	Men (N = 3768)	Women (N = 4135)	X^2
Insurance Coverage					0.34
Yes	86.3	79.5	80.4	85.1	
No	13.6	20.4	19.5	14.8	

$p = \leq 0.05$ * $p \leq .01$ ** $p \leq .001$ ***

Race-ethnicity is a significant independent variable ($X^2 = 42.91$; $p = .001$). There was a higher proportion of African American women with metabolic syndrome (11.7%) than African American men with metabolic syndrome (6.0%). There were proportionately more Caucasian men (80.9%) with metabolic syndrome than Caucasian women (73.7%) with metabolic syndrome. Yet, there was a similar proportion of Caucasian women without metabolic syndrome (75.2%) as Caucasian men without metabolic syndrome (75.5%). The two categories Mexican Americans and the other race category had relatively similar proportions of men and women with metabolic syndrome.

The remaining variables, a family history of diabetes ($X^2 = 60.15$; $p \leq .001$), a family history of cardiovascular disease ($X^2 = 11.38$; $p \leq .01$) and a past personal medical history of cardiovascular disease ($X^2 = 16.28$; $p \leq .01$) were all statistically significant. There was a fairly even distribution between men with metabolic syndrome who reported a family history of diabetes (52.1%) as men with metabolic syndrome who did not have a family history of diabetes (47.8%). Women with metabolic syndrome reported a proportionately higher percentage of family history of diabetes (60.2%) when compared to women with metabolic syndrome who did not have a family history of diabetes (39.7%). One-fifth of women (21.7%) and men (19.9%) with metabolic syndrome had a family history of cardiovascular disease. The proportion of men with metabolic syndrome who had a past medical history of cardiovascular disease (8.3%) was more than three times the proportion of women with metabolic syndrome who also had a past medical history of cardiovascular disease (2.4%).

Environmental Factors

The only environmental variable that demonstrated a statistically significant finding was household income. Household income was statistically significant ($X^2 = 8.01$; $p < .05$). More women (37.6%) with metabolic syndrome than men (25.6%) with metabolic syndrome reported a lower annual household income (< $20, 000).

Health Behaviors

Level of physical activity was statistically significant ($X^2 = 43.22$; $p \leq .001$). A higher proportion of women (78.9%) with metabolic syndrome than men (71.7%) with

metabolic syndrome reported that they were less active than their peers. Tobacco use was statistically significant ($X^2 = 25.84$; $p \leq .001$). Men (31.0%) with metabolic syndrome reported smoking cigarettes proportionally more than women (27.5%) with metabolic syndrome. The relationship is similar in men and women without metabolic syndrome.

Health Care Services

All of the cross tabulations of the variables in this domain were statistically significant with the exception of health insurance coverage. A usual source of health care ($X^2 = 135.8$) and frequency of health care contacts ($X^2 = 171.97$) were significant at the $p = .001$ level of significance. More women (87.1%) with metabolic syndrome than men (78.1%) with metabolic syndrome reported a usual source of health care. More women (86.1%) with metabolic syndrome than men (71.6%) with metabolic syndrome reported one or more contacts with a health care provider over the past twelve months.

This concludes the descriptive analysis of the study. In the next section, logistic regression analysis is used to further explore the impact of population characteristics, environmental factors, health behaviors and health care services on metabolic syndrome.

Multivariate Analysis

Logistic regression was used to determine the relationship between the independent variables, categorized by the domains of population characteristics, environmental factors, health behaviors and health care services, and the presence of metabolic syndrome. The variables, REGION and TOBACCO were not significant in the cross tabulations or in the initial regression analysis despite the addition of other independent

variables and were excluded from the final logistic regression model. METRO, a dichotomous variable of urban and rural status satisfies geographic locale and was maintained. Activity was retained to represent health behaviors in the model.

Prior to performing regression analysis, Pearson correlation coefficients were run on all variables. Pearson correlation coefficients were low with respect to metabolic syndrome and the independent variables. The correlation matrix of correlation coefficients can be found in Appendix B. The higher correlation coefficients involved race, region, education, and income. There was a higher correlation between Caucasians and African Americans (- .480), Caucasians and Mexican Americans (- .498), African Americans and Mexican Americans (- .426), region and Mexican Americans (- .415) and education and Mexican Americans (- .335). A higher correlation was found in household income and health insurance coverage (- .346), household income and education (- .328), and between a source of health care and frequency of contacts with a health care provider (- .340). Although these correlation coefficients were higher, they were acceptable given the large sample size. Variables with higher correlation coefficients were matched as potential interaction terms and included in the logistic regression analysis to clarify their effect on the dependent variable, metabolic syndrome.

Several interaction terms were analyzed for statistical significance with the logistic regression model. They were income with insurance, income with education, race with gender, and education with health insurance coverage. Statistical significance was evident in the later two terms, therefore, race and gender along with education and health

insurance coverage were retained as interaction terms. Including the interaction term education with health insurance coverage eliminated the lower level independent variable of health insurance. Health insurance coverage did not achieve statistical significance in the univariate, bivariate or multivariate analyses and did not effect the stability of the model with respect to the explanation of variance to the other variables or to the overall model.Therefore, in the final regression analysis, health insurance coverage was eliminated, though the higher level interaction term of education and health insurance coverage was retained. The results of the analysis including the interaction terms by logistic regression are displayed in Table 14.

The study results show the impact of the independent variables on the presence of metabolic syndrome. Model fit is indicated by a –2 Log Likelihood ratio of 1033.98 (df = 19, p = .00). The R^2 for this model is .0969. This indicates the strength of the relationship between the dependent and independent variables. This correlation explains the degree of variation of the dependent variable that can be explained by the independent variables. Thus, 9.6% of the variation of the dependent variable is explained by the independent variables. This will be discussed further in the final chapter.

Population Characteristics

Multiple factors proved significant for the presence of metabolic syndrome. Women were 30 % less likely to have metabolic syndrome than men were. African Americans were 46% less likely to have metabolic syndrome. However, when gender and race

Table 14.

Logistic Regression Results of the Likelihood of Metabolic Syndrome

Variable	Wald F	Adjusted Odds Ratio	95 % Confidence Interval
Population Characteristics			
Gender	13.46***		
Males		1.00	1.00, 1.00
Females		0.70	0.56, 0.87
Age	213.78***		
20 – 39		1.00	1.00, 1.00
40 – 64		3.82	3.12, 4.69
Race	25.20***		
Caucasian		1.00	1.00, 1.00
African American		0.54	0.41, 0.71
Mexican American		1.02	0.78, 1.32
Other		0.97	0.55, 1.71
Gender and Race[x]	7.26**		
Caucasian Men		1.00	1.00, 1.00
African American men		1.00	1.00, 1.00
Mexican American men		1.00	1.00, 1.00
Other men		1.00	1.00, 1.00
Caucasian women		1.00	1.00, 1.00
African American women		1.98	1.40, 2.80
Mexican American women		1.56	1.13, 2.15
Other women		1.12	0.54, 2.33
Family History Diabetes	38.41***		
Yes		1.00	1.00, 1.00
No		0.60	0.50, 0.72

Table 14 (continued)

Logistic Regression Results of the Likelihood of Metabolic Syndrome

Variable	Wald F	Adjusted Odds Ratio	95 % Confidence Interval
Family History Cardiovascular Disease	4.56		
Yes		1.00	1.00, 1.00
No		0.80	0.64, 1.01
Past Medical History Cardiovascular Disease	8.06*		
Yes		1.00	1.00, 1.00
No		0.55	0.35, 0.88
Environmental Factors			
Metro	7.30*		
Rural		1.00	1.00, 1.00
Urban		1.26	1.04, 1.53
Household Income	9.67**		
< 20,000		1.00	1.00, 1.00
≥ 20,000		0.74	0.60, 0.92
Education	12.02***		
< High school grad		1.00	1.00, 1.00
≥ High school grad		0.39	0.21, 0.71
Education & Health Insurance[x]	3.64*		
< High school /with insurance		0.70	0.49, 0.98
≥ High school/without insurance		1.18	0.86, 1.64

Table 14 (continued)

Logistic Regression Results of the Likelihood of Metabolic Syndrome

Variable	Wald F	Adjusted Odds Ratio	95 % Confidence Interval
Health Behaviors			
Physical Activity	30.07***		
Active		1.00	1.00, 1.00
Less Active		1.67	1.36, 2.06
Health Care Services			
Usual Source Health Care	6.51*		
Yes		1.00	1.00, 1.00
No		0.75	0.59, 0.96
Frequency Health Care	1.19		
No visits		1.00	1.00, 1.00
≥ 1 visit		1.12	0.89, 1.42

[x] Interaction Term

2 Log L Ratio = 1033.98, df = 19, R^2 = .0969, p = .00

p = ≤ 0 .05 * p = ≤ 0.01** p = ≤ 0.001***

interacted, African American women were nearly twice (AOR = 1.98; CI:1.40-2.80) as likely as Caucasian women and men to have metabolic syndrome. Mexican American women were one and one-half times (AOR = 1.56; CI:113–2.15) more likely than Caucasian women and men to have metabolic syndrome. Study participants between the

ages of 40–64 years were almost four times (AOR = 3.82; CI:3.12-4.69) more likely to have metabolic syndrome than those between 20-39 years of age. Participants without a family history of diabetes (AOR = .60; CI:0.50-0.72) were 40 % less likely to have metabolic syndrome than respondents who had a family history of diabetes. Participants were less likely to have metabolic syndrome if they did not have a family history of cardiovascular disease (AOR=0.80; CI:0.64-1.01) or a personal past medical history of cardiovascular disease (AOR=0.55;CI:0.35-0.88).

Environmental Factors

Urban residence (AOR = 1.26;CI:1.04-1.53) conferred a greater likelihood for metabolic syndrome than rural residence. The higher a household income (AOR = 0.74: CI:0.60-0.92), the less likely one had metabolic syndrome. The more education (AOR = 0.39; CI:0.21-0.71) the less likely one would have metabolic syndrome.

Health Behaviors

The less active an individual was (AOR = 1.67; CI: 1.36-2.06) the more likely metabolic syndrome was present.

Health Care Services

With respect to health care services, participants were less likely to have metabolic syndrome when there was no usual source of health care (AOR = 0.75; CI: 0.59-0.96). No significant difference was noted in the frequency of health contacts.

Hypothesis Testing

The following section is organized by hypotheses. Hypotheses are grouped within the collective domains proposed in the conceptual ecological framework of Henrik Blum (Blum, 1983). The results of the bivariate analysis presented in Table 13 are used to reject or fail to reject the null hypotheses. The multivariate results from the logistic regression analysis in Table 14 are used to reject or fail to reject the final null hypothesis. A summary of hypotheses is provided in Table 15.

Population Characteristics

The hypotheses regarding population characteristics comprise proportionately more variables, as compared to the other domains. The hypotheses tested include the impact of age, race-ethnicity, a family history of diabetes, a family history of cardiovascular disease, and a past medical history of cardiovascular disease on the presence of metabolic syndrome in men and women.

H_{1A} The prevalence of metabolic syndrome is similar for men and women when age is controlled. When metabolic syndrome was analyzed with respect to age there was a statistically significant difference between the 20-39 year age group with metabolic syndrome and the 40-64 year age group with metabolic syndrome ($X^2 = 261.1$; $p = < .001$). However, when age is profiled by gender, the significance of the difference disappears ($X^2 = 3.65$; $p = 0\ .085$). Thus, there are similar distributions of metabolic syndrome between men and women given the variable of age. Therefore, the null hypothesis for H_{1A} fails to be rejected.

Table 15.

Results of Hypotheses Testing

Population Characteristics	**Hypotheses**
H_{1A} The prevalence of metabolic syndrome is similar for men and women when age is controlled	Fail to Reject
H_{1B} The prevalence of metabolic syndrome is similar for men and women when race-ethnicity is controlled	Reject
H_{1C} The prevalence of metabolic syndrome is similar for men and women when a family history of diabetes is controlled.	Reject
H_{1D} The prevalence of metabolic syndrome is similar for men and women when a family history of cardiovascular disease is controlled.	Reject
H_{1E} The prevalence of metabolic syndrome is similar for men and women when a past medical history of cardiovascular disease is controlled.	Reject
Environmental Factors	
H_{2A} The prevalence of metabolic syndrome is similar for men and women when geographic residence is controlled.	Fail to Reject
H_{2B} The prevalence of metabolic syndrome is similar for men and women when income is controlled.	Reject
H_{2C} The prevalence of metabolic syndrome is similar for men and women when education is controlled	Fail to Reject

Table 15 (continued)

Results of Hypotheses Testing

Health Behaviors	**Hypotheses**
H_{3A} The prevalence of metabolic syndrome is similar for men and women when activity level is controlled.	Reject
H_{3B} The prevalence of metabolic syndrome I is similar for men and women when tobacco use is controlled.	Reject
Health Care Services	
H_{4A} The prevalence of metabolic syndrome is similar for men and women when a source of health care is controlled.	Reject
H_{4B} The prevalence of metabolic syndrome is similar for men and women when the frequency of health care contacts are controlled.	Reject
H_{4C} The prevalence of metabolic syndrome is similar for men and women when health insurance coverage is controlled.	Fail to Reject
H_O There is no difference in the prevalence of metabolic syndrome between men and women when age, race-ethnicity, a family history of diabetes, a family history of cardiovascular disease, a past medical history of cardiovascular disease, geographic residence, annual household income, education, activity level, a usual source of health care, and frequency of health care contacts, and health insurance are controlled.	Reject

H_{1B} The prevalence of metabolic syndrome is similar for men and women when race-ethnicity is controlled. Comparisons across race categories indicated significant associations. More than 20% of Mexican Americans and Caucasians had metabolic syndrome ($X^2 = 25.62$; $p = < .01$). African Americans represented 16.6 % and other minorities comprised 18.1% of participants with metabolic syndrome (See Table 12). When comparing men and women with and without metabolic syndrome by race, a larger proportion of African American women, Mexican American women, and women of other ethnic minorities, had metabolic syndrome compared to their male counterparts (see Table 13). Yet, a higher proportion of white men (80.9%) as compared to white women (73.7%) had metabolic syndrome. Results demonstrate that while gender alone was not statistically significant, the addition of race was significant ($X^2 = 42.91$; $p = < 0.001$). Since there were statistically significant differences between men and women with metabolic syndrome with regard to the variable of race, the null hypothesis for H_{1B} is rejected.

H_{1C} The prevalence of metabolic syndrome is similar for men and women when a family history of diabetes is controlled. A family history of diabetes is a risk factor for diabetes in men and women (ADA, 2001). A family history of diabetes was consistently significant across statistical analyses. A positive family history of diabetes was statistically significant for metabolic syndrome for men and women ($X^2 = 60.15$; $p = < 0.001$). A proportionately higher percentage of women with metabolic syndrome (60.2%) had a positive family history of diabetes as compared to men with metabolic

syndrome (52.1%) who reported a family history of diabetes. Participants were 40% less likely to have metabolic syndrome if they did not have a family history of diabetes (AOR 0.60; CI 0.50-0.72). Given that a statistically significance was noted in the analyses between men and women with metabolic syndrome and a family history of diabetes, the null hypothesis for H_{1C} is rejected.

H_{1D} The prevalence of metabolic syndrome is similar for men and women when a family history of cardiovascular disease is controlled. A family history of cardiovascular disease is a risk factor for the development of cardiovascular disease in men and women (NCEP, 2001). The definition of metabolic syndrome does not include cardiovascular disease, but implies an increased risk for the development of cardiovascular disease. In this study, a reported history of cardiovascular disease was statistically significant ($X^2 = 11.38$; $p = < 0.01$) among men and women with metabolic syndrome. There was a higher proportion of women (21.7%) with metabolic syndrome with a family history of cardiovascular disease when compared to men (19.9%) with metabolic syndrome and a family history of cardiovascular disease. Thus, the null hypothesis for H_{1D} is rejected.

H_{1E} The prevalence of metabolic syndrome is similar for men and women when a past medical history of cardiovascular disease is controlled. Metabolic syndrome increases the risk of a cardiovascular event not only because of its component clinical characteristics but the additive risks of the clinical characteristics that make up the syndrome (Fontbonne, & Eschwege, 1991; Castelli, et. al., 1986). Having reported a

past medical history of cardiovascular disease, specifically, having had a myocardial infarction before the age of 50 years, showed a significant association with metabolic syndrome ($X^2 = 16.28$; $p = < 0.01$). This finding is similar to that found in a previous study by Lehto et al. (2000). Due to the significant differences between men and women, when metabolic syndrome and a positive past medical history of cardiovascular disease, the null hypothesis of H_{1E} is rejected.

Environmental Factors

H_{2A} The prevalence of metabolic syndrome is similar for men and women when geographic residence is controlled. Geographic distribution to the Northeast, Midwest, South and West was not statistically significant when analyzed across those with and without metabolic syndrome and by gender. The regional categorizations may be too broad to capture differences. When analyzing residence by metropolitan area, designated as urban or rural status there was statistical significance ($X^2 = 17.22$; $p = < 0.01$) among those with and without metabolic syndrome (See Table 12). However, the statistical significance disappears when gender and metabolic syndrome are analyzed with regard to urban or rural status. As there were no statistically significant differences between men and women with metabolic syndrome with regard to geographic location, either by region or by metropolitan area, the results fail to reject the null hypothesis H_{2A}.

H_{2B} The prevalence of metabolic syndrome is similar for men and women when income is controlled. There was statistical significance in income levels ($X^2 = 7.63$; $p =$

< 0.01) between those with metabolic syndrome and those without metabolic syndrome (See Table 12). Further analysis by gender demonstrated that proportionately more women with metabolic syndrome (37.6%) reported an annual household income less than $20,000 as compared to men with metabolic syndrome (25.6%) who reported an annual income less than $20,000 ($X^2 = 8.01$; $p = < 0.05$). This study confirm that income and gender share a statistical significance when metabolic syndrome is present. Due to the significant differences between annual household income among men and women with metabolic syndrome, the null hypothesis of H_{2B} is rejected.

H_{2C} The prevalence of metabolic syndrome is similar for men and women when education is controlled. There was a statistically significant association ($X^2 = 35.71$; $p = < 0.001$) between metabolic syndrome and level of education. However, when the relationship between education and metabolic syndrome was further assessed, after adjusting for gender, the association disappeared. Level of education did have an interactive effect with health insurance and will be discussed at the conclusion of this section. Due to the fact that there were no statistical associations noted between men and women with metabolic syndrome and level of education, the null hypothesis of H_{2C} fails to be rejected.

Health Behaviors

H_{3A} The prevalence of metabolic syndrome is similar for men and women when activity level is controlled. In this study, proportionately more respondents with metabolic syndrome were less active (21.7%) than those with metabolic syndrome who

were more active (15.4%). A greater proportion of women with metabolic syndrome were reportedly less active than men with or without metabolic syndrome ($X^2 = 43.22$; $p = < 0.001$). Given that there was statistically significant association between men and women with metabolic syndrome and level of activity, the null hypothesis H_{3A} is rejected.

H_{3B} The prevalence of metabolic syndrome is similar for men and women when tobacco use is controlled. Habitual cigarette smoking is the most preventable cause of death in men and women in the United States. It is a risk factor for cardiovascular disease and chronic lung disease (LaCroix, 1991). While tobacco use was not statistically significant between those with metabolic syndrome and those without metabolic syndrome, there was an association among men and women with metabolic syndrome and their use of tobacco ($X^2 = 25.84$; $p = < 0.001$). Men with metabolic syndrome (31%) more often reported a history of cigarette smoking than did women with metabolic syndrome (27.5%). Thus, the null hypothesis H_{3B} is rejected.

Health Care Services

H_{4A} The prevalence of metabolic syndrome is similar for men and women when a source of health care is controlled. A higher proportion of individuals with metabolic syndrome reported a usual source of health care (21.4%) than did not have a usual source of health care (14.3%) at a level of statistical significance ($X^2 = 29.38$; $p = < 0.001$). More women with metabolic syndrome reported that they had a usual source of health care as compared to men with metabolic syndrome ($X^2 = 135.8$; $p = < 0.001$).

Attitudes among health care professionals and reasons for health care visits were not analyzed in this study. A usual source of health care is only one indicator of access and utilization of healthcare services. Given that this study found significant differences between men and women with metabolic syndrome and a usual source of health care the null hypotheses, H_{4A} is rejected.

H_{4B} The prevalence of metabolic syndrome is similar for men and women when the frequency of health care contacts are controlled. The frequency of health care contacts by individuals with metabolic syndrome and those without metabolic syndrome was not significant. However, women with metabolic syndrome reportedly made more frequent health care contacts than men with metabolic syndrome ($X^2 = 171.13$; $p = < 0.001$). Thus, the null hypothesis H_{4B} is rejected as there were statistically significant differences in the frequency of contacts made by men and women with metabolic syndrome.

H_{4C} The prevalence of metabolic syndrome is similar for men and women when health insurance coverage is controlled. No statistically significant difference for health insurance coverage was found among men and women with metabolic syndrome. The null hypothesis H_{4C} fails to be rejected as there were no significant differences in men and women with metabolic syndrome with or without health insurance coverage.

Logistic Regression Analysis

H_O There is no difference in the prevalence of metabolic syndrome between men and women when age, race-ethnicity, a family history of diabetes, a family history of

cardiovascular disease, a past medical history of cardiovascular disease, geographic residence, annual household income, education, activity level, a usual source of health care, and frequency of health care contacts, and health insurance are controlled. Logistic regression analysis was used to explore the impact of population characteristics, environmental factors, health behaviors, and health care services on the presence of metabolic syndrome. Tobacco use, frequency of health care and health insurance were not found to be statistically significant in the multivariate analysis. Gender, age, race, family history of diabetes, education and physical activity were all found to be highly significant ($p = < 0.001$). Gender, when interacted with race, and education when interacted with health insurance, had statistically significant interactive effects. Thus, the null hypothesis H_O as stated above is rejected.

Summary

This concludes the presentation of the results for factors that impact the presence of metabolic syndrome. In addition to several independent variables demonstrating significance, interactions occur between gender and race, and between education and health insurance that affect the prevalence of metabolic syndrome. Several variables were found to be statistically significant with regard to gender and metabolic syndrome. Although women were less likely to have metabolic syndrome, when race was interacted with gender, African American and Mexican American women became more likely to have metabolic syndrome than Caucasian women. Those less highly educated but with insurance were 30% less likely to have metabolic syndrome. Advanced age, inactivity

and urban residence were all more likely to indicate a higher risk of metabolic syndrome. If an individual had no family history of diabetes, no family history of cardiovascular disease, and no past medical history of cardiovascular disease there was a lower risk for metabolic syndrome. Those with a higher level of education and higher household incomes were less likely to have metabolic syndrome. Lastly, those without a usual source of health care were less likely to have metabolic syndrome. The next chapter includes a discussion of the study's findings, limitations and future implications.

CHAPTER 5: DISCUSSION

This chapter provides a discussion of the study findings. This discussion is organized by the domains within the conceptual framework. The four domains are population characteristics, environmental factors, health behaviors and healthcare services. The results from this study are analyzed with respect to previous research studies presented in the literature review. The potential impact of the results on clinical practice, limitations of the study and direction for future research are discussed in the concluding section.

Study Summary

This retrospective non-experimental design study explores the impact of gender, among other factors, on the presence of metabolic syndrome. The descriptive aspect of this study begins by replicating previous research using NHANES data, which cites the overall unadjusted prevalence of metabolic syndrome to be 21.8 % (Ford, et al., 2002) and 22.6% (Park, et al., 2003). This study found an unadjusted prevalence of 19.7 % . The ATP III definition for metabolic syndrome was utilized in this study and the two preceding studies cited.

Variation in descriptive statistics may be due to minor coding differences and the imposed age restriction for this analysis. For example, the lower prevalence found in this study is likely due to a designated study population between the ages of 20-64 years, whereas the Ford, et al. (2002) and Park, et al. (2003) studies had no upper age

limit. In the Ford, et al (2002) study, participants were eliminated if fasting < 8 hours, whereas this study and the Park, et al. study included those who were fasting a minimum of 6 hours. Despite these minor coding differences, findings in the Ford, et al. (2002) and Park, et al. (2003) studies were corroborated by this study.

This study is unique in that it examined gender among other factors associated with metabolic syndrome and related findings to potential risk for diabetes and cardiovascular disease. The multivariate analysis reflects the impact of population characteristics, environmental factors, health care behaviors, and health care services on metabolic syndrome as a model for analysis. It expands on previous research by continuing the descriptive analysis and adding inferential analyses.

The complex design of the NHANES data allows for the inclusion of the largest representative sampling of ethnic minorities in the United States. Unlike previous research, in which women have been under-represented, women comprise almost half the population sampled in NHANES. The descriptive study by Ford, et al. (2002), Park, et al. (2003) and this analysis, confirm that men and women exhibit metabolic syndrome equally, with the exception of African American women and Mexican American women who shared a disproportionate burden of metabolic syndrome than Caucasian women and all men. This research design is more inclusive of women and ethnic minorities than in past research. Thus, the findings from this study may be applied to a broader population.

Population Characteristics

While gender was not statistically significant by itself, when gender and race interacted in the logistic regression model, African American women and Mexican American women were more likely to have metabolic syndrome. Women were found to be 30% less likely to have metabolic syndrome (AOR = 0.70; CI:0.56-0.87). This raises concern about men and their risk for metabolic syndrome. This direction was not what was initially expected. This study is exploratory in terms of identifying at risk populations. Given the results from the regression analysis, men and women should both be screened for metabolic syndrome.

However, the likelihood of metabolic syndrome was higher for women of certain ethnic minorities, when compared to men and Caucasian women, and particular attention should be paid to screening African American and Mexican American women. The independent variable of race was statistically significant in univariate, bivariate and multivariate analyses. Although the analysis indicated a lower likelihood of metabolic syndrome among African Americans overall (AOR = 0.54;CI:0.41-0.71), the interactive effect between race and gender clarified results that were counterintuitive. If a woman was African American (AOR = 1.98; CI:1.40-2.80) or Mexican American (AOR = 1.56; CI:1.13-2.15), she was one and a half to two times more likely to have metabolic syndrome than Caucasian women and all men.

The ATP III definition requires 3 out of 5 clinical characteristics be present to diagnose metabolic syndrome. The clinical characteristics were delineated and profiled

by gender, age and race in the Ford, et al. (2002) study. In African American and Mexican American women a proportionately higher percentage of their clinical characteristics of metabolic syndrome were attributed to high blood pressure and abdominal obesity than to diabetes, high triglycerides or low HDL cholesterol levels, when compared to Caucasian women (Ford et al., 2002). Winkleby, Kraemer, Ahn, & Varady (1998) found a steeper incremental increase in high blood pressure with age in African American women than Caucasian women. Women of ethnic minorities may be more susceptible to certain characteristics that make up the metabolic syndrome. More focused research on women of ethnic minorities and the clinical characteristics that comprise the metabolic syndrome are needed to elucidate which factors have a greater effect on the development of this syndrome. Targeting efforts at specific clinical characteristics based on the demographic and risk profile may better identify populations at risk.

The identification of metabolic syndrome is important for both primary and secondary interventions. Primary prevention is "concerned with the development of disease in a susceptible or potentially susceptible population" whereas secondary prevention refers to "early diagnosis and prompt therapy to shorten or reduce the severity of disease" (Thomas, 1981). An important aspect of this study was to explore whether metabolic syndrome affects a younger cohort the same way it affects an older population.

The variable, age, was statistically significant in the univariate, bivariate and multivariate analyses. Individuals between the ages of 40-64 years (AOR = 3.82; CI:3.12-4.69) were almost four times more likely to have metabolic syndrome than those between 20-39 years of age. Advanced age is associated with the development of chronic disease and is a risk factor for diabetes and cardiovascular disease (Isomaa, et al., 2001). Diabetes and cardiovascular disease are more prevalent in older populations. As a risk factor, advanced age is defined as > 45 years for men and > 55 years for women (ADA, 2001 & NCEP, 2001). Those 65 years of age and older were excluded from this study. Presumably, the number of individuals with metabolic syndrome would be much higher had they been included.

The study sample was divided between individuals 20-39 years (53.9%) and 40-64 years (46.1%). Overall more individuals with metabolic syndrome were in the 40-64 years of age category, and a higher percentage of women (73.2%) with metabolic syndrome than men (68.9%) with metabolic syndrome fell in the 40-64 year age category. The reason for this is unknown. Men with metabolic syndrome may have a higher mortality rate in their younger years or women develop more characteristics as they grow older. More research is needed to explore what factors are present in relation to age and gender that make men or women more at risk for developing metabolic syndrome.

This research represented almost 300,000 women and 400,000 men with metabolic syndrome between the ages of 20-39 years of age. Given the rising incidence of type 2

diabetes, further research on primary and secondary prevention strategies in younger individuals with metabolic syndrome should be given consideration. Risks for metabolic syndrome increase in accordance with age for men and women. In spite of the age parameters delineated in this study, advanced age remained a significant predictor for the presence of metabolic syndrome.

A family history of cardiovascular disease was statistically significant across the analyses. Obtaining a family history of cardiovascular disease is important in obtaining risk assessment for metabolic syndrome. However, a larger percentage of individuals with metabolic syndrome had no family history of cardiovascular disease. Not having a family history of cardiovascular disease does not appear to eliminate the risk for metabolic syndrome. In the future, having a family history of metabolic syndrome may be equally important in the surveillance of metabolic syndrome in populations at risk.

An individual's past medical history of cardiovascular disease remained statistically significant throughout the analyses. Individuals without a past medical history of cardiovascular disease were 45% less likely to have metabolic syndrome (AOR = 0.55; CI:0.35-0.88). Women with diabetes are at an equivalent risk for cardiovascular disease as men without diabetes who already have cardiovascular disease. While younger women are less likely to experience cardiovascular disease, when they have evidence of cardiovascular disease they have a higher mortality rate than men of the same age (Vaccarino, et al., 1999). Cardiovascular disease reaches more gender equality in advanced years (Charney, 1999).

Given the high risk for cardiovascular disease in an individual with metabolic syndrome, it would be prudent for men and women to seek evaluation for the presence of cardiovascular disease. There were four times the proportion of men with metabolic syndrome and a past medical history of cardiovascular disease as compared to women with metabolic syndrome and a past medical history of cardiovascular disease. This is consistent with the literature in that only 1 in 17 women has had a cardiovascular event compared to 1 in 5 men by the age of 60 years (AHA, 1993).

While this study demonstrates what previous research has shown, that fewer younger women report cardiovascular disease, they are not exempt from developing it. More importantly, data from the National Registry of Myocardial Infarction showed that women younger than 50 years of age who were hospitalized for a myocardial infarction had a mortality rate twice that of men (Vaccarino, et al., 1999). This observation begs the question, do the women in the study population represent the survivors of myocardial infarctions but are unaware they have had a cardiovascular event? While women generally experience cardiovascular disease later than their male counterparts, women with diabetes, are equally at risk for a cardiovascular event as a man without diabetes and already has cardiovascular disease (NCEP, 2001). The National Ambulatory Medical Care Survey highlighted the fact that women were counseled less often than men on risk factors for cardiovascular disease (Vaccarino et al., 1999). Given that metabolic syndrome is a risk factor for cardiovascular disease, efforts geared to the more than one-half million women who are known to have

metabolic syndrome are essential to reduce morbidity and mortality associated with cardiovascular disease in women.

Strategies to reduce gender discrepancies in clinical practice include public awareness campaigns such as those initiated by the American Heart Association. Education on the risks of cardiovascular disease in women should receive equal attention among health professionals. Previous research has preceded launched initiatives in women and heart disease, therefore additional research is needed to discover whether these strategies have improved outcomes.

Environmental Factors

Geographic residence by metropolitan area was statistically significant in the regression model (AOR = 1.26 CI:1.04-1.53) but there were no statistically significant associations between residence and men and women with metabolic syndrome. Consistent with the literature, (Eberhardt et al., 2001) those who lived in an urban location were 26% more likely to have metabolic syndrome.

That a higher proportion of individuals living in an urban environment had metabolic syndrome may have more to do with socioeconomic development and opportunities in the United States. Individuals tend to migrate to larger cities where employment, housing and transportation needs are more easily attained. Lifestyle and dietary habits in an urban area may be linked to the development of metabolic syndrome.

Annual household income was a statistically significant factor in the analysis of metabolic syndrome and associated factors. Individuals who reported an annual household income that was equal to or greater than $20,000 were 26% less likely (AOR = 0.74 CI:0.60-0.92) to have metabolic syndrome. There is a proportionately higher prevalence of chronic disease when income, occupation and education are analyzed (Lantz, House, Leprowski, Williams, & Chen, 1998). Findings from this analysis support the literature with respect to income. Financial constraints negatively impact health. Considerations such as living conditions, adequate nutrition, and safe employment must be addressed in future research. Economic inequities and their relation to higher morbidity and mortality are evident in prevalence studies (Armstrong, Barnett, Casper & Wing, 1998). While women live longer than men, many women have fewer economic assets (Wamala, et al., 1999). Economic inequities affect both men and women. However, women suffer a disparate economic burden coupled with an inevitable higher risk for poor health.

Similar results were found with education. Individuals with a high school education or higher were 61% less likely (AOR = 0.39; CI:0.21-0.71) to have metabolic syndrome. This study confirms a study by Wamela, et al. (1999) that a lower level of education correlated with a higher risk for metabolic syndrome. The Wamela, et al. 1999) study used the WHO definition for metabolic syndrome in a study population of 300 healthy women between the ages of 30–65 years of age. This study used the ATP

III definition with a more robust sample of 10,134 individuals and had similar results for men and women.

Health Behaviors

This study found that the less active a participant was, the more likely they were to have metabolic syndrome. Individuals who were less active were 67% more likely to have metabolic syndrome (AOR = 1.67; CI:1.36-2.06). Obesity and physical inactivity are modifiable risk factors linked to metabolic syndrome. Impacting lifestyle choices would intuitively reduce the development of metabolic syndrome.

Habitual physical activity reduces the risk of developing a number of chronic conditions, particularly diabetes and cardiovascular disease (DPP, 2002; Depres & Lemarche, 1993). The less physically active a person is, the higher their risk for diabetes and cardiovascular disease (Haapanen et al., 1997; Mansone, Colditz, Stamfer, Williett, Krowlewski, et al., 1991). Women of ethnic minorities are twice as likely to be physically inactive as Caucasian women (Crespo, Keteyian, Heath, & Sempos, 1996; Hahn, Teutsch, Franks, Chang, & Lloyd, 1998).

Increasing physical activity may decrease the risk of metabolic syndrome by maintaining weight and reducing body fat. Unfortunately, increasing daily physical activity appears to be a difficult challenge for many individuals. Theoretically, the influence of technology has negatively impacted our level of activity. Industry sponsored health clubs, and programs such as the 10,000 step program sponsored by the

American Diabetes Association are examples of efforts to increase daily physical activity.

Lack of exercise and obesity have contributed to the growing incidence of type 2 diabetes in youth. School and community sponsored programs are one avenue for improving the health of our nation's youth. Health beliefs were not measured in this study. Qualitative research concerning beliefs and attitudes toward adopting healthy lifestyles is needed.

Health Care Services

Individuals who do not have a usual source of health care are 25% less likely to have metabolic syndrome (AOR = 0.75; CI:0.59-0.96). This may be due to ignorance of symptoms of metabolic syndrome or access issues to health care services. Many women have a usual source of health care. More men (21.8) reported that they did not have a usual source of health care than women (12.8%). This finding suggests that while men are at risk for metabolic syndrome, not having an identified source of health care did not produce an additive risk. In contrast, women were proportionately more likely to have an identified source of health care and were 30 % less likely to have metabolic syndrome. More qualitative and quantitative research concerning health care utilization by men and women with regard to general medical care are warranted.

Women have suffered disadvantages within the health care system. In an analysis of management of chest pain in men and women, Schulman, et al. (1999) demonstrated that African American women were less likely than Caucasian men to be referred for cardiac

catheterization. Whether a woman has a designated health care provider is not sufficient enough information to conclude that women are receiving adequate health care services. More research is needed concerning the access and utilization of health care services to men and women.

Frequency of health care contacts was significant in the bivariate analysis. Women (86.1%) with metabolic syndrome made more frequent contacts to a health care provider than men (71.6%) with metabolic syndrome ($X^2 = 171.97$; $p = .001$) yet failed to show statistical significance in the regression analysis. There is no information in the survey data as to the nature of the health care "contacts." They may have been face-to-face contacts or by telephone. Potential explanations for less frequent contacts could have been due to a lack of transportation, employment responsibilities or financial barriers. Women make more health care visits for childbearing concerns alone. Although women have historically made more health care visits to health professionals, women's health problems are not always treated as aggressively as they could be (Ayanian, Epstein, 1991). As noted earlier, while women utilize health care services more frequently, they receive less counseling on preventive health practices (Bertakis et al., 2000). Areas for future research would include further exploration of the quality of health care services for women and more specifically, evaluation for gender differences in the adoption of clinical care guidelines.

While health insurance was not significant in any of the analyses, it did have a statistically significant interactive effect with education. If an individual had insurance

but had less than a high school education (AOR 0.70; CI 0.49-0.98) they were 30% less likely to have metabolic syndrome. Given that participants 65 years of age have access to Medicare in the U.S., the variable of health insurance may have produced different results had individuals over the age of 65 were included in the study. In addition the elderly experience more chronic disease as a group, which may have affected frequency of health care contacts.

Health promotion requires health care services be available, accessible, and adequate to have a positive influence on outcomes. Findings within the health care service domain were not statistically significant. Further exploration as to the actual use of services and the quality of services is essential to better understand the impact of health care services on metabolic syndrome.

Study Limitations

Although the NHANE survey is voluminous, there were measures that were not collected that may have been beneficial to the study. The lack of additional variables contributed to the low R^2 of 0.9 leaving many of the factors that could explain the prevalence of metabolic syndrome unmeasured. For example, dietary habits, as well as a more detailed description of health care services, would be important inclusion variables for analysis.

Another limitation of this study is the lack of consensus on a definition and intervention strategy for metabolic syndrome. The ATP III definition is used in this study. Other definitions may have produced different results. The ATP III is the most

conservative criteria available, is fairly easy to evaluate in clinical practice, and has been used in previous studies with similar results (Ford, Giles & Dietz, 2002; Park et al., 2003; Wampala et al., 1999). However, a lack of consensus in the past has limited research efforts in establishing consensus guidelines for clinical practice. Achieving consensus on the definition would aid clinicians in better diagnosing those at risk for metabolic syndrome.

Proxy variables were used to measure certain characteristics when more specific information may have been more useful. The creation of dichotomous variables such as income, education and health care services and their designated levels of measurements may have limited the results. Socioeconomic status, level of education and income are disproportionately lower among ethnic minorities than in Caucasians. This fact presupposes a confounding variable of ethnic minorities, health insurance coverage and household income. There is the potential to overestimate the impact of ethnic minority status on metabolic syndrome. Socioeconomic factors were controlled for in the regression analysis. In a study by Winkleby et al. (1998) which used the NHANES data, socioeconomic status alone did not explain the disproportionate burden of cardiovascular risk factors in women of ethnic minorities.

The use of self-report survey data is another limitation of this study. All of the clinical data were measured, but many of the other characteristics were self-reported at a given point in time. Despite these limitations, the corroboration of results from

previous studies may be useful in translation to clinical practice. The next section will provide observations for clinical practice and future research.

Implications for the Future

If left untreated, the sum impact of metabolic syndrome has the potential for far greater morbidity and mortality than its component parts. The clinical characteristics that make up metabolic syndrome, hyperglycemia, hypertension, central obesity, and dyslipidemia are all positively influenced by healthy lifestyles, which include a low fat diet and habitual exercise. Social, cultural and psychological differences must be considered in planning long term intervention strategies.

Barriers to adopting healthy lifestyles include the following potential solutions. Perceived susceptibility of disease can impact whether individuals adopt preventive care strategies. A concerted effort is needed to increase awareness of the factors that define metabolic syndrome. More public awareness of the impact of lifestyles, specifically, obesity and inactivity, on metabolic syndrome and its inherent health risks are a positive step toward reducing the incidence of metabolic syndrome.

This study and others have looked at data obtained between 1988-1994. NHANES 1999-2000 is now available. Given the increasing incidence of obesity and diabetes, the prevalence of metabolic syndrome has likely increased as well. Analyzing data from currently available and future NHANE surveys may provide even more interesting results.

Inadequate knowledge of prevention strategies by health care professionals or individuals may limit advice given to those at risk for metabolic syndrome. Primary care providers need a better grounding in healthy lifestyles, specifically nutrition and exercise. Contact with health professionals is essential in delivering information on preventive measures. Therefore, access to health care information and professionals is a crucial component to successful delivery of health promotion messages. Although this study demonstrated that there were frequent health care contacts in those with metabolic syndrome, the survey was limited in that the context of health care contacts was unavailable. A prospective qualitative study may elucidate interactions that are associated with successful outcomes in counseling patients on healthier lifestyles. There has been progressively limiting reimbursement to health care providers for counseling patients. A mechanism for compensation of health professionals for providing this expert advice to clients may improve comprehensive counseling.

There is a low priority and inadequate funding for prevention programs among institutions and government. Dissemination of research findings to clinical practitioners and the impact of prevention programs are essential to making a change in policy from one of treatment and recovery to prevention. In addition, a vested interest by industry leaders to promote healthier lifestyles through marketing and advertising would benefit communities. Highlighting the costs in terms of morbidity related to metabolic syndrome, and potential loss of productivity in the workforce adds an economic component to motivate private industry in assisting with a national effort for supporting

healthy lifestyles. Thus, this research is important to public officials, pharmaceutical companies, marketing and advertising personnel, as well as the general public.

Unfortunately, the economic benefits of pharmaceuticals as therapies de-emphasize the preventive care efforts needed to reduce the incidence of metabolic syndrome. Although treatment for diabetes and cardiovascular disease is improving, the public needs to be aware that the quality of life that can be expected without disease is superior to having disease.

Intangible long term benefits in a society that embraces short term results may reduce the potential for front end financial and individual efforts (De Courten, McCarty, & Zimmet, 1999). It is more difficult to subscribe to a healthy lifestyle in a society in which technology has circumvented any concerted effort to commit to a healthier diet and exercise for its members. In an era of an ever-increasing cost of living, individuals are pressed to exchange work hours for time spent on personal health.

Conclusions

Limiting women's health to their reproductive status effectively limits the acknowledgement of a gender specific response to shared medical conditions. Results from this study should assist in the design of public health policy, clinical practice, and prevention programs for the screening and treatment of women at high risk for metabolic syndrome. Given the high risk for metabolic syndrome in African American women and Mexican American women, a culturally diverse and sensitive health promotion program would be a foremost consideration in program planning.

Population-based prevention programs must be a collaborative effort between health professionals and the community. A population-based strategy would address aspects of cultural and community life to ensure relevance and commitment by the community.

Metabolic syndrome is an important precursor in the clinical progression of diabetes and cardiovascular disease. Models for practice and intervention for metabolic syndrome are not developed. More prospective studies that address outcomes based on interventions are warranted.

Although a similar proportion of men and women have metabolic syndrome, women are less likely to develop metabolic syndrome while controlling for other factors. Individual characteristics, such as advanced age, ethnic minority status, a positive family history of diabetes and a personal history of cardiovascular disease are important considerations in the evaluation for metabolic syndrome. Socioeconomic factors such as, a lower income, a lower level of education and urban residence was associated with metabolic syndrome. Clinicians need to be more aware of factors that signify a risk for disease development and progression.

Identification of individuals with metabolic syndrome is a critical first step in the implementation of primary and secondary prevention efforts to those who are at greatest risk for disease. Further exploration of which factors may present the greatest risk for particular groups is a reasonable step toward targeted interventions. Those with metabolic syndrome are candidates for aggressive evaluation of cardiovascular disease using advanced technologies. Stratification of risk for metabolic syndrome would assist

in deciding whether the focus should be on education and supportive lifestyle changes or more aggressive medical management of blood pressure or both.

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Appendix A

Correlation Matrix

	Metabolic Syndrome	Non-Hispanic White	Non-Hispanic Black	Mexican American	Other	Gender	Age	Family History of Diabetes	Family History of CVD	Past Medical History of CVD	Metro	Region	Household Income	Education	Activity	Tobacco	Source of Healthcare	Frequency of Healthcare	Health Insurance
Metabolic Syndrome	1.000																		
Non-Hispanic White	.019	1.000																	
Non-Hispanic Black	-.062	-.480	1.000																
Mexican American	.046	-.498	-.426	1.000															
Asian/Native American	-.011	-.159	-.136	-.141	1.000														
Gender	-.025	-.009	-.037	.055	-.020	1.000													
Age	-.272	-.133	.055	.090	-.011	-.007	1.000												
Family history of diabetes	.099	-.011	.023	.011	-.050	-.118	-.014	1.000											
Family history of CVD	.033	.107	-.043	-.055	-.031	-.058	.002	.112	1.000										
Past medical history of CVD	.073	-.017	-.009	.027	-.002	.052	-.086	.003	.049	1.000									
Metro	-.060	-.193	.075	.079	.110	.009	.037	-.050	-.044	-.071	1.000								
Region	-.028	.208	.177	-.415	.056	-.019	-.051	.007	.029	-.013	.039	1.000							
Household Income	.037	-.287	.123	.174	.006	-.027	.082	-.018	-.008	.039	-.043	-.052	1.000						
Education	.102	-.256	-.072	.335	.007	.048	-.099	-.039	-.031	.051	-.023	-.144	.328	1.000					
Activity	-.069	.043	.030	-.069	-.012	.094	-.062	-.017	.005	.000	.016	.030	-.089	-.103	1.000				
Tobacco	-.028	.013	.078	-.077	-.033	.120	.028	-.014	.056	.005	-.034	.053	.122	.097	-.040	1.000			
Source of healthcare	.076	.108	.045	-.156	-.003	-.190	-.159	.083	.028	.042	-.075	.085	-.132	.098	.019	-.071	1.000		
Frequency of contacts	-.046	-.085	-.058	.143	.005	.199	.070	-.056	-.031	-.026	.004	-.080	.086	.088	-.004	.059	-.340	1.000	
Health insurance	.010	.209	.088	-.291	-.030	-.051	-.128	.028	.020	.011	-.035	.158	-.346	.267	.059	-.056	.282	-.204	1.000

Appendix B

Research Table

STUDY	PURPOSE	METHODS	RESULTS
Cardiovascular Risk Reduction – Hypertension			
Hypertension in Diabetes Study (UKPDS 38 - HIDS) (1998)	Effect of tight blood pressure control on diabetes related complications	RCT of 1,148 subjects with type 2 diabetes (637 men and 511 women)	Lowering blood pressure reduced the risk of developing microvascular complications
Heart Outcome Prevention Evaluation (HOPE) (2000)	Effect of blood pressure reduction on cardiovascular events in high risk patients	9,297 subjects (6,817 men and 2,480 women)	Intervention with ramipril reduced cardiovascular morbidity and mortality
Cardiovascular Risk Reduction – Cholesterol			
Scandinavian Simvastatin Survival Study (4S) (1994)	Effect of simvastatin on reducing cardiovascular mortality in persons with average cholesterol levels and previous MI	4,444 subjects (3,617men and 827 women) with a cohort of 202 subjects with diabetes	Intervention with simvastatin reduced cardiovascular mortality to an even greater degree in diabetics than in nondiabetics
Cholesterol and Recurrent Events Study (CARE) (1996)	Effect of pravastatin on reducing cardiovascular events	4,159 subjects (3,583 men and 576 women)	Intervention with pravastatin reduced cardiovascular events. Effect from drug treatment was greater among women

Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS) (1998)	Effect of lovastatin on reducing a first coronary event	6,605 subjects (5,608 men and 997 women)	Intervention with lovastatin reduced the relative risk of a first coronary event
Heart and Estrogen/Progestin Replacement Study (HERS) (1998)	Effect of hormone replacement therapy in reducing cardiovascular events	RCT of 2,763 women	No difference
Postmenopausal Estrogen/progestin Intervention trial (PEPI) (1995)	Effect of hormone replacement therapy in risk reduction of cardiovascular events	RCT of 875 women	HRT conferred a benefit by improving lipids-unopposed estrogen most cardioprotective
Estrogen Replacement Angiographic Study (ERA) (2000)	Effect of hormone replacement therapy in reducing cardiovascular events	RCT of 309 women	No difference
Cardiovascular Risk Reduction – Diabetes			
Diabetes Control and Complications Trial (DCCT) (1993)	Effect of glucose control on diabetes related complications	RCT of 1,441 subjects with type 1 diabetes	Lowering blood glucose reduced the risk of developing microvascular complications
United Kingdom Prospective Diabetes Study (UKPDS) (1998)	Effect of glucose control on diabetes related complications	RCT of 5,102 subjects with type 2 diabetes	Lowering blood glucose reduced the risk of developing microvascular complications

Nurses' Health Study	Prospective study of health related activities and conditions in women	Serial Survey of 121,700 female nurses	Obesity and lack of exercise were significant predictors of the development of diabetes
Diabetes Prevention Study (2001)	Effect of positive lifestyle on progression of IGT to diabetes	RCT 522 subjects	Delayed progression to disease by 58%
STOP-NIDDM Trial (2002)	Effect of medication (acarbose) on progression of IGT to diabetes	RCT 1,429 subjects with impaired glucose tolerance	Delayed progression to disease by 25%
San Antonio Heart Study (1991)	Prospective study of risk factors in the development of cardiovascular disease	RCT 1,125 subjects - approximately 50% Mexican American and 50% non-Hispanic white	Correlated cluster of risk factors "Syndrome X" as prevalent and predictive of cardiovascular disease
Paris Prospective Study (1991)	Prospective study of risk factors in the development of cardiovascular disease	7,028 males	Correlated cluster of metabolic abnormalities "Syndrome X" as prevalent and predictive of cardiovascular disease

Atherosclerosis Risk in Community Study (ARIC) (2000)	Prospective analysis of athersclerotic disease	15,792 subjects 3,524 African Americans.	Persons with hypertension had a greater risk of developing diabetes. Confirmed an association with metabolic risk factors called "Syndrome X" and an increased risk for cardiovascular related deaths. African Americans had a greater number of metabolic abnormalities associated with Syndrome X than non-Hispanic whites.
Quebec Cardiovascular Study (2000)	Prospective study of metabolic risk factors in the development of cardiovascular disease	287 males	The metabolic triad was predictive for cardiovascular disease

Vita