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After Controlling for Other Risk Factors, to What Extent Does the Level of Parity Account for the Differences in the Probability of Developing Diabetes Mellitus?

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AFTER CONTROLLING FOR OTHER RISK FACTORS, TO WHAT EXTENT DOES THE LEVEL OF PARITY ACCOUNT FOR THE DIFFERENCES IN THE PROBABILITY OF DEVELOPING DIABETES MELLITUS?

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AFTER CONTROLLING FOR OTHER RISK FACTORS, TO WHAT EXTENT DOES THE LEVEL OF PARITY ACCOUNT FOR THE DIFFERENCES IN THE PROBABILITY OF DEVELOPING TYPE II DIABETES MELLITUS?

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ABSTRACT

Diabetes mellitus is a serious problem for many Americans. The prevalence of diabetes mellitus in the U.S. is 7.0%, which is approximately 20.8 million of the population (Centers for Disease Control and Prevention [CDC], National Diabetes Facts Sheet, 2003). Of the 20 million people with diabetes in the United States, half are women. Minority and ethnic groups are the hardest hit by type 2 diabetes; the prevalence is at least 2-4 times higher among African American and Hispanic women than among White women (U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2005). In peer reviewed literature, both modifiable and non-modifiable risk factors were linked to type 2 diabetes. The purpose of this study is to answer the question: After controlling for other risk factors, to what extent does the level of parity account for the differences in the probability of developing type 2 diabetes mellitus? To further examine this issue, a secondary data analysis was performed utilizing the data from The National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study (NHEFS) (NCHS, 2000). The NHEFS is a national longitudinal study that was jointly initiated by the National Center for Health Statistics and the National Institute on Aging in collaboration with other Public Health Service agencies. It was designed to investigate the relationships between clinical, nutritional, and behavioral factors. Cox proportional hazards regression analysis indicated that there

were no statistically significant relationships found between changes in parity over time and type 2 diabetes mellitus after controlling for other variables including demographic characteristics, reproductive history, physiological history, and interaction variables. Therefore, the results suggest that there is no association between parity and the subsequent incidence of type 2 diabetes mellitus.

DEDICATION

I would like to dedicate this dissertation to my family who has given me their unconditional love and support throughout the dissertation writing process and to the memory of my loving uncle, Sergeant Leonard Williams, who will always be in my heart.

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TABLE OF CONTENTS

LIST OF TABLES

Table

LIST OF FIGURES

Figure

DEFINITION OF TERMS

1. Acanthosis nigricans: is a brown to black, poorly defined, velvety hyperpigmentation of the skin, usually present in the posterior and lateral folds of the neck, the axilla, groin, umbilicus, and other areas. The most common cause would be insulin resistance, usually from type 2 diabetes mellitus
2. Acidosis: too much acid in the body; acidosis is associated with diabetic ketoacidosis, lung disease, and severe kidney disease.
3. Acute: describes something that happens suddenly and for a short time. Opposite of chronic.
4. Adipose tissue: combination of fat cells.
5. Atherosclerosis: A process of progressive thickening and hardening of the walls of medium-sized and large arteries as a result of fat deposits on their inner lining.
6. Autonomic neuropathy: Disease of the nerves affecting mostly the internal organs such as the bladder muscles, the cardiovascular system, the digestive tract, and the genital organs. These nerves are not under a person's conscious control and function automatically (autonomically).
7. Blood glucose: the main sugar found in the blood and the body's main source of energy. Also called blood sugar.
8. Chronic: describes something that is long-lasting. Opposite of acute.

9. Diabetes mellitus (DM): a condition characterized by hyperglycemia resulting from the body's inability to use blood glucose for energy. In type 1 diabetes, the pancreas no longer makes insulin and therefore blood glucose cannot enter the cells to be used for energy. In type 2 diabetes, either the pancreas does not make enough insulin or the body is unable to use insulin correctly.
10. Diabetic acidosis: an emergency condition in which extremely high blood glucose levels, along with a sever lack of insulin, result in the breakdown of body fat for energy and an accumulation of ketones in the blood urine. Signs of DKA are nausea and vomiting, stomach pain, fruity breath odor, and rapid breathing. Untreated DKA can lead to coma and death.
11. Diabetic ketoacidosis: dangerously high levels of ketones. Ketones are acids that build up in the blood. They appear in the urine when your body doesn't have enough insulin. Ketones can poison the body. They are a warning sign that your diabetes is out of control or that you are getting sick.
12. Diabetic retinopathy: diabetic eye disease; damage to the small blood vessels in the retina. Loss of vision may result.
13. Direct costs: costs associated with an illness that can be attributed to a medical service, procedure, medication, and any other service requiring payment.
14. Endogenous insulin: insulin produced inside the body.
15. Gestational diabetes mellitus (GDM): a type of diabetes mellitus that develops only during pregnancy and usually disappears upon delivery.
16. Hyperglycemia: excessive blood glucose.

17. Hypertension: a condition present when blood flows through the blood vessels with a force greater than normal. Also called high blood pressure.
18. Hypoglycemia: a condition that occurs when one's blood glucose is lower than normal. Also called an insulin reaction.
19. Incidence: number of newly diagnosed cases of a disease in a given group or population.
20. Indirect costs: Costs associated with an illness that occur because an individual cannot work at his or her usual job due to premature death, sickness, or disability; lost or forgone productivity, including being temporarily incapacitated due to bed days, lost workdays, permanent disability and premature mortality.
21. Inflammatory markers: Tumor Necrosis Factor (TNF-ά), Interleukin-6 (IL-6), and C-reactive protein (CRP) induce chronic-low grade inflammation which impairs insulin-stimulated glucose uptake.
22. Insulin: a hormone that helps the body use glucose for energy.
23. Insulin resistance: the body's inability to respond to and use the insulin it produces. Insulin resistance may be linked to obesity, hypertension, and high levels of fat in the blood.
24. Kidney failure: a chronic condition in which the body retains fluid and harmful wastes build up because the kidneys no longer work properly. Also called end-stage renal disease (ESRD).
25. Modifiable risk factors for type 2 diabetes: they can be changed and include things like diet, exercise and smoking.

26. Nephropathy: disease of the kidneys. Hyperglycemia and hypertension can damage the kidneys, preventing kidneys from removing waste and extra fluids from the bloodstream.
27. Neuropathy: disease of the nervous system.
28. Nonketotic hyperosmolar syndrome: an emergency condition in which one's blood glucose level is very high and ketones are not present in the blood or urine. Can lead to coma or death if untreated.
29. Non-modifiable risk factors for type 2 diabetes: cannot be controlled, such as age, gender, race and ethnicity and family history.
30. Nulliparity: no live births among women
31. Parity: the number of live births a woman has delivered.
32. Peripheral neuropathy: nerve damage that affects the feet, legs, or hands.
33. Peripheral vascular disease (PVD): a disease of the large blood vessels of the arms, legs, and feet.
34. Pre-diabetes: when blood glucose levels that are higher than normal but not yet diabetic. Many people with pre-diabetes go on to develop type 2 diabetes within 10 years.
35. Prevalence: the number of people in a given group or population who are reported to have a disease.
36. Prevention: Primary prevention is stopping or delaying the onset of diabetes. Secondary prevention is early identification of diabetes and/or stopping or delaying the onset of complications. Tertiary prevention is stopping disability from disease and its complications.

37. Type 1 diabetes: a condition characterized by high blood glucose levels caused by a total lack of insulin; develops most often in young people but can appear in adults.
38. Type 2 diabetes: a condition characterized by high blood glucose levels caused by either a lack of insulin or the body's inability to use insulin efficiently; develops most often in middle-aged and older adults but can appear in young people.

CHAPTER 1

THE PROBLEM

During recent years, the link between weight gain and type 2 diabetes as well as the established risk factors for weight gain and type 2 diabetes has become clear. However, one of the factors that has uncertainties is parity. The reported relation between parity and diabetes is not consistent. The research literature is inconclusive. One reason that the literature is inconclusive is because the studies have not been conducted in a manner that allows longitudinal monitoring and the control for mediating factors. Given the inconclusive nature of the data on childbearing/parity and the later development of type 2 diabetes mellitus, the examination of the potential association between change in parity over time and type 2 diabetes mellitus is warranted. Specifically, the research purpose reported here is to determine the relationship between change in parity and type 2 diabetes mellitus development after controlling for other risk factors such as age, race, education level, income level, miscarriages, alcohol use, smoking status, physical activity, fat intake, BMI, hypertension, cholesterol, race and parity interaction, and parity and BMI interaction.

Overview of Diabetes

Type 2 diabetes mellitus imposes a serious burden on the public health of the United States. It is the sixth leading cause of mortality due to disease in the United

States and the fourth leading cause among ethnic groups, leading annually to more than 300,000 deaths (Anderson & Smith, 2005). Type 2 diabetes mellitus is "a serious condition that can have a detrimental impact on health, quality of life, and life expectancy," according to Huang and Goran (2003, p. 38). Approximately 20.8 million people across all ages, which total 7.0% of the population, have diabetes mellitus (National Institute of Diabetes and Digestive and Kidney Diseases, 2005). An estimated 5-10% of Americans diagnosed with diabetes have type 1 diabetes and 90-95% have type 2 diabetes. According to the National Institute of Diabetes and Digestive and Kidney Diseases (2005), complications of diabetes included diabetic neuropathy, diabetic retinopathy, hypoglycemia, gastroparesis, amputation, kidney disease, heart disease, hypertension, stroke, dental disease, and urologic problems. Twenty percent of the deaths in the U.S. in 2002 were among people with diabetes over 25 years of age (Centers for Disease Control and Prevention (CDC), 2003). The risk of mortality for diabetics is twice the risk of mortality for non-diabetics (National Institute of Diabetes and Digestive and Kidney Diseases, 2005). Also, the risk of death associated with diabetes is greater for younger people ages 25-44 and women.

The prevalence of diagnosed diabetes has steadily increased in the United States, from 5.76 million cases in 1980 to 11.1 million cases in 2000 (National Institute of Diabetes, 2005) to 13 million cases in 2003 (CDC, National Diabetes Facts Sheet, 2003) to 20.8 million in 2005 (National Institute of Diabetes and Digestive and Kidney Diseases, 2005).

The prevalence of diagnosed diabetes varies among different populations. Of the 20 million people with diabetes in the United States, half are women (National Institute

of Diabetes and Digestive and Kidney Diseases, 2005). Minority and ethnic groups are the hardest hit by type 2 diabetes; the prevalence is at least 2-4 times higher among African American, Hispanic, American Indian, and Asian Pacific Islander women than among White women (U.S. Department of Health and Human Services, 2005). Data from studies of nationally representative samples indicate that, compared with their white counterparts, African American women are more likely to have or to develop diabetes (Cowie, Harris, Silverman, Johnson, & Rust, 2003). For women aged 45-64 years, the prevalence was 7.8% among whites and 15.4% among blacks (National Institute of Diabetes and Digestive and Kidney Diseases, 2005).

Diabetes Mellitus is a disorder that affects the way the body digests and metabolizes food for growth and energy. It is a life-long disease marked by high levels of sugar in the blood. Diabetes Mellitus is characterized by hyperglycemia which is produced by lack of endogenous insulin, resistance to insulin, or both. Insulin is a hormone produced by the pancreas to control blood sugar (U.S. Department of Health & Human Services, 2005). The development of diabetes mellitus occurs when glucose (sugar) enters the bloodstream. Glucose is a source of fuel for the body. The pancreas produces insulin. The insulin moves the glucose from the bloodstream into muscle, fat, and liver cells, where the glucose can be used as fuel. Most people with diabetes mellitus have high blood sugar.

Type 1 diabetes mellitus occurs when the body stops producing insulin or produces too little insulin to regulate blood glucose level. It comprises about 10% of total cases of diabetes in the United States. Type 1 diabetes is typically recognized in

childhood or adolescence. It used to be known as juvenile-onset diabetes or insulin-dependent diabetes mellitus.

In type 2 diabetes, relative insulin deficiency usually occurs because of resistance to the actions of insulin in muscle, fat, and the liver and an inadequate response by the pancreatic beta cell (Edelman, 1998). This abnormality results in decreased glucose transport in muscle, elevated hepatic glucose production, and increased breakdown of fat. At the simplest level, food consumed is broken down into glucose. The glucose then passes into the bloodstream, where it is used by cells for growth and energy. For glucose to reach the cells, however, insulin must be present. A combination of insulin resistance and an inability of the pancreas to maintain adequate compensatory insulin secretion will cause type 2 diabetes (Henry, 1996). Symptoms of type 2 diabetes include: urinating frequently (polyuria), increased thirst (polydipsia), weight loss, weakness and lethargy, acanthosis nigricans and diabetic ketoacidosis (Ritchie, Ganapathy, Woodward-Lopez, Gerstein, & Fleming, 2003). At least 90% of people with diabetes have type 2 diabetes. It is typically recognized in adulthood, usually after age 45 years. It used to be called adult-onset diabetes mellitus, or non-insulin-dependent diabetes mellitus. These names are no longer used because type 2 diabetes does occur in younger people, and some people with type 2 diabetes need to use insulin (Krentz and Bailey, 2005).

Gestational diabetes is a form of diabetes that occurs during the second half of pregnancy. Although gestational diabetes typically goes away after delivery, women who have gestational diabetes are more likely than other women to develop type 2 diabetes later in life (Buchanan et al., 1998).

Complications

There are major acute and long term complications of diabetes. These include hyperglycemia with acidosis and nonketotic hyperosmolar syndrome. The latter could be acute, and potentially life-threatening outcomes of diabetes (National Institute of Diabetes, 2005). Over a long period of time, hyperglycemia damages the retina of the eye, kidneys, nerves, and blood vessels. There are four major long-term diabetic complications: retinopathy, nephropathy, peripheral neuropathy and autonomic neuropathy. The following damages to the body can occur:

- Damage to the retina from diabetes (diabetic retinopathy) is a leading cause of blindness.
- Damage to the kidneys from diabetes (diabetic nephropathy) is a leading cause of kidney failure.
- Damage to the nerves from diabetes (diabetic neuropathy) is a leading cause of foot wounds and ulcers, which frequently lead to foot and leg amputations.
- Damage to the nerves in the autonomic nervous system can lead to paralysis of the stomach (gastroparesis), chronic diarrhea, and an inability to control heart rate and blood pressure with posture changes (National Institute of Diabetes 2005).

Diabetes accelerates atherosclerosis, or the formation of fatty plaques inside the vascular system, which can lead to blockages or a clot (thrombus), which can lead to heart attack, stroke, and decreased circulation in the arms and legs (peripheral vascular disease) (Abraira et al., 1997).

In the short run, diabetes can contribute to a number of acute (short-lived) medical problems. Many infections are associated with diabetes, and infections are frequently more dangerous in someone with diabetes because of the body's normal ability to fight infections is impaired. To compound the problem, infections may worsen glucose control, which further delays recovery from infections.

Established Pathophysiolical Link between Increased Weight Gain/Obesity and Type 2 Diabetes Mellitus

Researchers have established a pathway between increased weight gain/obesity and the development of type 2 diabetes mellitus. According to Caterson and Gill, (2002), Colditz, Willet, & Manson, (1995), Formiguera and Canton, (2004), and Kahn, Hull; and Utzschneider, (2006), the role of obesity in the pathogenesis of type 2 diabetes mellitus has long been recognized. The pathway is illustrated in Figure 1 consists of the following: increased weight gain/obesity, promotes increased secretion of inflammatory markers by adipose tissue (fat cells), yielding an insulin resistance state which in turn causes an impaired glucose tolerance state, which results in β-cell deterioration/ β -cell failure, and the development of type 2 diabetes mellitus. The pathway is described in the following paragraphs.

Studies such as the Nurses' Health Study, the Health Professionals Follow-up Study, and other research studies have observed that increased weight gain/obesity is predictive of developing type 2 diabetes mellitus (Carey et al., 1997; Chan, Rimm, Colditz, Stampfer, & Willett, 1994; Colditz et al., 1995; Field et al., 2001; Holbrook,

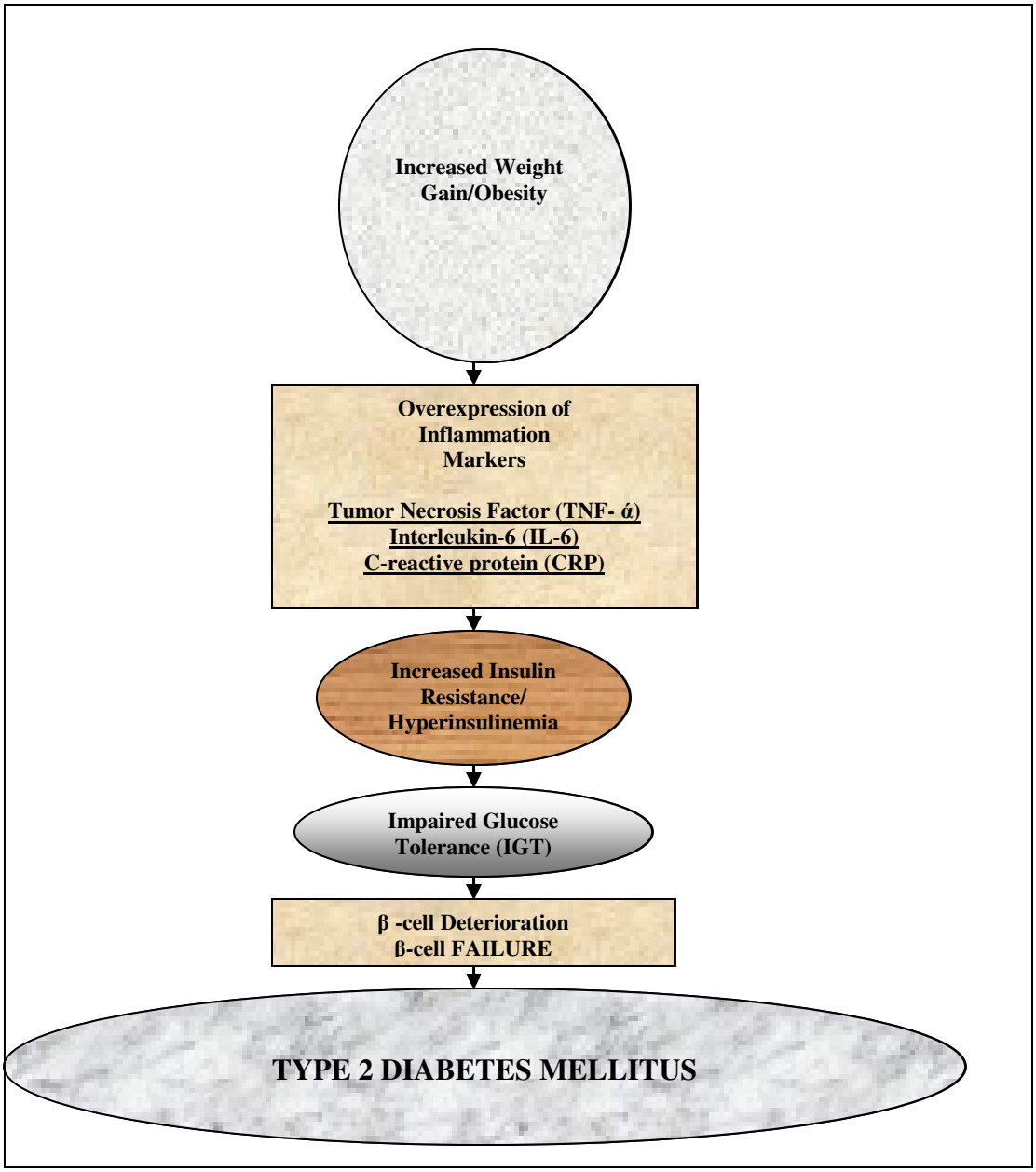

Figure 1. Model of Weight Gain/Obesity and Type 2 Diabetes Mellitus

Barrett-Conner, & Wingard, 1989). Obesity is characterized as an excess of adipose tissue (fat cells) (Calle & Kaaks, 2004; Kopelman, 2000). The adipose cells (fat cells) produce excessive amounts of free fatty acids, adipokines, and pro-inflammatory cytokines including TNF- α and IL-6 (Coppack, 2001; Fröhlich et al., 2000; Greenberg &

McDaniel, 2002; Mohamed-Ali et al., 1997; Moller, 2000). The over production of the pro-inflammatory cytokines such as TNF- α and IL-6 induce chronic-low grade inflammation which impairs insulin-stimulated glucose uptake and elevate plasma concentrations of an acute phase protein C-reactive protein (CRP) (Festa et al., 2000; Fröhlich et al., 2000; Ridker, Hennekens, Buring, & Fifai, 2000; Sattar & Greer, 2003). Elevated CRP concentration is an indicator of systemic inflammation (Festa et al., 2000; Fröhlich et al., 2000; Maachi et al., 2004; Sites et al., 2002; Yudkin, Stehouwer, Emeris, & Coppack, 1999). The over expression of the pro-inflammatory markers and chronic-low grade inflammation state contribute significantly to insulin resistance.

Insulin resistance is defined as the inability of cells or tissues to respond to normal levels or concentrations of insulin circulating in the body (Kadowaki et al., 2006; Shoelson, Lee, & Goldfine, 2006; Stephens, Lee, & Pilch, 1997; Weyer, Bogardus, & Pratley, 1999). The insulin resistant state seems to be a result of obesity and is known to be a major risk factor in the etiology of type 2 diabetes mellitus (Abbasi, Brown, Lamendola, McLaughlin, & Reaven, 2002; Boden, 1997Xu et al., 2003; Schulman, 2000). Many prospective epidemiological studies across various population groups indicate that type 2 diabetes frequently occurs after a progression of insulin resistance and a loss of insulin secretion (Ferrannini, 2005; Ferrannini, 2003; Kahn, 2003; Field et al., 2001). As a result of insulin resistance, the pancreas produces much more insulin than normal which leads to hyperinsulinemia. Reaven (1988) suggested in his Banting Lecture that insulin-stimulated glucose uptake and hyperinsulinemia are involved in the etiology and clinical course of type 2 diabetes. With further worsening of the insulin resistance state resulting in a markedly increased production of insulin

(hyperinsulinemia), the progression of impaired glucose tolerance (IGT) is categorized as the next stage associated with the natural history of type 2 diabetes mellitus (Despres, et al., 1995; Petersen & McGuire, 2005; Santomauro et al., 1999; Schulman, 2000).

According to Davies, Raymond, Day, Hales, & Burden, (2000); Dunstan et al., (2002); and The DECODA Study (2002); and Unwin and others (2002), IGT is an intermediate stage between normal glucose tolerance and overt type 2 diabetes mellitus. It can be identified by an oral glucose tolerance test in which blood glucose levels increase. They are greater than normal; however, not as great as individuals with type 2 diabetes mellitus. Fasting glucose levels are normal or slightly elevated. Literature indicates that individuals with IGT have an increased risk of type 2 diabetes mellitus. The diminishing pancreatic insulin secretion by the pancreatic β-cells in the IGT stage results in higher blood glucose levels which are toxic to β-cells. The results of the malfunctioning and/or failure of pancreatic β-cells lead to the deterioration of glucose homeostasis which ultimately leads to overt type 2 diabetes mellitus (Buchanan et al., 2000; Elbein, Hastedt, Wegner, & Kahn, 1999; Kahn & Foldfine, 1993; Unwin, et al., 2002; Tuomilehto et al., 2002;).

Association Between Childbearing/ Parity and Weight Gain

The pathway of the well established link between increased weight gain/obesity and type 2 diabetes has been reviewed in order to successfully develop a model to association between childbearing (parity) and increased weight gain/obesity which has an association with the development of type 2 diabetes mellitus. In a review of literature, ten studies

were conducted examining the relationship between parity and the development of type 2 diabetes. Four studies revealed a positive association with type 2 diabetes mellitus (Cheung, 2004; Kritz-Silverstein, 1989; Martin et al., 1984; Nicholson et al. 2006). Four studies revealed no association between parity and type 2 diabetes mellitus (Alderman et al., 1993; Boyko et al., 1990; Collins et al., 1991; Manson et al., 1992). One demonstrated a U- shaped association (increase of low and high parity increase type 2 diabetes) which increased the risk of type 2 diabetes (Simmons, 1992), and another study revealed an inverse relationship between decreased parity and type 2 diabetes (Hanley et al., 2002).

It has become clear during recent years that childbearing exerts important and lasting effects on women's health. Having children have been shown to affect later hormone secretion and other chronic diseases (Musey, Collins, Musey, Martino-Saltzman, & Preedy, 1987). A Swedish population-based study conducted by Villamor and Cnattinguis (2006) determined that weight gain during the time between pregnancies as well as pre-pregnancy weight gain is strongly associated with the risk of major maternal complications such as type 2 diabetes development.

Since there is a broad acceptance of the link between increased weight gain/obesity and the development of type 2 diabetes mellitus, the question arises, "To what extent does change in parity relates to the development of type 2 diabetes mellitus after controlling for other known risk factors"? Answering the research question leads to a brief overview of the pathophysiological process of type 2 diabetes mellitus development.

Figure 2 illustrates parity and weight gain and their association with type 2 diabetes mellitus development. Parity has been associated with the development of type 2 diabetes in middle-aged women through increased weight gain (Keppel & Taffel, 1993; Rookus, Rokebrand, Barema, & Deavrenbert, 1987; Smith, et al., 1994; Williamson et al., 1994; Wolf, et al., 1997). As seen in the literature, an interest in this association has come from a couple of things: a higher prevalence of type 2 diabetes development among women who have given birth in clinical studies (Kritz- Silverstein et al., 1989; Martin et al., 1984; Nicholson et al., 2006) and a pregnancy-induced insulin-resistant state that frequently results in the development of gestational diabetes (Beard, Fuster, and Annegers, 1984). Pregnancy may also lead to a long-term increase in body weight (Keppel & Taffel, 1993; Rookus, Rokebrand, Barema, & Deavrenbert, 1987; Smith, et al., 1994; Williamson et al., 1994; Wolf, et al., 1997), indirectly increasing the risk of type 2 diabetes.

In the literature, there have been other large prospective studies and one longitudinal study to determine if there is an association between parity and type 2 diabetes which revealed inconsistent findings (Boyko et al., 1990; Cheung, 2004; Collins et al., 1991; Kritz-Silverstein, 1989; Manson et al., 1992; Nicholson et al., 2006). In addition to the inconsistent findings in these studies, there were limitations in these studies in which certain variables were not available as well as limited statistical methods used during the analyses. Most of the studies identified utilized cross-sectional data.

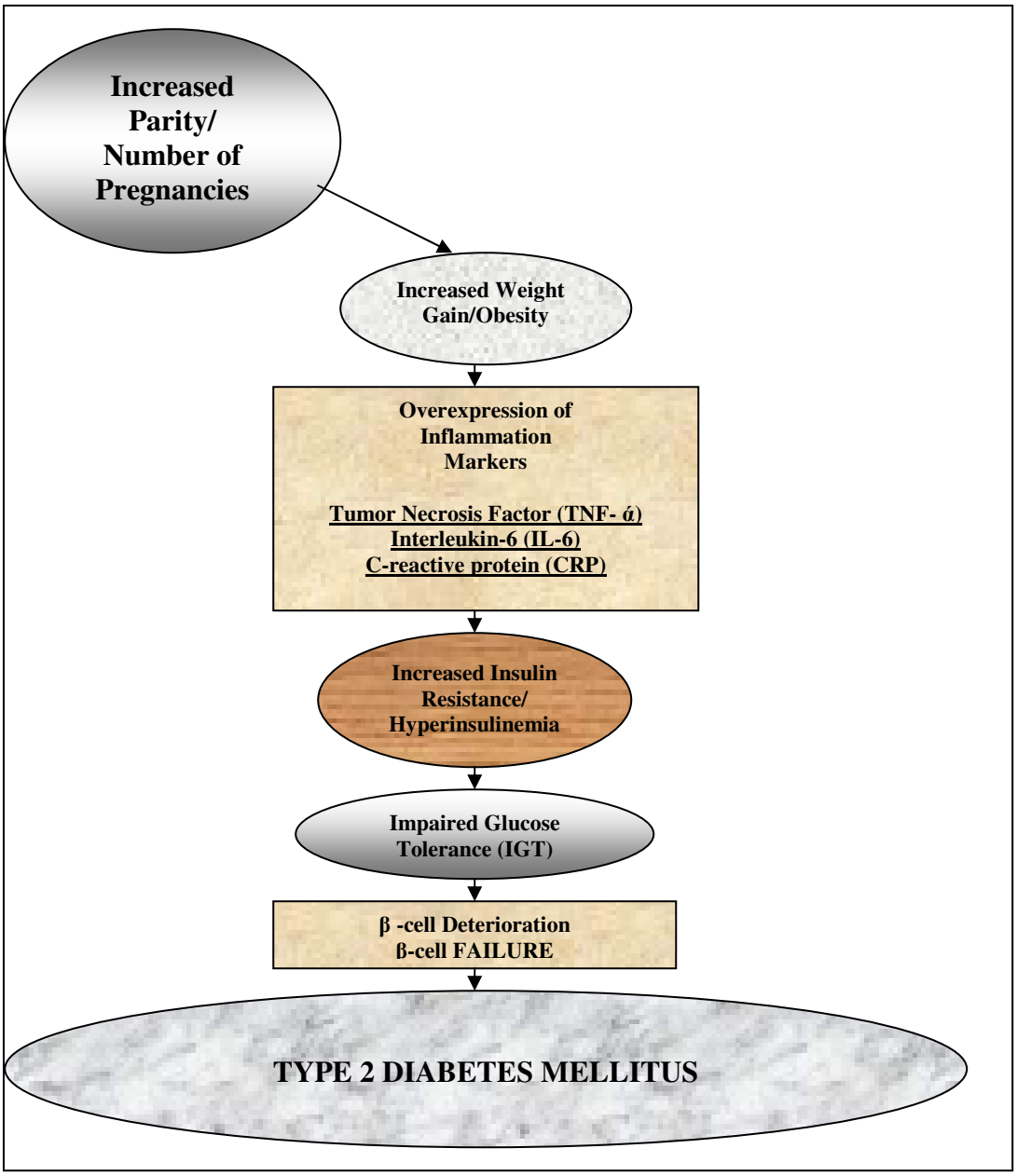

Figure 2. Model of the Physiologic Link Between Parity and Weight Gain/Obesity and Type 2 Diabetes Mellitus

There were three studies that found an association between parity and type 2 diabetes Cheung (2004), Kritz-Silverstein et al. (1989), Martin et al. (1984), and Nicholson et al. (2006) in which two of them controlled for age and or BMI, both of

which are important confounding factors. In the eight studies that have presented results adjusted for age and BMI, the findings have been highly inconsistent: two reported a positive relationship between parity and diabetes risk (Kritz-Silverstein, 1989; Nicholson et al., 2006), four found no effect (Alderman et al., 1993; Boyko et al., 1990; Collins et al., 1991; Manson et al., 1992), one demonstrated a U- shape association (increase of low and high parity increase type 2 diabetes) which increased the risk of type 2 diabetes (Simmons, 1992), and another study revealed an inverse relationship between decreased parity and type 2 diabetes (Hanley et al., 2002).

Nicholson and others (2006) performed a longitudinal analysis of data from the Atherosclerosis Risk in Communities study to examine the presence and strength of an association between parity and diabetes. Their results indicated a strong relationship between among women with five or more births. Most of the risk was due to sociodemographic factors and higher obesity, ascertained by responses to a questionnaire survey. Sociodemographic factors that were studied included: age, race, income, education, and family history. A prospective analysis was done on women without diabetes at baseline and a series of modeling was developed for the groups of parity.

Purpose

The purpose of the present study is to consider whether change in parity is associated with the subsequent development of type 2 diabetes mellitus. There is no doubt that there is an established link between weight gain and type 2 diabetes mellitus development. However, given the inconclusive nature of the previous research studies

and their varying methodological approaches, the examination of the potential association between change in parity over time and type 2 diabetes mellitus is warranted. The present study conducted a longitudinal analysis on whether change in parity is associated with type 2 diabetes mellitus development while controlling for mediating factors among women in the United States, using the NHANES I Epidemiologic Follow-up Study (NCHS, 2000). There have been over two hundred publications produced utilizing the rich data from the NHEFS. However, there has not been a study done utilizing the data to determine if there is an association between change in parity and subsequent type 2 diabetes mellitus development. Specifically, the research question examined the relationship between change in parity and type 2 diabetes mellitus development after controlling for other mediating factors such as age, race, education level, income level, miscarriages, alcohol use, smoking status, physical activity, fat intake, BMI, hypertension, cholesterol, race and parity interaction, and parity and BMI interaction, which included investigating the interaction of parity and race in relation to type 2 diabetes mellitus development and observing whether the interaction effect between parity and BMI had an influence on type 2 diabetes mellitus development. The following specific research question guided the approach to studying this general overall problem: (1) To what extent does change in parity account for the differences in the probability of developing type 2 diabetes mellitus after controlling for other risk factors?

Significance of the Research

Methodoligically, the present study is significant. Since this research is based on national data, its findings were representative of the U.S. population. Thus, the results were more generalizable than previous studies. There are few studies on the association of parity and type 2 diabetes mellitus that are based on national data such as the one used in this study. The present study also addresses the limitations of prior research studies. In other words, most of the reviewed studies on the relation of parity and type 2 diabetes mellitus were seen to suffer from the limitations of smaller sample sizes or have been carried out with special groups selected on the basis of characteristics such as race. For example, Kritz-Silverstein, Barrett-Conner, & Wingard (1989) collected data among 1186 upper-middle-class Caucasian women in southern California as part of the Rancho Bernardo Heart and Chronic Disease Survey. Simmons (1992) only studied South Asian and European women during The Coventry Diabetes Study while Martin, Hopper, Dean, Campbell, and Hammond (1984) studied 396 Maltese-born Melbourne residents of Victoria and Italian-born residents of Victoria. Collins, Dowse, and Zimmet (1991) studied five population groups: Micronesians of Kiribati and Naurau, Melanesians, migrant Asian Indians, and mixed-ethnic population of Mauritius.

Although some studies used national data to carry out their investigations, they were cross-sectional rather than longitudinal which prevents temporal sequencing which is necessary to establish an association between the exposure and outcome variables. For example, Boyko, Alderman, Keane, and Baron (1990) used data from the Second National Health and Nutrition Examination Survey to study self-reported health status

among American women while Hanley and others (2002) used the Sandy Lake Health and Diabetes Project population-based cross-sectional study.

Oleckno (2002) defines cross-sectional studies as those studies which focus on a broad sampling of different persons of different ages, races different educational and income levels, and other related factors of a single population at a single point in time. Longitudinal studies observe one sample several times on the dependent variable at different age levels and, therefore, by definition, at different times of measurement.

Wiley and Camacho (1990) point to the fact that cross-sectional data are unable to reveal the direction of the relationship between personal health practices and health status, gives reason to suspect that the least part of association between such behaviors as exercise, height/weight ratios, and concurrent health status results from the effects of poor health on these factors rather than the reverse. That is, it is not clear whether good personal health practices preceded good health or visa versa. This kind of problem as noted by Wiley and Camacho (1980) can be solved or eliminated by longitudinal data.

Inherent limitations of cross-sectional studies exist; however, the major limitation of most cross-sectional studies is the temporal sequence between exposure (parity level) and outcome (type 2 diabetes mellitus). Temporal sequencing is necessary to establish an association between the exposure and outcome variables. This is seen in longitudinal data analyses (Oleckno, 2002). While the cross-sectional studies provide important and useful information, it seems as though the association of parity and type 2 diabetes mellitus is not completely understood. Therefore, the need to continue to study the effect of parity on type 2 diabetes mellitus utilizing longitudinal data is warranted.

Large scale health surveys like the first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study (NHEFS) offer the ability to minimize selection bias in the estimation of associations between variables in a sampled target population. When interest focuses on the association of a risk factor and the development of a disease, however, the inference from a single cross-sectional survey is somewhat limited. One can examine the association between a risk factor and the development of a disease much better with longitudinal follow-up that records the development of the disease. The NHEFS national population based data was created by the CDC's National Center for Health Statistics (NCHS). In 1970, the U.S. Secretary of the Department of Health, Education and Welfare (now the Department of Health and Human Services) called for a task force to develop a national surveillance system to conduce clinical observations, professional assessments and record dietary intake patterns. The product of this task force was the NHANES I, II, III, IV, and the NHEFS. There have been four waves of the NHEFS, 1) 1982-1984, 2) 1986, 3) 1987, and 4) 1992. There was also a Hispanic Health and Nutrition Examination Survey conducted from 1982-1984 to capture data on the Hispanic population in the U.S. The NHANES has effectively provided longitudinal surveillance data regarding the health status on the U.S. population since 1971 (CDC, 2003).

The NHEFS is a large national longitudinal study that was jointly initiated by the National Center for Health Statistics and the National Institute on Aging in collaboration with other Public Health Service agencies. It was designed to investigate the relationships between clinical, nutritional, and behavioral factors. The NHEFS is the first U.S. investigation of its size and scope to follow the same group of people over a period

of approximately twenty years (Cox, et al., 1997). The NHEFS dataset is a nationally representative census based geographic sample of non-institutionalized civilian U.S. population NHANES I aged 25-74 years who completed the medical examination. It contains anthropometric data, diet recall, self reported medical history, clinical measurements, health status at examination, exposure information and DNA samples. There have been eight surveys conducted since 1960. Most analysts of the NHEFS are interested in assessing the relationship between a set of risk factors measured at baseline and some out come event (NCHS, 2000). The follow-up and data-collection rates in the NHEFS have been very high. Ninety-six percent of the study population has been successfully traced at some point through the 1992 follow-up. Tracing rates for each completed wave ranged from 90 to 94% and interview rates ranged from 91 to 96% of those traced. The three major objectives of the NHEFS are to study risk factors associated with morbidity and mortality, changes over time in participants' characteristics, and the natural history of disease and functional impairment.

Questionnaires were administered using household and telephone interviews. The 1982-1984 interview was administered during an in-house visit; whereas, the remaining years' interviews were administered via telephone. Only one person per household is represented in the sample questionnaire. The questionnaire included items on a variety of different subject areas (NCHS, 1997) seen in Table 1.

Table 1

Subject Areas in the NHEFS, 1992 Sample Questionnaire

	Items in the Sample Questionnaire	
Demographic, Health, and Behavioral Related Items		
	❖ Acculturation	❖ Kidney condition
	❖ Alcohol Use*	❖ Medical conditions
	❖ Audiometry	❖ Miscellaneous pain
	❖ Balance	❖ Physical activity and fitness*
	❖ Blood Pressure*	❖ Physical functioning
	❖ Cardiovascular disease	❖ Occupation
	❖ Demographic information*	❖ Oral health
	❖ Dermatology	❖ Osteoporosis
	❖ Diabetes*	❖ Respiratory health and disease
	❖ Dietary supplements	❖ Smoking and tobacco use*
	❖ Diet behavior and nutrition*	❖ Social support
	❖ Early childhood	❖ Tuberculosis
	❖ Female Medical History*	❖ Vision
	❖ Immunization	❖ Weight history*

Subject Areas with an asterisk (*) were included in this study

Theoretical Framework

The theory behind the analysis can be summarized by a conceptual framework by Sandra Black (2002) regarding risk factors for the development of diabetes. The model illustrates that social factors and demographic characteristics contribute to 1) behavioral factors, 2) genetic vulnerability, 3) psychological factors, and 4) clinical factors which contribute to the incidence of diabetes and diabetes related complications (Black, 2002). This model is similar to the Social Ecology Model (SEM) developed by McLeroy,

Bibeau, Steckler, and Glanz (1988) which is often applied when attempting to understand health issues.

The Social Ecology Model (SEM) provides a set of conceptual and methodological principles for organizing comprehensive, community-based, health promotion initiatives. The SEM is unique in that it takes into account the physical environment and its relationship to people at intrapersonal, interpersonal, organizational, community, and public policy levels. The ecological perspective on health promotion programs, as proposed by McLeroy, Bibeau, Steckler, and Glanz (1988), provides an excellent look at health promotion programs from a contextual perspective. It has implications to both explain health behavior and design related health promotion interventions. As a means to explain health behavior, the SEM approach forces one to look for the cause of a health issue or problem from multiple perspectives. Intra-personal, social and cultural, and physical environmental factors influence health behaviors and are a part of the social ecological models of health which were defined by Sallis and Owen (1997).

The SEM also addresses the socioeconomic, cultural, political, environmental, organizational, psychological, and biological determinants of health (Stokols, 1996). The conceptual model offers a model for the integration of multiple perspectives into the planning of interventions for behavior change. The theory also proposes that lasting behavior change requires programs that target multiple levels of influence (Emmons, 2000). There are levels of influence which include intrapersonal factors, interpersonal processes, institutional factors, community factors, and public policy (McLeroy, Bibeau, Steckler, and Glanz, 1988).

The intrapersonal factors consist of the person being able to change their behaviors which are influenced by knowledge, skills, beliefs, attitudes, and self-confidence (McLeroy, Bibeau, Steckler, and Glanz, 1988). Personal characteristics and behaviors are associated with the development of diabetes and obesity (Kaplan, Everson, & Lynch, 2000). Interpersonal processes consist of those who provide social support for the individual. They are family, friends, neighbors, and co-workers which play an influential role in the health behaviors of individuals (McLeroy, et al., 1988). There are also institutional factors which influence health behaviors of the individual which include schools, churches, and work places. They provide social support for behavior change and can significantly influence health and health behaviors (McLeroy, et al., 1988). The next level is community factors which consist of neighborhoods, businesses, and community centers. They are all associated with the influence on health and health behavior of an individual (McLeroy, et al., 1988). The final level is public policy which consists of local, state, and national levels. Public policy influences health and health behavior change through those regulatory channels (McLeroy, et al., 1988).

In the present study, the demographic factors and socioecological factors which were most remote helped to guide the development of the comprehensive model tested. There was no data available on depression, cognition, or genetic vulnerability. However, there was data on some behavioral factors and some clinical factors. Two different models were combined to develop the present study. One model was physiological and the other model was socioecological. The physiological model determined what was tested physiologically such as blood pressure, cholesterol level, and BMI. The socioecological model tested behavioral, demographic, and social factors such as parity,

ethnicity, economic status, physical activity, age, education, smoking status, drinking status, and fat intake. The combined model helped to determine a broader ecological perspective of the association of change in parity and subsequent type 2 diabetes mellitus development.

Determining the effect of the change in parity as a risk factor for the development of diabetes could contribute to defining more effective and specific strategies for decreasing the development of type 2 diabetes in women in the future. The ecological theories state that health is affected not only by the presence of environmental factors but also by the reciprocal relationship that exists among the environmental factors and health that impacts the health status of individuals. Health education awareness programs characterizing potential long-term consequences of the metabolic and lifestyle changes associated with pregnancy and the increased risk of diabetes could be developed and implemented. The interventions would target lifestyle changes (behavioral factors) such as proper diet and adequate exercise.

Overview of the Research Study

The report of this research is divided into different chapters. The first chapter is devoted to the statement of the problem, overview and background for the study, and significance for the research. The second chapter discusses the review of literature on what is currently known about the established pathophysioligical link between weight gain/obesity and type 2 diabetes mellitus and the relationships between parity, other health indicators and type 2 diabetes mellitus. Chapter three is devoted to methodology.

In chapter four, the results of the research study are reported. A discussion of the results for the study and implications for future research are presented in chapter five.

CHAPTER 2

LITERATURE REVIEW

This review of the literature examined studies concerning the prevalence of diabetes, indirect and direct costs of diabetes, the relationship between parity, established risk factors, the putative physiologic links between weight gain/obesity and type 2 diabetes mellitus, and the ethnic disparities in the development of type 2 diabetes. The factors examined in this study are parity, established risk factors, demographic characteristics, social effects, and behavioral factors which are identified in Black's (2002) diabetes framework.

This review is divided into four major sections. The first section is the general review of literature on type 2 diabetes mellitus. The second section is a review of those studies showing the association between parity and weight gain. The review of studies continue with (3) a review of those studies showing the relationship of other risk factors associated with the development of type 2 diabetes mellitus independent of weight gain, (4) a review of those studies revealing the relationships between parity and other health indicators and type 2 diabetes mellitus, (5) a comparison of epidemiologic and intervention studies regarding the association between parity and type 2 diabetes mellitus, and (6) a review of those studies showing the impact of race/ethnicity on the risk for type 2 diabetes mellitus. This section concludes with a summary of all of the reviewed studies provided in Table 2.

Diabetes Mellitus

The prevalence of diabetes is alarmingly high, and according to projections based on the U.S. Census Bureau, cases of diagnosed diabetes will steadily increase. The Census Bureau has approximated that there will be 39 million cases of diagnosed diabetes by 2050, implying an increase in diagnosed diabetes prevalence from 4.4% in 2000 to 9.7% in 2050 (Boyle et al., 2001). In the past two decades, the excess incidence of type 2 diabetes seen in African-Americans may be attributable to differences in the distribution of the risk factors, or the impact of the risk factors may have on ethnicity (Lipton, Liao, Cooper, & McGee, 1993). Data from studies of nationally representative samples indicate that, compared with their white counterparts, African American women are more likely to have or to develop type 2 diabetes (Cowie et al., 2003). For women aged 45-64 years, the prevalence was 7.8% among Whites and 15.4% among Blacks. Thus, African American women are more than 100% more likely to develop type 2 diabetes than Caucasian women (Lipton et al., 1993). According to the literature, a possible explanation for the disparity between African American women and Caucasian women is the racial differences in the known risk factors for type 2 diabetes such as adiposity/obesity, family history of diabetes, and socioeconomic factors (Lipton et al., 1993).

Another public health concern is the cost of diabetes, especially with such alarming prevalence projections. Based on the changing demographics, diabetes will cost $156 billion in 2010 and $192 billion in 2020 (American Diabetes Association (ADA), 2003). A burden is placed on the U.S. economy with diabetes related treatment. In 2002, diabetes cost an estimated $132 billion; these costs include both health care expenditures

and lost productivity. Diabetics spend twice as much per capita on direct medical expenditures compared to non-diabetics (ADA, 2002).

Established Physiological Links Between Weight Gain/Obesity and Type 2 Diabetes

As stated previously, researchers have established a pathway between increased weight gain/obesity and the development of type 2 diabetes mellitus. The model illustrates the various processes that an individual goes through during the pathophysiological process of type 2 diabetes mellitus development. They are: (1) increased weight gain/obesity, (2) increased secretion of inflammatory markers by adipose tissue (fat cells), (3) insulin resistance state, (4) impaired glucose tolerance state, (5) β-cell deterioration/ β -cell failure, and (5) the development of type 2 diabetes mellitus. Since there is a broad acceptance of the link between increased weight gain/obesity and the development of type 2 diabetes mellitus, the question arises, "How does increased parity relates to increased weight gain/obesity which is associated with the development of type 2 diabetes mellitus"? Answering the proposed question leads to a brief overview of the pathophysiological process of type 2 diabetes mellitus development.

According to Caterson and Gill, (2002), Colditz, Willet, and Manson, (1995), Formiguera and Canton, (2004), and Kahn, Hull, and Utzschneider, (2006), the role of obesity in the pathogenesis of type 2 diabetes mellitus has long been recognized. Studies such as the Nurses' Health Study, the Health Professionals Follow-up Study, and other research studies have observed that increased weight gain/obesity is predictive of developing type 2 diabetes mellitus (Carey et al., 1997; Chan, Rimm, Colditz, Stampfer,

& Willett, 1994; Colditz et al., 1995; Field et al., 2001; Holbrook, Barrett-Conner, & Wingard, 1989). A Swedish population-based study conducted by Villamor and Cnattinguis (2006) determined that weight gain during the time between pregnancies as well as pre-pregnancy weight gain is strongly associated with the risk of major maternal complications such as type 2 diabetes development.

Obesity is characterized as an excess of adipose tissue (fat cells) (Calle & Kaaks, 2004; Kopelman, 2000). The adipose cells (fat cells) produce excessive amounts of free fatty acids, adipokines, and pro-inflammatory cytokines including TNF- α and IL-6 (Coppack, 2001; Fröhlich et al., 2000; Greenberg & McDaniel, 2002; Moller, 2000; Mohamed-Ali et al., 1997). The over production of the pro-inflammatory cytokines such as TNF- α and IL-6 induce chronic-low grade inflammation which impairs insulin-stimulated glucose uptake and elevate plasma concentrations of an acute phase protein C-reactive protein (CRP) (Festa et al., 2000; Fröhlich et al., 2000; Ridker, Hennekens, Buring, & Fifai, 2000; Sattar & Greer, 2003). Elevated CRP concentration is an indicator of systemic inflammation (Festa et al., 2000; Fröhlich et al., 2000; Maachi et al., 2004; Sites et al., 2002; Yudkin, Stehouwer, Emeris, & Coppack, 1999). The over expression of the pro-inflammatory markers and chronic-low grade inflammation state contribute significantly to insulin resistance.

Insulin resistance is defined as the inability of cells or tissues to respond to normal levels or concentrations of insulin circulating in the body (Kadowaki et al., 2006; Shoelson, Lee, & Goldfine, 2006; Stephens, Lee, & Pilch, 1997; Weyer, Bogardus, & Pratley, 1999). The insulin resistant state seems to be a result of obesity and is known to be a major risk factor in the etiology of type 2 diabetes mellitus (Abbasi, Brown,

Lamendola, McLaughlin, & Reaven, 2002; Boden, 1997; Xu et al., 2003; Schulman, 2000).

Many prospective epidemiological studies across various population groups indicate that type 2 diabetes frequently occurs after a progression of insulin resistance and a loss of insulin secretion (Ferrannini, 2005; Kahn, 2003; Ferrannini, 2003; Field et al., 2001). As a result of insulin resistance, the pancreas produces much more insulin than normal which leads to hyperinsulinemia. Reaven (1988) suggested in his Banting Lecture that insulin-stimulated glucose uptake and hyperinsulinemia are involved in the etiology and clinical course of type 2 diabetes. With further worsening of the insulin resistance state resulting in a markedly increased production of insulin (hyperinsulinemia), the progression of impaired glucose tolerance (IGT) is categorized as the next stage associated with the natural history of type 2 diabetes mellitus (Petersen & McGuire, 2005; Santomauro et al., 1999; Schulman, 2000; Despres, et al., 1995).

According to Dunstan et al., (2002), Davies, Raymond, Day, Hales, and Burden, (2000), The DECODA Study (2002), and Unwin and others, (2002), IGT is an intermediate stage between normal glucose tolerance and overt type 2 diabetes mellitus. It can be identified by an oral glucose tolerance test in which blood glucose levels increase. They are greater than normal; however, not as great as individuals with type 2 diabetes mellitus. Fasting glucose levels are normal or slightly elevated. Literature indicates that individuals with IGT have an increased risk of type 2 diabetes mellitus. The diminishing pancreatic insulin secretion by the pancreatic β-cells in the IGT stage results in higher blood glucose levels which are toxic to β-cells. The results of the malfunctioning and/or failure of pancreatic β-cells lead to the

Table 2.

Comparison of Literature on the Association of Parity and Diabetes

#	STUDY	Study Design Population	Nature of the Statistical Analysis	Parity defined	Outcome Variable criteria used	Dependent Variables and controlled variables	Inferred Findings	Association between Parity & Diabetes YES/NO
1	Parity and Risk of Type 2 Diabetes (Nicholson et al, 2006)	Prospective cohort of African American and Caucasian women; Follow-up 9 years	Cox proportional hazards regression	Number of live births	2-h PG ≥200 mg/dl during an oral glucose tolerance test	Sociodemographic, clinical, and lifestyle factors	Higher parity was associated with increased risk of type 2 diabetes mellitus	Change in parity, increase type 2 diabetes mellitus YES
2	Is parity associated with earlier diagnosis of type 2 diabetes (Cheung, 2004)	Cohort from diabetes data base; 2102 Caucasian Australian women	Retrospective Multivariate linear regression	Number of live births	The age of diagnosis of type 2 diabetes.	Corrected for age	Small association of parity of 5 or more and age of diagnosis of diabetes; Effect disappeared with parity 0-5.	Yes (very small effect); parity and age of diagnosis of diabetes YES

Table 2. (*Continued*).

Comparison of Literature on the Association of Parity and Diabetes

#	STUDY	Study Design Population	Nature of the Statistical Analysis	Parity defined	Outcome Variable criteria used	Dependent Variables and controlled variables	Inferred Findings	Association between Parity & Diabetes YES/NO
3	Association of parity with risk of type 2 diabetes and related metabolic disorders (Hanley et al, 2002)	Crossectional Population based study Canadians n=383	Logistic and linear regression analyses	Number of live births	2-h PG ≥200 mg/dl during an oral glucose tolerance test	Age, waist circumference	Parity associated with decreased risk of diabetes; nulliparous women associated with elevated fasting insulin and proinsulin	Increase parity decrease diabetes; Decrease parity and increased diabetes INVERSE RELATIONSHIP
4	Reproductive history, glucose tolerance, and NIDDM in Hispanic and non-Hispanic white women (Alderman et al, 1993)	Hispanic and non-Hispanic white women 20-74 years	Linear and Logistic regression	Number of live births	2-h PG ≥200 mg/dl during an oral glucose tolerance test	Subscapular skin-fold thickness	Childbearing was related to lower insulin levels	No association NO

Table 2. (*Continued*)

Comparison of Literature on the Association of Parity and Diabetes

#	STUDY	Study Design Population	Nature of the Statistical Analysis	Parity defined	Outcome Variable criteria used	Dependent Variables and controlled variables	Inferred Findings	Association between Parity & Diabetes YES/NO
5	Parity and incidence of non-insulin dependent diabetes mellitus (Manson, et al, 1992)	Prospective cohort study; 113,606 nurses Follow-up 12 years	Cox proportional hazards regression analysis	Number of live births	Not given	Age, BMI, family hx, age at first birth, hormone	Importance of controlling for variables; no association	No association NO
6	Parity, ethnic group and the prevalence of type 2 diabetes: the Coventry Diabetes Study (Simmons, D, 1992)	Cross – sectional n=2096 and n=1148 Asian and European women	Logistic regression analysis	Number of live births	Not given	Age, BMI	U shape association; Nulliparity (no live births) and multi-parity (5 or more live births) increase prevalence of diabetes	U shaped association 1-2 live births no association; but no live births and 5 or more live births there is an association

Table 2. (*Continued*).

Comparison of Literature on the Association of Parity and Diabetes

#	STUDY	Study Design Population	Nature of the Statistical Analysis	Parity defined	Outcome Variable criteria used	Dependent Variables and controlled variables	Inferred Findings	Association between Parity & Diabetes YES/NO
7	Evidence against association between parity and NIDDM from five population groups (Collins et al, 1991)	Pacific and Indian Ocean island nations n = 204, n = 62, n = 390, n = 247, and n= 1333	Logistic Regression analysis	Number of live births	Not given	Age, BMI, family history	There is little if any independent association between parity and diabetes	No association NO
8	Effects of childbearing on glucose tolerance and NIDDM prevalence (Boyko et al, 1990)	NHANES I 3057 women	Logistic Regression analysis	Number of live births	Not given	Age, BMI, education, income	No association after controlling for the variables; prior to that, there was an association	No association NO

Table 2. (*Continued*).

Comparison of Literature on the Association of Parity and Diabetes

#	STUDY	Study Design Population	Nature of the Statistical Analysis	Parity defined	Outcome Variable criteria used	Dependent Variables and controlled variables	Inferred Findings	Association between Parity & Diabetes YES/NO
9	The effects of parity on the later development of non-insulin-dependent diabetes mellitus or impaired glucose tolerance (Kritz-Silverstein et al, 1989)	Population-Based sample 1186 women	Logistic regression analysis	Number of live births	Not given	Age, obesity, family history,	Parity was associated with a significant increased risk of diabetes	Increase parity, increase diabetes YES
10	Glucose tolerance and mortality in diabetes mellitus in Maltese-born residents of Victoria (Martin et al, 1984)	Maltes-born residents 396 women	Multivariate analysis	Number of live births	Not given		Glucose tolerance was correlated with family hx of diabetes, age, obesity, and parity	Increase parity, increase diabetes YES

deterioration of glucose homeostasis which ultimately leads to overt type 2 diabetes mellitus (Elbein, Hastedt, Wegner & Kahn, 1999; Kahn & Foldfine, 1993; Tuomilehto et al., 2002; Buchanan et al., 2000; Unwin, et al., 2002).

The pathway of the well established link between increased weight gain/obesity and type 2 diabetes has been reviewed in order to successfully develop a model to show an association between increased parity and increased weight gain/obesity which has an association with the development of type 2 diabetes mellitus. However, for this study, an analysis was conducted to determine if there is an association between change in parity and type 2 diabetes mellitus which is independent of increased weight gain which is seen in Figure 3.

Association Between Parity and Increased Weight Gain

Increased parity has been associated with increased weight gain and higher risk of obesity in women persisting beyond one year postpartum (Keppel & Taffel, 1993; Rookus, Rokebrand, Barema, & Deavrenbert, 1987; Smith, et al., 1994; Williamson et al., 1994; Wolf, et al., 1997). Significant weight is gained during pregnancy in most women's lives. In the Stockholm Pregnancy and Weight Development Study, 40-50% of women attributed the onset of their obesity to childbearing, and 73% reported retaining 10 kg after pregnancy (Rossner, 1992; Rossner & Ohlin, 1995).

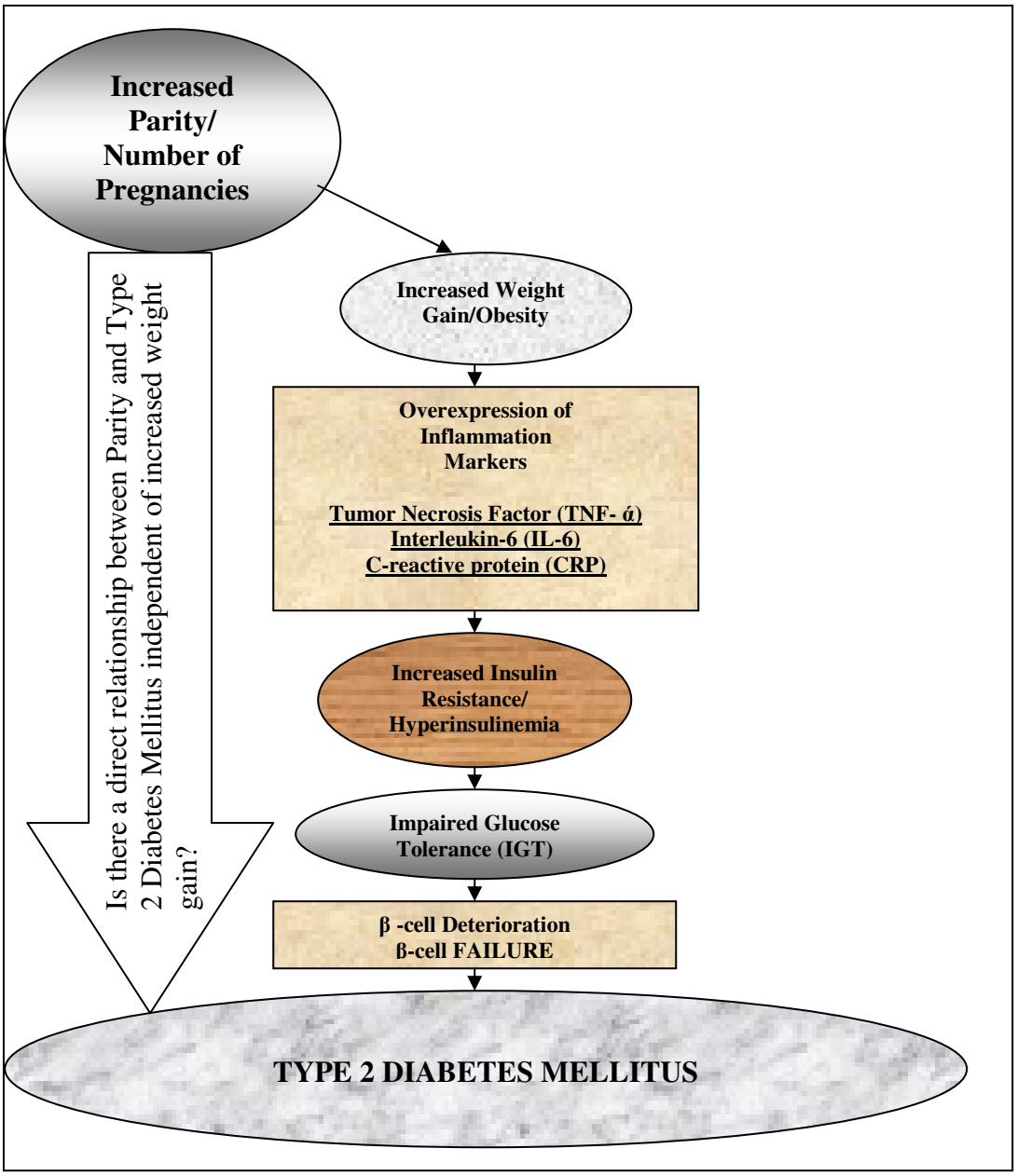

Figure 3. Model of the Physiologic Link Between Changes in Parity and Type 2 Diabetes Mellitus

Research studies of pregnant women suggest that pregnancy-related weight gain range from 0.5 to 1.5 kg for Caucasian women and up to 3 kg for African-American women by 6 – 18 months postpartum (Keppel & Taffel, 1993; Ohlin & Rossner, 1990;

Rookus et al., 1987; Schauberger, Rooney, & Brimer, 1992; Williamson et al., 1994). Researchers have indicated that there are several physiological mechanisms that have been proposed to explain the association of changes in parity and increased weight gain/obesity among women. In a cross-sectional study, many of the physiological changes have been shown to persist for years after childbearing (den Tonkalaar, et al., 1990). They are (1) increased glucocorticoid activity (Harris, Ellison, Richter, de Wet, and Levin, 1998), an overload of fat tissue deposits in the femoral area during pregnancy (Kay, Folsom, Prinas, Potter, and Gapstur, 1990), pregnancy related insulin resistance (Godsland, 1996; Kritz-Silverstein, Barrett-Conner, and Wingard, 1989; Ness et al., 1993), and hormonal changes due to fewer ovulatory cycles (Gunderson & Abrams, 2000). However, in addition to the physiological changes, pregnancy related weight gain as well as post partum weight retention may also be associated with changes in diet (excess caloric intake) and physical activity (decreased or no physical activity).

There have been several studies published regarding the association of the changes in parity and weight gain/obesity. An increase in BMI was found to be associated with changes in parity in the Nurses' Health Study among 41,000 Iowa women aged 42-67 (Manson, et al., 1992). The results from a Massachussetts case-control study revealed that five or more births among women increased their chance of being obese compared with nulliparous women (Palmer, Rosenburg, & Shapiro, 1992). In a population study of women aged 35-68 who participated in the Framingham Heart Study, researchers found a significant increase in BMI in association with increased parity (Ness et al., 1993). Among men and women in the Rancho Bernardo Study, investigators found an association between the number of children and obesity many years after childbearing

(Barrett-Connor, 1997; Kritz-Silverstein, et al., 1997). The BMI was positively associated with the number of biological children (Barrett-Connor, 1997). A Finland study revealed that the number of children among women aged 25-84 was associated with the prevalence of obesity (Heliovaara & Aromaa, 1981). In a study of Swedish women with two or more children, change in parity was linked to a change of average weight after pregnancy by approximately 2 kg when compared to nulliparous women (Cederlof & Kaij, 1970). There has also been a more recently published study from Sweden regarding the association of increased parity and obesity among women aged 45-73 years (Lahmann, Lissner, Gullberg, & Berglung, 2000).

Researchers have found that there is an association between increased parity and increased weight gain/obesity. Excess weight gain during pregnancy and failure to lose weight after pregnancy are identifiable predictors of long-term obesity. The accepted association between weight gain/obesity and type 2 diabetes mellitus, as well as the proposed association between changes in parity and weight gain/obesity is seen previously in Figure 2.

Other Risk Factors Associated With the Development of Type 2 Diabetes Mellitus Independent of Weight Gain

Research indicates that physical inactivity, high saturated fat intake, and offsprings of diabetic pregnancies are risk factors of type 2 diabetes independent of weight change. However, the more recent American guidelines suggest that high blood pressure, low plasma high-density lipoprotein cholesterol (HDL-C) level and high triglyceridaemia are additional independent risk factors. (ADA, 2003),

Longitudinal studies have clearly indicated that decreased physical activity (sedentary lifestyles) increases the risk of developing type 2 diabetes regardless of the degree of adiposity (Helmrich, Ragland, Leung, & Pafenbarger, 1991; Kriska et al., 1993; Manson et al., 1992;). Offsprings of diabetic pregnancies including gestational diabetes are often large and heavy at birth, tend to develop obesity in childhood and are at high risk of developing type 2 diabetes at an early age (Pettitt et al., 1988). These studies reveal that those born to mothers after they have developed diabetes have a three-fold higher risk of developing diabetes than those born before (Dabelea, et al., 2000).

In observational epidemiological studies, a high saturated fat intake has been associated with a higher risk of impaired glucose tolerance, and higher fasting glucose and insulin levels (Feskens, et al., 1995; Feskens & Kromhout, 1990; Parker et al., 1993). Higher proportions of saturated fatty acids in serum lipid or muscle phospholipid have been associated with higher fasting insulin, lower insulin sensitivity and a higher risk of type 2 diabetes (Folsom, Ma, McGovern, & Eckfeldt, 1996; Vessby et al., 1994; Vessby, Tengblad, & Lityhel, 1994).

In intervention studies, replacement of saturated by unsaturated fatty acids leads to improved glucose tolerance (Uusitupa et al., 1994; Vessby et al., 1980). Long-chain polyunsaturated fatty acids do not, however, appear to confer additional benefit over monounsaturated fatty acids in intervention studies (Vessby et al., 2001). In observational studies, a high intake of total fat has been shown to predict the development of impaired glucose tolerance and the progression of impaired glucose tolerance to type 2 diabetes (Feskens et al., 1995; Marshall, Hoag, Shetterly, & Hamman, 1994).

The Relationships Between Parity and Other Health Indicators and Type 2 Diabetes

The relationship between parity, other health indicators, and type 2 diabetes mellitus has been examined in several published studies. The definition of parity in all of the studies was the number of live births the participants experienced. The literature suggests that there may be an association between parity and diabetes mellitus. It is a controversial topic and has been debated for many years. Recent studies on the topic have been conducted and yield mixed findings. Table 2 illustrates the comparison of the various studies and their inconsistent findings. The design methods and outcomes in the research studies are summarized then compared and contrasted.

To validate the findings from previous study indicating that multi-parity is associated with an increased risk of the development of type 2 diabetes, Nicholson et al. (2006) explored the relationship of those factors by performing a secondary data analysis on the data from the Atherosclerosis Risk in Communities Study to determine the association between parity and diabetes. It was a population-based, longitudinal study consisting of a sample of 7,024 African American and Caucasian women with 9 years of follow-up. An initial survey was conducted in 1986 through 1989 and the follow-up surveys in 1990 through 1998.

The main aim of the study was to determine the relation of parity with diabetes, accounting for the contribution of clinical, physiologic and sociodemographic factors using a longitudinal approach. At the first visit, participants were asked to fast for 12 hours after which blood was collected and insulin levels were measured. Information was retrieved from questionnaires concerning the women's history of physical activity, smoking, and health related variables. Parity was defined as the number of live births at

the initial visit. Other categories regarding parity were also listed such as no live births (nulliparity), etc. Diabetes was determined by the American Diabetes Association diagnostic criteria. A Cox proportional regression analysis was performed by using a modeling approach which also included adjusting for confounding variables which included: sociodemographic and familial factors (age, race, income, education level, and family history of diabetes), then lifestyle related factors (total caloric intake, current smoking, and physical activity), then reproductive health-related factors (menopause, age at menopause, usage of birth control pills and hormone replacement therapy) and finally inflammatory markers. The researchers showed that higher parity was associated with the increased risk of type 2 diabetes independent of sociodemographic factors. The association between five or more live births and diabetes was attenuated however, remained significant after additional adjustment for BMI. The limitations of the study revealed that there was no generalizability to other racial groups (Native Americans) with higher rates of diabetes. Also, Nicholson and others (2006) were not able to discern between non-live births due to miscarriages.

Compared to the other research studies regarding the association of parity and the risk of type 2 diabetes mellitus development, this study's strengths consisted of utilizing standardized measures of exposures, outcomes, behavioral factors, and laboratory measures to examine potential mechanisms of the association between parity and diabetes whereas other studies were not able to provide such measures and did not find an association between parity and diabetes mellitus (Manson et al., 1992).

In another study, Cheung (2004) conducted a study on women with a diagnosis of type 2 diabetes to determine the association between parity and type 2 diabetes mellitus

development. His study was aimed at detecting the effect of parity on an already predisposed population of women in The Wentworth Area Diabetes Service database. Self-reported information such as date of birth, age at diagnosis of diabetes, parity, BMI, family history of diabetes, and smoking was retrieved from women with type 2 diabetes since 1993.

The sample for the study consisted of 2,102 European respondents with a mean age of 62 years. A multivariate linear regression analysis was performed to ascertain if there was an association between parity and the age of diagnosis of type 2 diabetes after controlling for BMI, date of birth, family history, and smoking. Cheung (2004) found a relationship between parity of 5 or more and the age of diagnosis of diabetes; however, the effect was small. He concluded that with each additional pregnancy, diabetes occurred only 0.25 years earlier. There was little effect with a parity of five or less. The outcome of the multivariate analysis indicated that is a very small association between higher parity and the age of diagnosis of diabetes exists.

In their study of the association of parity with the risk of type 2 diabetes, Hanely and others (2002), did not support Nicholson's and Cheung's results. The researchers wanted to answer the following questions: 1) Is parity associated with risk of type 2 diabetes? 2) Is parity associated with variation in concentrations of insulin and proinsulin among non-diabetic women? Data for their cross-sectional study were collected through questionnaires from the Sandy Lake Health and Diabetes Project which is a population-based sample of 383 non-diabetic women participants aged 12-79 years. Associated risk factors and other measures studied were age, glucose levels, insulin levels, pro-insulin levels, and BMI.

Information on the number of live births and diagnosed diabetes was obtained from questionnaires. After an oral glucose tolerance test was administered, diabetes was diagnosed based on the criteria from the World Health Organization. Multiple logistic regression analyses were performed while adjusting for age: 1) parity as a continuous variable and 2) parity as a dichotomous variable. When linear and logistic regression analyses were used to analyze the data, the researchers showed that nulliparity is associated with an increased risk of diabetes in a Native Canadian population as well as non-diabetic nulliparous women had significantly elevated concentrations of fasting insulin and proinsulin compared to non-diabetic parous women. In other words, their findings indicated that women who experienced one live birth had a significant reduced risk of diabetes compared with women who never experienced giving birth. These findings were consistent with other studies in other populations such as Pima Indian women that are known to suffer from higher rates of diabetes (Charles et al., 1994). The limitations of the study included not having information on abortions, miscarriages, or stillbirths.

Alderman and others (1993) studied the relationship of parity and type 2 diabetes in Hispanic and non-Hispanic white women who participated in a population-based study in Colorado's San Luis Valley (Alderman et al., 1993). Data for their population-based case-control epidemiological study were collected from randomly sampled 196 diabetic participants (case) and a control sample of 735 participants, who were 20-74 years of age. The diabetic and non-diabetic participants were administered a glucose tolerance test, physical examination, and standardized interview.

When multiple logistic regression analyses were used to analyze the data, the results indicated childbearing was associated with lower insulin levels and had little effect on later risk of diabetes development. After adjusting for BMI, parity was not related to type 2 diabetes in Hispanic and non-Hispanic white women.

In another study, Manson et al., (1992) using longitudinal data from 113,606 women ages 30 to 55 years in the United States participating in the Nurses' Health Study, studied the association between parity and subsequent incidence of type 2 diabetes mellitus. In their study, the researchers gathered information regarding previous diagnosis of diabetes, other major illnesses, as well as age, height and weight, number of pregnancies, and the use of oral contraceptives and hormones. All questionnaires were mailed in 1976 with supplemental follow-up questionnaires from 1976 to 1988 which provided information on parity. The participants did not have type 2 diabetes, coronary heart disease, stroke or cancer at baseline and were followed for 12 years.

When proportional hazards models were used to analyze the data, the results revealed that there was no association between parity and the later development of type 2 diabetes mellitus after controlling for age and BMI. The follow-up rate for this study was high, 92% across categories of parity. That is, the results from the study are unlikely to be biased by losses of follow-up since the rate is so high. The results were consistent with another study by Boyko and others (1990) that controlled for age, BMI, educational level, and socioeconomic status as well as with another study by Collins and associates (1991) which controlled for BMI and age.

Another study in which parity is correlated with type 2 diabetes is the Coventry Diabetes Study (Simmons, 1992). He compared parity and the prevalence of type 2

diabetes among 1148 Asian and 2096 European women aged 30-64 years. A cross-sectional diabetes screening program for women in the United Kingdom was conducted. The researcher analyzed the data from the cross-sectional screening program to determine the effect of parity on the later development of type 2 diabetes mellitus. A survey was given to the participants in which information regarding the number of live births, age, diabetic history, height and weight, and blood glucose levels were taken.

The results of the logistic regression analysis revealed that Asian and European women with five or more live births who are 30-64 years of age have a higher prevalence of type 2 diabetes than subjects with only one or two children. Simmons found a U-shaped relationship between parity and the prevalence of type 2 diabetes mellitus, with a high prevalence among nulliparous women (women with no live births). This finding is also seen in the findings from the study conducted by Green, Beral, and Moser (1988) in which a U-shaped relationship between mortality with type 2 diabetes mellitus and parity with a decreased change of type 2 diabetes mellitus following two deliveries.

In their study of the association of parity with the risk of type 2 diabetes, Collins and others (1991), did not support Nicholson's and Cheung's results. The researchers wanted to answer the following questions: 1) Is parity associated with risk of type 2 diabetes? 2) Is parity associated with variation in concentrations of insulin and proinsulin among non-diabetic women? Data for their cross-sectional study were collected through questionnaires from the Sandy Lake Health and Diabetes Project which is a population-based sample of 383 non-diabetic women participants aged 12-79 years. Associated risk factors and other measures studied were age, glucose levels, insulin levels, pro-insulin levels, and BMI.

Information on the number of live births and diagnosed diabetes was obtained from questionnaires. After an oral glucose tolerance test was administered, diabetes was diagnosed based on the criteria from the World Health Organization. Multiple logistic regression analyses were performed while adjusting for age: 1) parity as a continuous variable and 2) parity as a dichotomous variable. When linear and logistic regression analyses were used to analyze the data, the researchers showed that nulliparity is associated with an increased risk of diabetes in a Native Canadian population as well as non-diabetic nulliparous women had significantly elevated concentrations of fasting insulin and proinsulin compared to non-diabetic parous women. In other words, their findings indicated that women who experienced one live birth had a significant reduced risk of diabetes compared with women who never experienced giving birth. These findings were consistent with other studies in other populations such as Pima Indian women that are known to suffer from higher rates of diabetes (Charles et al., 1994). The limitations of the study included not having information on abortions, miscarriages, or stillbirths.

Collins, Dowse, and Zimmet, (1991) compared the association of parity and type 2 diabetes in five population groups. Collins and others (1991) investigated the association between parity and the development of type 2 diabetes from five population-based surveys from four Pacific and Indian Ocean island nations.

The sample for the study consisted of 2736 respondents of Micronesian, Melanesian, and Mauritian backgrounds who were 40 years of age and older and were not diagnosed with diabetes mellitus at the time of the survey. This method of exclusion was done similar to Kritz-Silverstein, Barrett-Connor, and Wingard, (1989). All data

were obtained through personal interviews in which information regarding number of pregnancies and live births was retrieved. A glucose tolerance test was administered and the results were determined based on the criteria from the World Health Organization. All other information on reproductive and family history of diabetes was collected during the interview.

When a logistic regression analysis was conducted on the cross-sectional data adjusting for age, BMI, and family history, the researchers concluded that there was no independent association between parity and type 2 diabetes in the studied populations. These results were not corroborated by Kritz-Silverstein and associates (1989) in which their study found no association between parity and type 2 diabetes mellitus.

In their study of the effects of childbearing on glucose tolerance and type 2 diabetes mellitus, Boyko, Alderman, Keane, and Baron, (1990) supported Collins et al. (1991) results. Data for Boyko and others' study were derived from the Second National Health & Nutrition Examination Survey, a stratified sample of civilian, non institutionalized population of the United States. The survey composed of 3057 participants who underwent clinical and laboratory evaluation for the presence of diabetes mellitus. A positive diagnosis of diabetes was determined by the results of the glucose tolerance test, previous diagnosis of diabetes, or the use of hypoglycemic medication. Parity was determined by the number of live births by each woman at the initial interview. Data were analyzed using logistic regression analysis adjusting for age, BMI, education, and income.

Their findings indicated that the prevalence of type 2 diabetes increased with the increasing number of live births; however, after the adjustment for age, BMI, education,

and income, the magnitude of the association became attenuated. Specifically, they found that childbearing experience is not associated with the development of type 2 diabetes mellitus because the results of the analysis did not show a consistent increase in type 2 diabetes prevalence with increased childbearing after adjustment for age, BMI, education, and income. They concluded that women who have given birth have a greater tendency to develop diabetes primarily due to their age and BMI. The researchers did not find evidence to suggest that bearing children independently caused an increase in type 2 diabetes mellitus prevalence. Similar findings were revealed in the study by Manson and others (1992) in which they adjusted for age, BMI, and family history.

On the other hand, Kritz-Silverstein and others (1989) examined the effect of parity on the later development of type 2 diabetes mellitus in a sample of 1186 women 40 years of age and older. Their cross-sectional study was based on data collected from a sample of 1186 participants in the Rancho Bernardo Heart and Chronic Disease Survey. The survey was used to obtain information regarding the number of pregnancies, the number of live births, and height and weight measures.

The aim of the study was to determine if parity was associated with the later development of type 2 diabetes mellitus. Using logistic regression to analyze their data, Kritz-Silverstein et al. (1989) found that parity is associated with a statistically significant increase in the risk of type 2 diabetes mellitus and that the risk is independent of age and obesity. This association was seen many years after childbearing. The findings were similar to those in the Cheung's study in which he found that there was an association between parity and age in regards to type 2 diabetes mellitus prevalence.

In another study, Martin et al. (1984) reached similar conclusions when he studied the association between parity and type 2 diabetes mellitus. His aim was to determine if there was a correlation between parity and type 2 diabetes mellitus. Martin et al. (1984) administered glucose tolerance tests to 200 Maltese-born women residents of Melbourne, Australia. Their cross-sectional study was based on data collected through via survey to test for diabetes. Information regarding diabetes status, family history of diabetes, number of children, weight, dietary habits, smoking and alcohol habits, and oral contraceptives use were obtained.

Logistic regression results indicated that the correlation between the number of children and type 2 diabetes was significant. In other words, the results revealed that there is an association of increased parity and the prevalence of type 2 diabetes mellitus. There are other closely related studies in which parity is associated with increased insulin, metabolic syndrome, and still-birth occurrence (Kritz-Silverstein, Barrett-Conner, Wingard, & Friedlander, 1994; Lao et al., 2006; Sicree, Hoet, Zimmet, King, & Coventry, 1986). There is also an editorial review found in the literature which implies that race, parity, and gestational diabetes are risk factors for type 2 diabetes and suggests two possible explanations for the higher incidence of type 2 diabetes in African American women when compared to Caucasian women (Kahn & Williamson, 2000).

A summary of studies discussed in this section is presented in Table 2 at the end of this chapter. These studies show discrepancies in their results. For example, Cheung (2004), Kritz-Silverstein and associates (1989), Martin et al. (1984) and Nicholson et al, (2006), found an association between parity and type 2 diabetes. Others have failed to confirm this relationship (Alderman and others, 1993; Boyko and others, 1990; Collins et

al., 1991; Manson and associates, 1992). However, Hanley and others (2002) found an inverse relationship between parity and the risk of type 2 diabetes mellitus development. Specifically, that diabetes is associated with decreased parity. Also, Simmons (1992) found a U-shaped relationship between parity and type 2 diabetes development. Moreover, that low parity and higher levels of parity is associated with the increased risk of type 2 diabetes mellitus development. The studies identified were limited to a certain population and geographical region in addition to problems inherent in cross-sectional analyses (Collins et al., 1991; Kritz-Silverstein et al., 1989; Manson et al., 1992; Martin et al., 1984). Some previous studies have controlled for different variables such as age of the participant and BMI and while others have not (Martin et al., 1984; Simmons, 1992). One study has controlled for modifiable risk factors such as physical activity and caloric intake (Manson et al., 1992). Other limitations that some of the studies shared were the lack of information on abortions, miscarriages, and stillbirths. Thus, non-live birth pregnancy outcomes could not be ascertained.

To address the population and geographical limitations, the non-adjusted variables and modifiable risk factors, problems with cross-sectional analyses, and the lack of information on abortions, miscarriages, and still births, an analysis of the existing data from the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study (NHEFS) was performed. The NHEFS is a national longitudinal population-based study that was designed to investigate the association between factors measured at baseline and the development of specific health conditions such as diabetes mellitus by assessing changes over time in participants' characteristics (National Center for Health Stastics (NCHS), 2000).

The proposed study addresses the population and geographical limitations by utilizing data from the NHANES I Epidemiologic Follow-up Study (NHEFS) which originally collected data from a national probability sample of the Unites States civilian non-institutionalized population which assured that the different units in the population had equal probabilities of being chosen (NCHS, 2000). Adjusting for variables and modifiable risk factors was performed on the confounding factors to determine the association of parity and the probability of developing type 2 diabetes mellitus. The independent variable, parity, was the total number of live births. The outcome variable, diabetes mellitus, was based on the American Diabetes Association criteria: physician-diagnosed diabetes, current use of diabetes medications, or fasting glucose levels $\geq$ 126 mg/dl. If the participants have any one of the listed criterion, they were considered to have type 2 diabetes mellitus. Confounders were age, BMI, race, hypertension status, cholesterol status, and physical activity. Other covariates included were hormone use, education level, stillbirths, miscarriages, and/or abortions.

Most of the studies identified utilized cross-sectional data analyses. Inherent limitations of cross-sectional studies exist; however, the major limitation of most cross-sectional studies is the temporal sequence between exposure (parity level) and outcome (type 2 diabetes mellitus). Temporal sequencing is necessary to establish an association between the exposure and outcome variables. This is seen in longitudinal data analyses (Oleckno, 2002). While the cross-sectional studies provide important and useful information, it seems as though the association of parity and type 2 diabetes mellitus is not completely understood. Therefore, the need to continue to study the effect of parity on type 2 diabetes mellitus utilizing longitudinal data is warranted.

To address the limitations of cross-sectional data analyses, a secondary data analysis of the existing data from The National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study (NHEFS) was performed. It is a longitudinal population-based study that was designed to investigate the association between factors measured at baseline and the development of specific health conditions such as diabetes mellitus by assessing changes over time in participants' characteristics (NCHS, 2000).

There were several population of women used in the various analyses of the studies seen in Table 2. Four studies included Caucasian and African American women (Boyko et al., 1990; Kritz-Silverstein et al., 1989; Manson et al., 1992; Nicholson et al., 2006). One study consisted of mainly Australian women (Cheung, 2004). Another study consisted of Hispanic and non-Hispanic women (Alderman et al., 1993). The remaining four studies included Pacific and Indian Ocean Islanders, Asian and Europeans, and Canadians (Collins, et al., 1991; Hanley et al., 2002; Martin et al., 1984; Simmons, 1992).

The definition of parity in all of the studies was the number of live births the participants experienced. Half of the studies performed logistic regression analyses while the others performed multivariate linear regression analyses. Eight studies controlled for age and/or BMI as well as sociodemographic variables (Boyko et al., 1990; Cheung, 2004; Collins et al., 1991; Kritz-Silverstein et al., 1989; Hanley et al., 2002; Manson et al., 1992; Nicholson, et al., 2006; Simmons, 1992;). Four of the eight studies used the logistic regression model for their analysis while controlling for age and/or BMI (Collins et al., 1991; Hanley et al., 2002; Nicholson et al., 2006). Four of the eight studies used multivariate regression or logistic regression analyses while controlling for age and/or

BMI (Cheung, 2004; Kritz-Silverstein et al., 1989; Manson, et al., 1992; Simmons, 1992). One study did not control for age or BMI (Martin et al., 1984). Another study controlled for subscapular skinfold thickness (Alderman et al., 1993). Other variables that were controlled in addition to age, BMI, and subscapular skinfold thickness were family history, age at first birth, hormone levels, lifestyle factors, and waist circumference. The outcome variable used was the diagnosis of type 2 diabetes. The criteria used in the studies for the diagnosis of type 2 diabetes were: 1) 2-h PG ≥200 mg/dl during an oral glucose tolerance test. The tests were performed as described by the World Health Organization, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water, 2) presently taking medicines for diabetes mellitus, or 3) the age of diagnosis of type 2 diabetes. The covariates used were: age, BMI, obesity, family history waist circumference, sociodemographic, clinical, lifestyle factors, education, and income. A summary of studies discussed in this section is presented in Table 2.

Comparison of Epidemiologic and Intervention Studies Regarding the Association Between Parity and Type 2 Diabetes Mellitus

The relationship between parity and the risk of developing type 2 diabetes was examined in the above studies. There were studies that found an association between parity and type 2 diabetes (Cheung, 2004; Kritz-Silverstein et al., 1989; Martin et al., 1984; Nicholson et al., 2006) in which two of them controlled for age and or BMI, both of which are important confounding factors. In the eight studies that have presented results adjusted for age and BMI, the findings have been highly inconsistent: three

reported a positive relationship between parity and diabetes risk (Cheung, 2004; Kritz-Silverstein, 1989; Nicholson et al., 2006), three found no effect (Collins et al., 1991; Manson et al., 1992; Boyko et al., 1990), one demonstrated a U shape association (increase of low and high parity increase type 2 diabetes) which increased the risk of type 2 diabetes (Simmons, 1992), and another study revealed an inverse relationship between decreased parity and type 2 diabetes (Hanley et al., 2002).

One out of the ten studies was a longitudinal study in which a logistic regression analysis was performed controlling for two of the main confounders, age and BMI (Simmons, 1992). However, one of the limitations was not having information to discern between non-live births due to miscarriage. The study was done correctly. The researchers took into account the confounders as well several limitations. Fortunately, the NHEFS contains the variables regarding miscarriages and number of live births.

There have been convincing findings from studies associating excessive weight gain and central adiposity with the development of type 2 diabetes. The association has been repeatedly demonstrated in longitudinal studies in different populations, with a varying gradient of risk apparent with increasing levels of BMI, adult weight gain, waist circumference or waist-to-hip ratio. It has been established that waist circumference or waist-to-hip ratio (reflecting abdominal or visceral adiposity) are more powerful determinants of subsequent risk of type 2 diabetes than BMI (Boyko et al., 2000; Chan et al., 1994; Colditz et al., 1990; Despres, 2001; Despres, Lemieux, & Prud'homme, 2001). Central adiposity has been shown to be a determinant of insulin resistance, the underlying abnormality in most cases of type 2 diabetes (Despres, 2001). In several randomized controlled trials, a decrease in weight has been shown to reduce the risk of progression

from impaired glucose tolerance to type 2 diabetes (Knowler et al., 2002; Tuomilehto et al., 2002).

Impact of Race/Ethnicity on the Risk for Developing Type 2 Diabetes Mellitus

There are racial/ethnic disparities in the prevalence of Type 2 Diabetes Mellitus. In 2005, African Americans and Hispanics in the United States had the greatest prevalence of diagnosed Diabetes Mellitus than their U.S. Caucasian counterparts across all age groups (U.S. Department of Health and Human Services, 2005). All population groups in the U.S. are experiencing an increase in the prevalence of Diabetes Mellitus; however, the increase is greater among minority groups (U.S. Department of Health and Human Services, 2005). According to the data from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK, 2005), 3.2 million African Americans which is 13.3% of that population and 2.5 million Hispanics which is 9.5% of that population in the United States 20 years and older diagnosed have diabetes mellitus compared to 13.1 million Caucasians which is 8.7% of that population (NIDDK, 2005). The data from the National Diabetes Surveillance System indicate that among adults aged 45-65 years, the prevalence of diagnosed diabetes is approximately 16.9% for African American males with a standard error (SE) of 1.34, 15.9% for African American females with an SE of 1.07, 13.3% for Hispanic males with an SE of 1.10, 15.9% for Hispanic women with an SE of 1.18, 10.1% for Caucasian males with an SE of 0.37, and 8.6% for Caucasian females with an SE of 0.34 (U.S. Department of Health and Human Services, 2005). Also, clinical and preventive studies that suggest that type 2 diabetes was

disproportionately affect children who are Native Americans, African-American and Hispanics/Latinos (Caprio, 2002; Ludwig & Ebbeling, 2001; Pinhas-Hamiel et al., 1996; Ritchie et al., 2003). There is a greater impact in the minority population. The prevalence of Diabetes is at least 2-4 times higher among African American, Hispanic, American Indian, and Asian Pacific Islander women than among Caucasian women (Bolen, Rhodes, Powell, Bland, & Holtzman, 2000; CDCP, 2005; Harris, et al., 1998). Eliminating the racial disparities among the minority populations (African Americans, Hispanics and others) in health and health care by 2010 is an overarching goal of Healthy People 2010 and the President's Initiative on Racial and Ethnic Disparities. Their aim is to "reduce the overall rate of clinically diagnosed diabetes" (U.S. Department of Health and Human Services, 2002).

Research studies have suggested that racial differences in the excessive risk of type 2 diabetes mellitus prevalence is associated with the increased prevalence of established risk factors which are low socioeconomic status, family history of diabetes, adiposity, and physical inactivity (Carulli et al., 2005; Lipton, et al.,1993; Robbins, Vaccarino, Zhang, & Kasi, 2000). African Americans and other minority groups are socially and economically disadvantaged. The socioeconomic inequalities in health have been attributed to a many of the mechanisms that may act as intermediate risk factors for diabetes (Knowler, McCance, Nagi, & Pettitt, 1993; Lynch, Kaplan, & Shema, 1997; Robbins, et al., 2001). The risk factors include poor nutrition, overweight, increased rates of poor health behaviors such as smoking and alcohol consumption, stress, and limited access to health care (Knowler, et al., 1993; Lynch et al., 1997; Robbins, et al., 2001). Research studies have indicated that in the U.S., there is an inverse relationship

between socioeconomic status (education and income) and diabetes mellitus prevalence (Brancati, Whelton, Kuller, & Klag, 1996; Cowie, et al., 1993; Drury , Danchik, & Harrisl, 1985). Brancati et al., (1996) and Robbins et al., (2000) revealed that the prevalence of type 2 diabetes is higher at a lower socioeconomic level which is an important marker of access to health care and health-related behaviors which is strongly associated with race in the United States. In a prospective cohort of 2646 African American and 9461 Caucasian adults aged 45 to 64 years who participated in the Atherosclerosis Risk in Communities Study (ARIC), Brancati, Kao, Folsom, Watson, and Szklo, (2000) found that African Americans are at greater risk of developing type 2 diabetes compared with their Caucasian counterparts and have higher blood pressure levels prior to the development of type 2 diabetes (Brancati et al., 2000). The excess risk was greater among African American women who had less education, indicated a family history of diabetes, greater measures of adiposity /obesity (increased BMI), and decreased levels of physical activity (Brancati et al., 2000).

Brancati and others (2000) conducted a community-based prospective study to determine the extent to which excess diabetes risk in African Americans was explained by racial differences in established diabetes risk factors. The findings suggested that the established risk factors in African American women were worse than in Caucasian women. African American women had less education, increased family history of type 2 diabetes, and greater levels of adiposity (increased BMI). In the baseline data from the ARIC study Brancanti et al. (2000), a prediabetic state was reported 3 to 9 years before the onset of type 2 diabetes in African Americans compared to Caucasian counterparts.

It has been well established that there is a clear association between obesity and the development of type 2 diabetes (Hamman, 1992; Manson, et al., 1992). Obesity is an important health problem for most minority populations, especially lower-income women in the African American and Hispanic populations. According to the National Center for Health Statistics (2006), the prevalence of obesity in the United States is far greater in the minority populations. The markedly high prevalence of obesity is more pronounced in women than in men. The prevalence of obesity in African American women is 51% and 40% in Hispanic women compared to 31.5% in Caucasians. The prevalence for obesity in African America men is 31.2 % and 30.5% in Hispanic males compared to 31.0% in their Caucasian counterpart (National Center for Health Statistics, 2006). In addition to the established risk factors, investigators have found that type 2 diabetes results from the interaction between a genetic predisposition and behavioral (life style) and environmental risk factors (Bracanti et al., 1996; Huang & Goran, 2003; Neel, 1962). There is strong evidence that behavioral and environmental risk factors such as obesity and physical inactivity are modifiable risk factors which are determinants of type 2 diabetes (Hamman, 1992; Manson, et al., 1992; Tuomilehto, Tuomilehot-Wolf, Zimmett, Alberti, & Knowler, 1997; Tuomilehto & Wolf, 1987). Women are at greater risk for inactivity, particularly as they age. African American and Hispanic women are more likely than Caucasian women to be physically inactive (Sundquist, Winkleby, & Pudaric, 2001). The Diabetes Prevention Program (DPP) included 3234 participants from minority groups that suffer disproportionately from type 2 diabetes such as African Americans, Hispanics, Asian Americans and Pacific Islanders, and American Indians. The study also included other high risk groups such as individuals 60 years of age and older, women with a history of

gestational diabetes, and participants with a family history of diabetes. The goal of the study was to determine if lifestyle intervention would prevent or delay the onset of type 2 diabetes in those individuals with impaired glucose tolerance (IGT). Weight loss and increased physical activity strategies were taught to the participants during the intervention. The findings suggested that lifestyle intervention worked well in all of the ethnic groups regardless of sex and age (The Diabetes Prevention Program Research Group, 2002). There was a 58% reduction in the incidence rate of type 2 diabetes compared to the metaformin group (The Diabetes Prevention Program Research Group, 2002).

Past research studies on pregnant women reveal that pregnancy-related weight gain estimates are greater for African-American women (3 kg) compared to Caucasian women (0.5-1.5 kg) 6-18 months after pregnancy (Gunderson & Abrams, 2000; Olson, Strauderman, Hinton, & Pearson, 2003; Wolfe et al., 1997). Since African-American women are disproportionately affected by obesity and type 2 diabetes compared to their Caucasian, an analysis of secondary data was performed to determine if there is a direct association between increased parity and type 2 diabetes prevalence independent of weight gain as well determining if there is an interaction effect between parity and race.

It has been established that there are racial disparities in the prevalence of diabetes. Research studies have suggested that racial differences in the excessive risk of type 2 diabetes mellitus prevalence is associated with the increased prevalence of established risk factors which are low socioeconomic status, family history of diabetes, adiposity, and physical inactivity (Carulli et al., 2005; Lipton et al.,1993; Robbins et al., 2000).

In the present research study, the data from NHANES I (baseline study) and the NHANES I Epidemiologic Follow-up Study is used to examine the effects of changes in parity over time on the risk of type 2 diabetes developments in women after controlling for all other risk factors including race. Specifically, to determine if there is an independent prognostic significance of the effect of changes in parity on the risk of developing type 2 diabetes in African American women as well as determining if there is an interaction effect between race and parity.

So far, there are limited research studies that have examined the effects of changes in the level of parity over time and the increased risk of type 2 diabetes. This study of the NHANES I Epidemiologic Follow-up Study focuses on sections related to diabetes and other related medical conditions and complications, demographic information, physical functioning and activity, and items related to the health behaviors of individuals and their diabetes risk factors seen in Table 1.

CHAPTER 3

METHODOLOGY

This chapter presents the methodology, including the source and collection of data, and the analytical procedures used for studying the research questions and hypotheses related to the variables contained in the model. The main variable for the present research study is the level of parity. Thus, the outcome variable used is type 2 diabetes mellitus. The interest, however, is the relation between the change in parity overtime and the increased risk of type 2 diabetes mellitus development. Covariates included in the study at baseline which are also included in the model: age, race, income, education, physical activity, alcohol use, smoking status, hypertension, cholesterol level, fat intake, BMI, number of miscarriages, parity and race interaction variable, and parity and BMI interaction variable .

This chapter begins with steps taken to select the sample for the first survey (NHANES I Survey) and to collect data. Further, this chapter discusses how the selected cohort was traced to participate in the NHEFS (NHANES I Epidemiologic Follow-up Study), including choosing of proxies for those cohort members who were deceased or incapacitated. Second, this chapter discusses the way in which all variables, the dependent and all independent variables are operationalized and conceptualized to be entered into the analysis. The statistical analysis technique to be used in the research study is also specified, and the rationale for selecting the specific statistical technique is provided. The chapter further discusses the assumptions for the specified statistical

technique, and how these assumptions are tested to determine violation by the data. This chapter closes with a presentation of the statistical analysis plan.

Data Information

The data used in this study are taken from the National Health and Nutrition Examination Surveys (NHANES I and NHANES I Epidemiologic Follow-up Study). The first National Health and Nutrition Examination Study (NHANES I) was conducted from 1971 to 1974 by the National Center for Health Statistics (NCHS), on a probability sample of the U.S. non-institutionalized civilian population, ages 1 – 74. This was augmented in 1974 – 1975 with a sub-sample of adults 25 -74 years of age, from the same original sample (NCHS, 1979).

A major purpose of the NHANES I Survey was to measure and monitor indicators of the nutritional status of the American people through dietary intake data, biochemical tests, physical measurements, and clinical assessments for evidence of nutritional deficiency. Although NHANES I provided a wealth of information on the prevalence of the health conditions and risk factors, the cross-sectional nature of the original survey limited its usefulness in studying the effects of clinical, environmental, and behavioral factors, and in tracing the natural history of disease. Therefore, a follow-up study was needed to investigate the relationship between factors measured at baseline and the subsequent medical conditions. To obtain such information, the NHANES I Epidemiologic Follow-up Study (NHEFS) was initiated (NCHS, 1979).

The NHANES I Epidemiologic Follow-up Study (NHEFS), originated as a joint project between the National Center for Health Statistics (NCHS) and the National Institute on Aging (NIA). The 1982-1984 initial follow-up of the cohort was funded primarily by NIA, with additional financial support from the following components of the National Institutes of Health (NIH) and Public Health Service agencies: National Cancer Institute; National Institute of Mental Health; National Institute on Alcohol Abuse and Alcoholism; National Heart, Lung, and Blood Institute; National Institute of Neurological and Communicative Disorders and Stroke; National Institute of Arthritis, Diabetes, Digestive, and Kidney Disease; National Institute of Allergy and Infectious Diseases; and the National Institute of Child Health and Human Development. All of these agencies were involved in both developing topics important to their specialty areas and designing procedures to collect data that would address these issues (Cohen et al., 1987; Cox et al., 1992; Cox et al., 1997; Engel, Murphy, Maurer, & Collins, 1978; Finucane et al., 1990; NCHS, 1979; NCHS, 1987).

The goal for the NHANES I Epidemiologic Follow-up Study was to examine the relationship of baseline clinical, nutritional, and behavioral factors assessed in NHANES I to subsequent morbidity and mortality. The size and scope of the population in NHEFS provide a unique opportunity not only to relocate more limited studies, but also to examine etiologic relationships in a large, heterogeneous nationally representative population (NCHS, 1979).

Survey Design

The following discussion, as well as the subsequent discussion on data collection, is a summary of the research design of the NHANES I, the NHANES 1 Augmentation, and NHEFS studies as it is presented in the Plan and Operation of the Health and Nutrition Examination Survey (1971-1975) (NCHS, 1979).

It should be noted that the sample for the present research study includes U.S. non-institutionalized adults 25-74 years of age. This sub-sample was extracted from the original probability sample of the U.S. non-institutionalized civilian population, ages 1-74 years, from which data for the first Health and Nutrition Examination Survey (NHANES I) was collected. As a result, the procedures employed in the sample design for the 1971-1974 original sample are the same for this particular sub-sample. The only exception is that from July 1974 through September 1975, this sub-sample of adults was given additional examination components which focused on other aspects of health. These additional components were designated as the "detailed" components in contrast with the somewhat simpler nutrition examinations. In other words, in addition to the interviews and tests that were performed among all participants in NHANES I original sample, the participants in this particular sub-sample received a more detailed, standardized health examination, which was continued through September 1975. Other examinations of this specific sub-sample included assessment of their overall health care needs and personal health behavior.

It was realized that the early 1970's were the times when interests in personal health behavior and its association with personal health status was at its peak. Researchers were more interested in explaining how individuals' personal health

practices were associated with personal health status. In particular, researchers were more interested in linking personal health behavior with mounting chronic diseases, a link which health professionals and epidemiologists were trying to understand. Therefore, this particular sub-sample was selected because the participants were believed to be capable of practicing healthful personal health behavior, and they were a group believed to be at risk of developing chronic diseases that seemed to increase with age.

No particular over-sampling of sub-groups of the population was done in this sub-sample (e.g., women of childbearing age were not over-sampled as they were for the major nutrition study of NHANES I). This process was important to prevent increased sampling error. Since each participant in the sample had a known, non-zero selection probability, over-sampling of a particular group would have eliminated that known non-zero equal chance for other members to be included in the sample. Over-sampling would also have caused the sample to be heavily weighted in favor of the over-sampled group, resulting in unrepresentativeness. The results of the study would also be misleading.

The original sample for the NHANES I (National Health and Nutrition Examination Survey I) included about 30,000 persons who were 1 to 74 years old at the beginning of the survey. This sample provided for over-sampling of special sub-groups such as the elderly, women of child-bearing age, people in poverty areas and children. These were the groups believed to be high risk of malnutrition and premature death. However, only a little more than 96% were interviewed. About 75% (20,749) were examined (NCHS, 1979).

The NHANES I Augmentation Survey sample included 20,749 persons age 25 to 74 years. Of the persons included in the sub-sample for the present research study, only

14,407 (70%) completed the health examination which was required of all subjects (NCHS, 1979). Overall response rate is one guide to the representativeness of the sample. If a high response rate is achieved, there is less chance of significant response bias than if a low response rate is achieved (Bailey, 1982). Further, Bailey notes that a response rate of at least 50% is adequate for analysis and reporting. A response rate of at least 60% is good (Babbie, 1982). The fact the researchers managed to successfully complete the examination of 70 percent of the respondents in this study suggests the response rate is very good. Although percentage rates are rough guides with no statistical basis, it is assumed this high response rate had no response bias. Therefore, the sample in this research study is said to be representative.

Survey Design for NHANES I

The sample design for NHANES I was developed essentially from a set of specifications that took into consideration the requirements and limitations placed upon it. Eight specifications were considered to be of primary importance. (1) The target population was the civilian, non-institutionalized population 1 to 74 years of age residing in the coterminous United States, with one exception. All people residing on any of the reservation lands set aside for the use of American Indians were excluded from the research. (2) For the nutrition component, broad national estimates were made annually, with more detailed estimates published upon completion of a 2-year cycle. For the detailed examination, broad national estimates were based on data collected during 2-year cycles, with more detailed estimates made after completion of the two successive 2-year

cycles. (3) Three mobile examination centers similar to the ones used in the earlier cycles were used. Therefore, with appropriate modifications, the survey was based on administrative and logistical procedures that were developed over a period of ten years. A team examined about 20 persons per day; of these, all received the nutrition examination; operationally, the three caravans visited a maximum of about 65 primary sampling units (PSU's) over a period of approximately two years. (4) A team stayed at least three weeks at a stand because of the expense of moving and the need to allow enough time in an area to give sample persons adequate time to be examined. (5) About 20% of the sample should be selected from the population classified at or below the poverty level. Other groups of special interest included pre-school children, women of childbearing age, and the aged. (6) The estimates from the survey were two kinds: (a) distributions of the population by specified characteristics such as height, weight, blood pressure, and selected biochemical determination; and (b) prevalence in the population of selected chronic conditions, particularly those in the arthritic, respiratory, and cardiovascular groups. (7) Maximum target tolerances for sampling variability were set for several key statistics, permitting a general analysis by broad geographic regions, population size groups, and other major sub-groups such as income, race, age, and sex. (8) Data from the 1960 Decennial Census were used in the sampling procedures until 1970 data became available.

Study Designs and Methods for NHANES I Epidemiologic Follow-up Surveys

The population of the follow-up survey (NHEFS) included the 14,407 participants who were 25 to 74 years of age when they were examined in NHANES I (1971-1975). Thus, the ages of the participants in this sample ranged from 32 to 86 years at the time of the follow-up. At the 1987 NHEFS, the ages of the participants ranged from 37 to 91 years, and 42 to 96 years at the time of the last follow-up in 1992. An attempt was made trace all of these examinees to their current address. However, only ninety-three percent (93%) was successfully traced and seven percent (7%) was lost to the survey. Consequently, the attrition rate was very good since only 7% of the members of the cohort was lost to data collection.

According to Menard (1991), a high attrition rate of 50% or more usually limits the generalization of the results to only the respondents who were retained in the study. However, since the attrition rate for the present study was only seven percent (7%), we can conclude that the results of the analysis were generalized beyond the respondents who were retained in the study.

Proxies were provided for those examinees who were incapacitated or deceased. In order to be accepted as a proxy respondent, the individual had to answer correctly the verification questions which were used to establish the identity of the deceased NHANES I participant. Persons who had lived with the subject were the preferred proxies. Thirty-seven percent of the proxy respondents were spouses of the subject, 39 percent were children, 10 percent were siblings, and the remaining 14 percent had various connections with the subject such as a friend, neighbor, and other relative (NCHS, 1979).

Until the initiation of the NHEFS, the NHANES I examinees had not been contacted by the NCHS or any of the NIH collaborators. Since the validity of longitudinal studies is dependent on completeness of follow-up, extensive and varied efforts were made to trace and establish the vital status of all NHEFS participants. A person was considered successfully traced if the person or a proxy (in case of those deceased or incapacitated) correctly responded to a set of verification questions establishing the participant's identity. All persons who could not be traced were considered lost to follow-up.

The fact of death had to be confirmed by a death certificate or a proxy interview. In some cases, information about death of a subject was obtained from neighbors or other tracing contacts. Although this information was noted in the record, these persons were considered lost to follow-up unless the information was verified by a proxy interview or a death certificate. As of August 1984, 93% of the study population was successfully located – 11, 358 were alive at follow-up, and 2, 022 were deceased. However, the success of tracing efforts varied by age, race, and sex (NCHS, 1979).

The demographic characteristics of the sample for NHANES I and NHEFS surveys are compared with those of persons, 25 years and above reflected in the 1974 and the 1984 U.S. Census data. The characteristics of both samples and those of the United States population are somewhat at variance. However, the difference in percentage distributions for both samples and the national population is not large, especially in sociodemographic characteristics as race, sex, and marital status. The percentage distributions for people who had completed high school and those who had some college education are also compatible with the national data. The income categories also show

similarities with incomes of the general population for the years 1974 and 1984 as well as the other follow-up years.

During the time of the NHANES I survey, the income levels of most participants were below $20,000. The income level was perhaps comparable to households' income for the rest of the U.S. population at the time, as reflected in the 1974 U.S. Census. For example, the 1974 U.S. Census shows the median income for a household to be $11,197. However, during the time of the follow-up survey (NHEFS, 1981-1984), the income levels were much improved (e.g., 36.3% of the households had incomes of $20,000 and above). These figures also compare well with household's income for the rest of the U.S. population as reported by the U.S. Census (1984).

Bailey (1982) states that a sample is more representative of the population from which it is selected if the characteristics of the sample closely approximate those same characteristics in the population. Based on the above discussion, since characteristics of the sample for the present research study have shown to approximate those of the U.S. population, it can be concluded that this sample is representative. Furthermore, the type of sampling procedure used (stratified probability sampling) in sample selection for the present study and the size for the sample (20,749 in NHANES I and 11,358 for NHEFS) both affect the degree of representativeness of the sample – decreasing the probability of sampling error.

According to Pedhazur (1982), a study for which the results can be generalized to the population has external validity. However, generalizability can be limited by lack of representativeness resulting from changes in the original sample relative to its status at the time the sample was drawn. Changes in the sample size or attrition rate particularly

threaten internal validity of the study (Pedhazur, 1982). In the present study, the attrition rate was approximately seven percent (7%) for the follow-up studies. Nesselroade (1988) points out that a small attrition rate may not be problematic to the representativeness of the sample. Thus, the results for the present study were generalizable.

Data Collection

This section deals with the procedures involved in the collection of the data used for this present study. A description of the variables and the validity and the reliability of these variables are provided.

Baseline Data Collection Procedure (NHANES I)

Data in NHANES I survey was obtained by means of household interviews, general medical histories, 24-hour dietary intake recall interviews, food frequency interviews, food program questionnaires, general medical examinations, dental, dermatological and ophthalmological examinations, anthropometric measurements, and 24 hematological, blood chemistry, and urological laboratory determinations.

In addition to the information received on all examined persons by means of the above questionnaires, procedures and measurements, data were gathered using a medical history supplement, supplementary questionnaires concerning arthritis, respiratory and cardiovascular conditions (when applicable); a health care needs questionnaire; a general well-being questionnaire; an extended medical examination; X-rays of the chest and hip

and knee joints; audiometry; electrocardiography; spirometry; pulmonary diffusion and tuberculin tests; along with additional laboratory determinations.

Detailed examinations were given by dentists, ophthalmologists, and dermatologists with an assessment of need for treatment. In addition, personal or telephone interviews were conducted by pre-trained interviewers. Questionnaires were divided into two sections; one section covered the demographic information of the respondent while the second covered the medical history.

An advance letter, announcing the forthcoming arrival of an interviewer from the U.S. Bureau of the Census, was mailed to each household that fell into the sample area. The interviewer subsequently visited the household to ascertain its composition and to administer a questionnaire, the primary purpose of which was to obtain demographic information. The questionnaire was administered to each potential sample person that was available and competent enough to respond to the questions. In the event that a potential sample person was not at home at the time of interview, any responsible adult in the household was asked to respond to the questions for the absent person.

For the main part of the survey, the medical history was taken in the sample person's home by an interviewer of the Health Examination Representative (HER), visited the sample person's home after the Census interviewing was complete and sample selection made. In addition to asking the medical history questions, the interviewer had the important responsibility of enlisting the sample person in the survey, gaining his or her cooperation and consent to the examination. The HER had to explain the purpose of the survey and convince sample person to make an appointment for the examination.

Further, the interviewer also administered a Food Programs Questionnaire and a General Medical History.

When administering the questionnaires the interviewer administered the questions in private to encourage openness and honesty on the part of the respondent and enhance the feeling of confidentiality. The fact that the respondent feels a sense of confidentiality when answering a questionnaire reduces any sense of bias and errors, while increasing the validity and reliability of the data.

During the continuation of the detailed sample (NHANES I Augmentation Survey of adults 25-74 years); Census interviewers replaced Health Examination Representatives (HER) in administering most of the material in the medical history forms as a part of the initial household interview phase of the survey. Because of this change in interviewers, the task of asking certain "sensitive" questions (e.g., those relating to kidney and bowel function) was given to the examining physician.

Examinations and interviews were conducted in a specially equipped and designed mobile examination centers that traveled to survey locations throughout the country. The survey team consisted of a physician, dentist, medical and health technicians, and dietary and health interviewers. A large staff of interviewers conducted the household interviews (NCHS, 1979).

In each location, local health and government officials were notified of the upcoming survey. Households in the survey received an advanced letter and booklet to introduce the survey. Local media also featured stories about the survey. To facilitate and encourage participation, transportation was provided to and from the examination center and participants received remuneration (NCHS, 1979).

In addition to the information received on all examined persons by means of the above questionnaires, procedures, and measurements, interviewers used a medical history supplement; supplementary questionnaires concerning arthritis, respiratory and cardiovascular conditions (when applicable); a health care needs questionnaire; a general well-being questionnaire; and extended medical examination; X-rays of the chest and hip and knee joints; audiometry; electrocardiography; spirometry; pulmonary diffusion and tuberculin tests; along with additional laboratory determinants to gather data.

Data Collection for NHANES I Epidemiologic Follow-up Surveys

The primary purpose of the NHEFS is to investigate the association between factors measured at baseline and the development of specific health condition. Three major objectives for study in the NHEFS cohort are Miller (1978) the morbidity and mortality associated with suspected risk factors; National Center for Health Statistics (1977) changes over time in participants' risk factor characteristics, and Engel et al, (1978) the natural history of chronic disease and functional impairments due to disease. To date, the NHEFS comprises a set of four follow-up surveys. The first was conducted between 1982 and 1984, the second in 1986, another in 1987, and the fourth in 1992. The first follow-up wave, conducted between 1982 and 1984, included all participants who were 25 to 74 years of age at the NHANES I baseline examination (n=14,407). The second follow-up wave, conducted in 1986, on the other hand, included only persons who were 55 to 74 years of age at the NHANES I baseline examination (n=3,980). The third and fourth follow-up waves were conducted in 1987 (n=11,750) and 1992 (n=11,195)

included all non-deceased participants of the NHANES I who were 25 to 74 years of age at baseline examination, regardless of whether they had been successfully traced or interviewed earlier. Each follow-up wave consisted of first tracking the participant or proxy to a current address, conducting interviews with the participant or proxy, abstracting records from health care facility stays and collecting death certificates for deceased participants (Cox et al., 1997).

Contacting Study Participants

Keeping in contact with study participants was done using a large variety of sources. The first step to tracking study participants was to contact directory assistance in the area where the participant had last been known to live. Other sources used after directory assistance inquiries included post office address inquiries, social security administration inquiries, state department of motor vehicle listings and credit bureau checks for participants and relatives and spouses of participants who were included in the household composition listings obtained in NHANES I. If participants were not located by the above means, directory searching was undertaken to locate residents living on the block where the subject was last known to have resided. If located, the persons were contacted to determine whether they were familiar with the whereabouts of the study participant. Any participant identified using the above means was considered a possible match and subjected to verification procedures.

Respondents for possibly-matched subjects were contacted and administered a tracking questionnaire to correctly establish the participant's identity. Once the name of

the subject was verified, the respondent was requested to supply at least two of the following items: the participant's date of birth, participant's address at the time of the last study contact, or the participant's household composition at the time of the last study contact. A participant's death was required to be confirmed by either a proxy interview or a death certificate.

Data Collection for Interviews

An attempt was made to interview all subjects identified during tracking. During the 1982 to 1984 follow-up wave, the interview was conducted in-person wherever the participant resided, including in nursing homes, prisons, mental health facilities, or occasionally, at some other convenient location (for example at a parent's home). The interviews included a 76 page Subject questionnaire and a physical measurement component which lasted for about 2 hours. Several questions related to the occurrence of hypertension, angina, myocardial infarction, claudication, and stroke were administered. Current smoking, as of the NHANES I baseline examination, was determined for the 11,348 persons who did not undergo detailed examination at baseline from responses to these questions or the same questions administered at a later follow-up wave. The validity of such information on tobacco use has been reviewed elsewhere (Machlin et al., 1989). The participant's pulse rate, blood pressure (three consecutive readings), and weight were measured at the end of the interview.

In contrast to the 1982-1984 interview procedures, the interviews in subsequent NHEFS follow-up waves were conducted over the telephone using a computer-assisted

telephone interview (CATI) system and did not include physical measurements (Cohen et al., 1987; Cox et al., 1997; Finucane et al., 1990). When a telephone number was not available, the respondent was sent a mail questionnaire to complete. Questions regarding the occurrence of coronary by-pass surgery and pacemaker procedures were added to the subsequent follow-up waves. Each set of questions on a particular condition also included a question to ascertain whether or not the subject had been for that condition since the beginning of the current decade. Whenever possible, the questionnaire was designed to retain item comparability between NHANES I and NHEFS in order to measure change over time. However, questionnaire items were modified, added, or deleted when necessary to take advantage of current improvements in questionnaire methodology (NCHS, 1979).

Quality Assurance Procedures

Thorough quality assurance procedures were instituted in all four waves of the follow-up data collection. A 3-day program of physical measurements training and an intensive 8-day interview training session was held for data collectors who participated in the 1982-1984 follow-up study. Questionnaires were edited in the field by interviewers so that the participants could be easily re-contacted if there were discrepancies or missing section in key items. Fifteen percent of the questionnaires were randomly selected for validation. This was done primarily by telephone and, if necessary, by mail. Additional questionnaires were selected for verification if the data were believed to be false.

In subsequent waves of data collection, a computer-assisted telephone interviewing (CATI) system was used. This computer program drove the questionnaire so that the correct skip patterns were followed and the appropriate questions were displayed on the computer monitor. The skip patterns are based on information gathered either from previous data collection waves or from responses provided during the interview. Edit and logic checks are incorporated into the data collection system itself, thus improving the quality of data. In addition, ten percent of the telephone interviews were validated.

Application of the Data to the Current Study

In this section, the outcome variable, exposure variable, and covariates used in this study are presented. Conceptualization and operationalization of these variables are provided. Each variable is defined and the way it is used to solicit responses from the sample is discussed.

Outcome Variable

A diagnosis of diabetes was based on the 1997 American Diabetes Association criteria which included a reported history of physician-diagnosed diabetes mellitus. Specifically, each person was asked whether a doctor had ever told the person that he/she had diabetes mellitus. Responses to the various conditions are therefore, coded as: 1 yes, 2 no, 8 don't know, or 9 not ascertained. Each condition is recoded with 1 representing

that the participant had type 2 diabetes mellitus, 0 representing that the participant did not have type 2 diabetes mellitus, while 8 and 9 are coded as missing. Since the present study is longitudinal, classification of type 2 diabetes was determined at the beginning of the NHANES 1 survey (baseline) and at follow-up surveys (NHEFS) in order to observe any change in participants' diabetic status from the beginning of the survey to the end of the follow-up.

In this research study, type 2 diabetes mellitus classification was used to conceptualize the diabetes status variable because the secondary nature of the data did not allow for a different conceptualization. That is, in order to conceptualize this variable properly in this longitudinal study, definitions changed over the years but for purposes of this analysis, the initial recorded type 2 diabetes status was used regardless of potential misclassifications.

Exposure Variable

The independent variable used in the research study was parity which was examined at baseline (NHANES 1) and during the follow-up surveys (NHEFS) to measure any changes over time in the level of parity and its association with type 2 diabetes diagnoses. Parity was defined as the total number of live births. It was measured as an interval level variable to prevent the loss of variability. As parity was not coded consistently in the 1982, 1987, and 1992 follow-up surveys, a default judgment was made that the parity measures of women who were older than 45 years of age during the baseline survey (1971-1975) were used during the 1982 (time 1), 1987 (time 2), and

1992 (time 2) follow-up survey analyses. The rate of birth for women 45 years of age and older was only .08% in 1971 compared to the younger age groups (National Center for Health Statistics, 2005). Statistics show as women age beyond 45 years, their childbearing decreases dramatically. Therefore, a default judgment was made that the parity measures of women who were older than 45 years of age during the baseline survey (1971-1975) were used during the 1982 (time 1), 1987 (time 2), and 1992 (time 2) follow-up survey analyses. This was done to allow parity to be stable across the time periods for women for whom data were missing and for whom there was a likelihood they were beyond childbearing age. The other variables listed in the present study that changed over time from baseline (1971-1975) throughout the three follow-up time periods include age, BMI, parity, and diabetes. The remaining variables, race, education level, income, blood pressure, cholesterol level, fat intake, alcohol, smoking, and physical activity did not change. These variables were measured at baseline and their baseline measures were used during the three follow-up time periods.

Independent Variables

There are several independent variables in this study. The variables examined are age, race, income, education level, physical activity, alcohol use, smoking status, hypertension, cholesterol level, Body Mass Index (BMI), fat intake, and number of miscarriages. Information on demographics, education level, physical activity, alcohol use, smoking status, hypertension, cholesterol level, Body Mass Index (BMI), fat intake, and number of miscarriages was obtained at baseline survey (NHANES I) and during the

follow-up visits. Weight and height were measured and BMI was calculated as weight in kilograms divided by height in meters squared.

Age**:** This variable is operationalized by the respondents' actual age at the time of the initial interview (NHANES I Survey). During the NHANES I interview, respondents' ages ranged from 25 to 74 years of age, while during the follow-up surveys (NHEFS) the ages ranged between 32 and 86 years old. This variable is treated as an interval level variable. This is done to examine the variation between all of the ages.

Race**:** This is a categorical variable which was operationalized to include only Caucasian and African American participants. This was done in order to observe the variation in the relation of parity to type 2 diabetes mellitus development among the two racial groups. Since there was little representation from other races and a small sample size (n = 148), only African American women and Caucasian women were examined. This was also done to maximize the variable. This variable was recoded in such a way that a value of 1 represents Caucasians and 2 represents African Americans.

Income**:** This variable is operationalized as the recode of "annualized family income for 1974." The income variable is an ordinal variable in the data set that has been recoded within the data into different levels. The different income levels ranged from under $1,000 to $25,000 and above. The respondents were asked "which of these income groups represents your family total annual income"? The variable was dichotomized based on a median cut. The variables were listed as 1) less than $20,000 and 2) greater than $20,000. This was done to prevent inflation in the standard errors during the Cox Regression Hazard analysis.

Education**:** This variable indicates the education level of the individual respondents and was examined at baseline. The variable is operationalized by asking the respondents to state the highest grade of regular school ever attended. In order to allow for better manipulation during analysis, this variable was also recoded. The variable was recoded in such a way that the education levels were 0 – 4, with 0 representing those with no education, 1 representing those who attended grades 1-8, with 2 representing those who attended grades 9-12, with 3 representing those who graduated from high school, and with 4 representing those who graduated from college.

Physical Activity**:** This variable is defined by measures indicating whether a respondent is moderately active or inactive during the NHANES I survey. The variable is operationalized by asking the respondents the following question: In your usual day, aside from recreation, how active are you? The variable was dichotomized due to the skewness of the data. The codes were listed as 1 representing moderately and highly active and 2 representing inactive.

Alcohol use**:** This is a continuous variable which represents the amount of alcohol participants consume over a period of 24 hours at baseline. Measured at interval level, it is operationalized by the actual number of alcoholic beverages of either wine, beer, or liquor a participant consumes in a period of 24 hours. The number of alcohol beverages is represented by codes 01-54 in a period of 24 hours. The variable was recoded to 1 representing alcohol use and 2 representing no alcohol use. This was done to maximize the variable representation because the data set was highly skewed. There were too many participants who reported 0. Therefore, the variable was dichotomized due to the skewness.

Body Mass Index (BMI)*:* This variable is a continuous variable which represents the weight in kilograms divided by meters squared (kg/m^2). The variable was operationalized by asking the participants their weight and height measurements at baseline and during all of the follow-up surveys.

Smoking status**:** This variable is a dichotomous variable. The variable was operationalized by asking the participants at baseline (NHANES I survey), "Do they currently smoke? The variable was recoded to 1 representing yes and 2 representing no. This was done to maximize the variable representation.

Blood pressure**:** This variable is an interval level variable and was operationalized by asking the question: "What is your blood pressure"? The blood pressure measures are listed in (mmHg/mmHg).

Cholesterol level**:** This variable is a continuous variable and was operationalized by asking the question at baseline (NHANES I): "What is your cholesterol level"? The variable was listed as (mg/dl).

Fat intake**:** This variable is a continuous variable which represents the amount of fat consumed in a day. The variable is operationalized by asking the question at baseline (NHANES I survey): "How much fat is consumed in a day"?
The participants were asked to estimate their daily fat intake. If they were not sure, they summarized their daily food intake and the data collector estimated their fat intake by reviewing a standardized chart. The variable was listed in (g).

Total number of miscarriages**:** This variable is a continuous variable which represents the number of miscarriages occurred which was measured at baseline. The

variable is operationalized by asking the question: "How many miscarriages have you had"?

Statistical Analysis Plan

The core research question for this study is to what extent does the level of parity account for the differences in the probability of developing type 2 diabetes mellitus after controlling for other risk factors?

The sub-questions for this study:

1. To what extent does the level of parity between baseline and the initial follow-up (baseline vs. time 1) account for the differences in probability of developing type 2 diabetes mellitus?
2. To what extent does the level of parity between baseline and the second follow-up (baseline vs. time 2) account for the differences in probability of developing type 2 diabetes mellitus?
3. To what extent does the level of parity between baseline and the third follow-up (baseline vs. time 3) account for the differences in probability of developing type 2 diabetes mellitus?
4. To what extent does the interaction effect between parity and race account for the differences in the probability of developing type 2 diabetes mellitus at baseline to time 1, time 2, and time 3?
5. To what extent does the interaction effect between parity and BMI account for the differences in the probability of developing type 2 diabetes mellitus at baseline to

time 1, time 2, and time 3?

As a first step in the investigation of associations between change in parity and the risk of type 2 diabetes mellitus development, potential confounders of this relationship were identified through literature review and theory as potential confounders of the data set.

The Cox's proportional hazards regression analysis was used to examine the relationship of baseline risk factors to incidence of type 2 diabetes mellitus development (Allison et al, 2001). This model assumes the hazard rate (incidence of type 2 diabetes mellitus) of an individual *j* with risk factors represented by the vector *x* is a constant multiple, exp (B_jX_j), of the baseline hazard rate at all times. The Cox proportional hazards model is the preferred model for analyzing data from the National Health and Human Examination Survey because it takes into account differential follow-up time and does not require that survival time be exponentially distributed (Ingram & Makuc, 1994). The Cox proportional hazards model can be generalized for non-proportional hazards. It uses the combination of the model and the estimation method. The model assesses the relationship between a set of risk factors and disease incidence. This is the preferred model for analyzing data from the NHEFS because it takes into account differential follow-up time. The Cox Proportional Hazard Model is:

$$h(t) = [h_0(t)]\, e^{(b_1 X_1 + b_2 X_2 + \ldots b_k X_k)}$$

This model can also be expressed as the Relative Hazard and as the Log-Relative

Relative Hazard:

$$\left(\frac{h(t)}{h_0(t)} \right) = e^{(b_1 X_1 + b_2 X_2 + \ldots b_k X_k)}$$

Log-Relative:

$$\ln \left(\frac{h(t)}{h_0(t)} \right) = (b_1 X_1 + b_2 X_2 + \ldots b_k X_k)$$

Dividing both sides of the Cox Proportional Hazard Model by $h_0(t)$ gives you the hazard ratio or relative hazard. The log-relative hazard is derived by taking the logarithm of both sides of the hazard ratio.

Where

- h (t) = the hazard function at time t
- $h_0(t)$ = the baseline hazard or hazard for an individual when the value of all of the independent variables equal zero.
- Exp (b) is the hazard ratio or relative hazard. The ratio indicates the expected change in the risk of the event when X changes from 0 to1. (i.e. 1 = presence of the characteristic X).
- b_k = regression coefficient

The Cox Proportional Hazard Model

1. Predicts the hazard function h (t) – The probability that an event will occur at time (t).
2. Makes no assumptions about the nature or shape of the hazard function
3. Assumes that changes in levels of the independent variables produces proportionate changes in the hazard function, independent of time.
4. It also assumes a log-linear relationship between the hazard function and the independent variables.

With the risk factors inserted, the resulting Cox regression model:

$$h(t) = [h_0(t)]\, e^{(b_1 \text{number of live births} + b_2 \text{age} + b_3 \text{race} + b_4 \text{education level} + b_5 \text{income} + b_6 \text{BMI} +}$$

b_7 parity * race + b_8 parity * BMI + b_9 total miscarriages + b_{10} systolic blood pressure + b_{11} diastolic blood pressure +

b_{12} cholesterol + b_{13} drink + b_{14} physical activity + b_{15} fat intake)

- When X = 0, h (t) = [h_0 (t)] (1), since $e^0 = 1$
- When X = 1, h (t) = [h_0 (t)] $e^{(b_1)(x_1)}$
- Where b_1 = Cox regression coefficient, determined by partial likelihood estimation.

The partial likelihood model discards the first part of the general model and treats the second part, the partial likelihood function, as though it were an ordinary likelihood function. The estimates are derived by finding values of β that maximize the partial likelihood (Allison, 1995).

With <u>all</u> of the variables inserted in the model:

h (t) = [h_0 (t)] $e^{(b_1}$ number of live births + b_2 age + b_3 race+ b_4 education level+ b_5 income + b_6 BMI +

b_7 parity * race + b_8 parity * BMI + b_9 total miscarriages + b_{10} systolic blood pressure + b_{11} diastolic blood pressure +

b_{12} cholesterol + b_{13} drink + b_{14} physical activity + b_{15} fat intake)

The Cox proportional hazards model assumes changes in levels of the covariates produces proportionate changes in the hazard function, independent of time. It is an estimate of the relative risk of type 2 diabetes diagnosis.

The estimation method used is the partial likelihood estimation of b_k. The process begins by determining the likelihood of the baseline hazard function [h_0 (t)], when $b_k = 0$. It is called the hazard for a chance or null model. The likelihood (L) is determined by taking the risk of type 2 diabetes mellitus at each point (t) and multiplying them together.

- $L = \Pi_{i=1}^{j} [h (t_i)]$

Chi –square tests were conducted to determine whether the addition of the variable *number of pregnancies or parity* results in a significant decrease in the -2LL.

Models were initially fitted using only the variable of interest. In subsequent stages of fitting, other variables were added to the model, as well as interaction terms involving the variable of interest. The statistical significance of such terms was evaluated using the likelihood ratio test at 0.05 significance level. The proportional hazards assumption was checked using time-dependent interaction terms evaluated with the same criteria (Allison, 1995). Data from participants beyond 65 years of age were censored at 65 years.

Statistical Analysis Plan for Research Sub-Question 1

To what extent does the level of parity between baseline and the initial follow-up account for the differences in probability of developing type 2 diabetes mellitus? To examine whether parity at baseline and change in parity during the initial follow-up survey were associated with future type 2 diabetes mellitus development, a descriptive analysis of all variables was performed. After testing for continuous variables and proportionality assumptions, a series of models adjusting for potential confounders to estimate the relative hazard (RH) of developing diabetes was conducted. Parity was added to the model first. This was done to determine the relation between parity and type 2 diabetes. Parity was examined first to see if parity was significant prior to controlling for other known risk factors. Covariates were then added to the model to determine their prognostic significance of the change in parity over time and the risk of type 2 mellitus

development. In step 1, parity was added to the model to determine if there was an association between change in parity over time and type 2 diabetes mellitus development. In step 2, demographic characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity & BMI interaction variable, and parity & race interaction variable) were added. In step 3, reproductive history (miscarriages) was added. In step 4, physiological history (hypertension status and cholesterol level) variables were added. In step 5, the final step, the behavioral factors (alcohol use, smoking status, physical activity, and fat intake) were added to the model.

Statistical Analysis Plan for Research Sub-Question 2

To what extent does the level of parity between baseline and the second follow-up survey account for the differences in probability of developing type 2 diabetes mellitus? To examine whether parity at baseline and change in parity during the second follow-up survey were associated with future type 2 diabetes mellitus development, a descriptive analysis of all variables was performed. After testing for continuous variables and proportionality assumptions, a series of models adjusting for potential confounders to estimate the relative hazard (RH) of developing diabetes was conducted. Parity was added to the model first. This was done to determine the relation between parity and type 2 diabetes. Parity was examined first to see if parity was significant prior to controlling for other known risk factors. Covariates were then added to the model to determine their prognostic significance of the change in parity over time and the risk of type 2 mellitus development. In step 1, parity was added to the model to determine if there was an

association between change in parity over time and type 2 diabetes mellitus development. In step 2, demographic characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity and BMI, and parity & race) were added. In step 3, reproductive history (miscarriages) was added. In step 4, physiological history (hypertension status and cholesterol level) variables were added. In step 5, the final step, the behavioral factors (alcohol use, smoking status, physical activity, and fat intake) were added to the model.

Statistical Analysis Plan for Research Sub-Question 3

To what extent does the level of parity between baseline and the third follow-up survey account for the differences in probability of developing type 2 diabetes mellitus*?* To examine whether parity at baseline and change in parity during the third follow-up survey were associated with future type 2 diabetes mellitus development, a descriptive analysis of all variables was performed. After testing for continuous variables and proportionality assumptions, a series of models adjusting for potential confounders to estimate the relative hazard (RH) of developing diabetes was conducted. Parity was added to the model first. This was done to determine the relation between parity and type 2 diabetes. Parity was examined first to see if parity was significant prior to controlling for other known risk factors. Covariates were then added to the model to determine their prognostic significance of the change in parity over time and the risk of type 2 mellitus development. In step 1, parity was added to the model to determine if there was an association between change in parity over time and type 2 diabetes mellitus development.

In step 2, demographic characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity and BMI, and parity and race) were added. In step 3, reproductive history (miscarriages) was added. In step 4, physiological history (hypertension status and cholesterol level) variables were added. In step 5, the final step, the behavioral factors (alcohol use, smoking status, physical activity, and fat intake) were added to the model.

Statistical Analysis Plan for Research Sub-Question 4

To what extent does the interaction effect between parity and race account for the differences in probability of developing type 2 diabetes mellitus? In the present study, baseline data and follow-survey data were examined to determine the interaction effect between parity and race in the subsequent development of type 2 diabetes. In step 2, demographic characteristics, BMI, age, race, income level, education level, BMI, parity and BMI, and parity and race were added to the model.

Statistical Analysis Plan for Research Sub-Question 5

To what extent does the interaction effect between parity and BMI account for the differences in probability of developing type 2 diabetes mellitus? In the present study, baseline data and follow-up survey data were examined to determine if the interaction effect between parity and race is associated with type 2 diabetes. In step 2, demographic characteristics, BMI, age, race, income level, education level, BMI, parity and BMI, and parity and race were added to the model.

The present study used methods to estimate variances that take into account sample clustering and stratification of the NHANES I sample in Cox proportional hazards models (Ingram & Makuc, 1994; Korn et al., 1997). However, weights were not included in this estimation. Sample weights calculated for the NHANES I survey are highly variable and skewed to the right. Weights for all 14,407 persons included in the NHEFS range from 442 to 68,027, encompassing a 154 fold difference between the smallest and largest weight (Ingram & Makuc, 1994). Strong right skewing of the weights is also apparent. For instance, the 98th percentile weight for the total NHEFS sample is 22,209, considerably smaller than the maximum sample weight of 68,027 (Ingram & Makuc, 1984). An individual with a large sample weight may have a large and possibly undesirable influence on estimates, particularly if that individual has an unusual value for the variable of interest. In addition, because of the variability of the sample weights, weighted standard errors tend to be considerably larger than the unweighted standard errors (Ingram & Makuc, 1994; Korn & Graubard, 1991). Ingram and Makuc (1994) discuss the use of weights in regression analyses of the NHEFS sample and noted that trimming weights at the 98th percentile produced a marked change in the size of regression coefficients and their standard errors. After trimming, the results of analyses including weights were similar to unweighted results. The authors also state that given the high variability and skew of the sample weights, it is not clear that the weighted analyses are appropriate (Ingram & Makuc, 1994). Another approach is to use an unweighted analysis but include the variables utilized in determining the sample weights, age, race, and sex (Ingram & Makuc, 1994; Korn & Graubard, 1991; Korn et al, 1997). Such an analysis represents a compromise that avoids the statistical inefficiency of a

weighted analysis (Korn & Graubard, 1991). This last option was employed in all of the analyses presented here parity and its relationship to the development of type 2 diabetes mellitus in the NHEFS cohort. In the analysis of the NHEFS cohort, neither stratification nor weights were used in the analyses as participants were being compared to themselves.

CHAPTER 4

RESULTS

In this chapter, the empirical findings associated with the research question and the research sub-questions outlined in chapter three are presented. Cox proportional hazards regression analysis was performed to answer the research questions. Various statistical parameters such as Hazard Ratios (HR's), Confidence Intervals (CI's), and -2 log likelihood (-2LL) values, and *p*-values were used to evaluate the research questions.

The criterion that is used in this research with respect to meaningfulness is a Wald test for significance value for each covariate and a -2LL test for the model overall. The findings were considered statistically significant if the *p*-values were $< .05$.

Descriptive Results for NHANES I 1971-1975 (Baseline Data)

Tables 3 and 4 show baseline characteristics of 6,530 out of 8,596 female participants aged 25 to 74 years without type 2 diabetes mellitus in the NHANES I. There were 2066 women in the study in which their type 2 diabetes mellitus status was missing. This reduced the sample size to 6,530. The mean age of the sample was 47 years (SD = 16) at baseline. Most of the participants were Caucasian women who had an average income range of approximately $5,000 to $9,999 (30.7%, n = 2007) and only possessed a twelfth grade education level (36%, n = 2353). A majority of this sample did not perform any

moderate physical activity (64.2%, n = 2362), consumed alcohol (66.0%, n = 4315), and smoked (72.6%, n = 597).

Table 3

Demographic and Health Related Variables of 6530 Adult Women Without Type 2 Diabetes Mellitus

	NHANES I (1971-1975) Sample (baseline)	
Variable	n	Mean (SD)
Age (yr)	6530	47.2 (15.5)
BMI (kg/m^2)	3865	25.6 (5.7)
Hypertension (systolic)	6480	134.7 (10.1)
Hypertension (diastolic)	6485	84.7 (9.6)
Parity	6530	3.4 (1.4)
Cholesterol level (mg/dl)	6530	251.0 (15.3)
Fat intake (g)	6530	60.1 (15.2)
Total miscarriages	5862	0.62(1.1)

N = 6530
NHANES 1971-1975

Table 4

Demographic and Health Related Characteristics of 6530 Adult Women Without Type 2 Diabetes Mellitus

	NHANES I (1971-1975) Sample (baseline)	
Variable	n	%
Physical activity (moderate)	3680	
1 = Yes	1318	35.8
2 = No	2362	64.2
Alcohol use	6530	
1 = Yes	4315	66.0
2 = No	2215	34.0

Table 4 (*Continued)*

Demographic and Health Related Characteristics 6530 Adult Women without Type 2 Diabetes Mellitus

	NHANES I (1971-1975) Sample (baseline)	
Variable	n	%
Smoking status	822	
1 = Yes	597	72.6
2 = No	225	27.4
Race	6530	
White	5394	83.0
Black	1136	17.0
Income (annual)	6530	
Under $1,000	243	3.7
$1,000-4,999	1997	30.6
$5,000-9,999	2007	30.7
$10,000-14,999	1256	19.2
$15,000-19,999	601	9.2
$20,000-24,999	227	3.5
$25,000 and over	199	3.1
Education level	6530	
None	71	1.1
1^{st}-8^{th} grades	1515	23.2
9^{th}-11^{th} grades	1263	19.3
12^{th} grade	2353	36.0
1^{st}-3^{rd} years of college	1068	16.4
4^{th} year of college	213	3.3
College graduate	47	0.7

N = 6530
NHANES 1971-1975

Table 5 illustrates the incidence of type 2 diabetes in the sample. The incidence rate was defined as the number of women who had newly developed diabetes during the 10 years of follow-up. The incidence of diabetes during the 10-year follow-up was also determined by each category of childbearing: no live births, one to two live births, three to four live births, and five or more live births respectively. Confidence intervals for incidence rates were calculated (Oleckno, 2002). There were 21, 49, 29, and 34 incident

cases of type 2 diabetes mellitus among women with no live births, one to two live births, three to four live births, and five or more live births. Approximately 3.2% of the sample was diagnosed with type 2 diabetes by a clinician. Incidence rates ranged from 7.4 per 1,000 person years (95% CI 5.6-9.2) in women with 3 to 4 live births to 8.0 per 1,000 person years (95% CI 6.1-9.9) in women with 5 or more live births to 10.1 per 1,000 person years (95% CI 8.0-12.2) in women with 1 to 2 live births. The incidence of diabetes among women with no live births was 6.5 per 1,000 person years (4.8-8.1).

Table 5

Incidence Rate and Confidence Intervals (CI) of Diabetes by Childbearing Categories, NHEFS 1982-1992

		NHEFS 1982-1992		
Incidence rate of type 2 diabetes	No live births	1-2 live births	3-4 live births	5 or more live births
Number of incident diabetes	21	49	29	34
Incidence rate per 1,000 person - years (95% CI)	6.5 (4.8-8.1)	10.1 (8.0-12.2)	7.4 (5.6-9.2)	8.0 (6.1-9.9)

Table 6 shows baseline established risk factors for diabetes mellitus of 6530 African American and Caucasian women. Apart from age and cholesterol level, the profile of established risk factors for diabetes mellitus was clearly worse in African

American women than in their Caucasian counterparts. In particular, African American women had fewer years of formal education, had more children, were more likely to develop pre-hypertension, had greater measures of BMI, and reported less physical activity. Typical consumption of alcoholic beverages and smoking were lower, and daily fat intake were higher in African American women than in white women; however, alcohol consumption and smoking differences were not statistically significant.

Table 6

Diabetes Mellitus Related Risk Factors of 6530 Women Without Diabetes Mellitus at Baseline NHANES I (1971-1975) Among African American and Caucasian Women

	Race	
Variable	African American	Caucasian
n	1136	5394
Age (yrs)	47.9 ± 15.4	47.2 ± 15.5
Income (annual) (%)		
$10,000 or greater	69.2	30.5
Education (%)		
< High school	61.6	16.0
High school graduate	23.4	41.8
College graduate	15.0	42.2
BMI (kg/m^2)	27.8 ± 6.7	25.1 ± 5.4
Systolic Blood Pressure (mmHg)	146.0	132.6
Diastolic Blood Pressure (mmHg)	94.3	82.9
Alcohol users (%)	32	38
Current Smokers (%)	14	31
Physical activity (moderate) (hrs/wk)	62	74
Fat intake (mg)	61.1 ± 32.7	55.2 ± 35.0
Parity	3.8 ± 2.9	3.3 ± 1.3
Cholesterol (mg/dl)	238 ± 14.1	290 ± 15.9

Data are means ± SD; All *p* values were < .05 for all variables except smoking and alcohol.

The Assumption of Multicollinearity

The assumption of multicollinearity states that none of the independent variables is perfectly correlated with another independent variable or linear combination of other independent variables. According to Lewis-Beck (1976), with non-experimental social science data, the independent variables are virtually always intercorrelated, that is, multicollinear. However, it is only when this problem becomes extreme ($r > .80$) that serious estimation problems often arise (Lewis-Beck, 1976).

When the assumption of multicollinearity is violated, there are usually serious estimation problems. That is, parameter estimates become unreliable, while estimated regression coefficients become so unstable that they may fail to achieve significance due to large standard errors. In other words, the regression coefficients may be over-estimated (Lewis-Beck, 1976).

Asher (1976) had argued multicollinearity poses severe problems to aggregate data rather than survey data. Thus, he reasoned, "The random measurement error component of the scores is likely to be cancelled, whereas in survey data random measurement error attenuates correlation coefficients, thereby making the problem of multicollinearity less likely" (Asher, 1976). This implies that multicollinearity is a characteristic of the sample rather than of the population.

If high multicollinearity is detected, it can be corrected by increasing the sample size if the sample is small. However, if the sample is fixed, one can correct high multicollinearity by combining those independent variables that are highly intercorrelated into a single indicator. Another way of correcting high multicollinearity is to discard those independent variables that are collinear. The examination of the Variance Inflation

Factor (VIF) of the independent variables for the present research study criterion cut-off was 4. All of the VIF's for the independent variables were 4 or less. Therefore, the assumption of multicollinearity was not violated in the present study.

Cox Proportional Hazards Regression Results

1. Cox Proportional Hazards Regression Results for the First Research Sub-question

The first research question seeks to determine to what extent does the level of parity between baseline (1971-1975) and the initial follow-up (1982-1992) account for the differences in probability of developing type 2 diabetes mellitus?

A longitudinal analysis of the 6530 women without diabetes at baseline in the NHANES I cohort and incidence of type 2 diabetes during the NHEFS 1982-1984 using Cox proportional hazards regression model was conducted. In step 1, parity was added to the model to determine if there was an association between change in parity over time and type 2 diabetes mellitus development. In step 2, demographic characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity and BMI, and parity and race) were added. In step 3, reproductive history (miscarriages) was added. In step 4, physiological history (hypertension status and cholesterol level) variables were added. In step 5, the final step, the behavioral factors (alcohol use, smoking status, physical activity, and fat intake) were added to the model. The Relative Hazards changed as the variables were added to the model. The results indicated that having one or more children does not increase the risk of developing type 2 diabetes mellitus. Table 7 illustrates that during the follow-up analysis for 1982, there was not a

statistically significant relationship between parity and type 2 diabetes mellitus development (RH=.721, 95% CI .491-.1.058, p >.05). After controlling for demographic characteristics, reproductive history, physiological factors, and interaction variables, parity was not statistically significant. There was a statistically significant relationship between age and subsequent type 2 diabetes mellitus development (RH = 1.060, 95% CI 1.033-1.087, p < .05). As the women in the study age increased by one year, there was a 6% increase in risk type 2 diabetes. Age remained significant after controlling for demographic variables, reproductive factors, and physiological factors. The interaction between parity and BMI became significant only after adding miscarriages to the model (RH = 1.020, 95% CI 1.003-1.037, p < .05). As the interaction between parity and BMI increased, there was a 3% increase in risk of developing type 2 diabetes. A similar result was seen in the relationship of total miscarriages and type 2 diabetes (RH = 1.906, 95% CI 1.417-2.565, p < .05). As miscarriages increased, there was a 90% increase in hazard of developing type 2 diabetes. There were no other statistically significant relationships found.

Table 7

Relative Hazards for Women Who Developed Type 2 Diabetes Mellitus During the NHEFS (1982)

Variables added	β	SE	RH	95% CI
n = 4317, diabetes = 177				
Step 1- Parity				
Parity	-.327	.196	.721	(.491-1.058)

Table 7 (*Continued)*

Relative Hazards for Women Who Developed Type 2 Diabetes Mellitus During the NHEFS (1982)

Variables added	β	SE	RH	95% CI
n = 782, diabetes = 25				
Step 2- Demographic characteristics				
Parity	-1.275	.794	.279	(.059-1.325)
Age	.058	.013	1.060*	(1.033-1.087)
Race	1.054	1.099	2.868	(.333-24.720)
Education level	.098	.651	1.103	(.308-3.954)
Income (annual)	-.337	.572	.714	(.233-2.190)
BMI	.009	.047	1.009	(.920-1.107)
Parity and Race interaction	-.462	.294	.630	(.354-1.122)
Parity and BMI interaction	.015	.008	1.016	(.999-1.032)
n = 781, diabetes 25				
Step 3- Reproductive history				
Parity	-.1120	.810	.326	(.067-1.595)
Age	.062	.013	1.064*	(1.037-1.092)
Race	.880	1.204	2.411	(.228-25.544)
Education level	.178	.712	1.195	(.296-4.822)
Income (annual)	-.216	.567	.806	(.265-2.447)
BMI	-.028	.049	.972	(.883-1.070)
Parity and Race interaction	-.620	.296	.538	(.301-.960)
Parity and BMI interaction	.020	.009	1.020*	(1.003-1.037)
Total miscarriages	.645	.151	1.906*	(1.417-2.565)
n = 772, diabetes 23				
Step 4- Physiological history				
Parity	-.886	.813	.421	(.086-2.069)
Age	.041	.016	1.042*	(1.009-1.076)
Race	.829	1.263	2.292	(.193-27.232)
Education level	-.040	.709	.961	(.239-3.860)
Income (annual)	.240	.659	1.272	(.350-4.624)
BMI	-.038	.055	.963	(.865-1.071)
Parity and Race interaction	-.594	.328	.552	(.291-1.050)
Parity and BMI interaction	.019	.009	1.020*	(1.001-1.039)
Total miscarriages	.611	.159	1.842*	(1.349-2.515)
Systolic Blood Pressure	.553	.310	1.739	(.947-3.195)
Diastolic Blood Pressure	-.053	.282	.948	(.546-1.648)
Cholesterol level	.135	.776	1.145	(.250-5.241)
n = 345, diabetes 2				
No other models were able to be fitted				

X^2=3.576 at Step 1; Δ X^2 = 28.263 at Step 2; Δ X^2 = 12.751 at Step 3; Δ X^2 = 3.854 at Step 4. * $\rho < .05$.
β, the estimate of the regression coefficient; S.E., standard error of coefficients; R.H., relative hazard

2. Cox Proportional Hazards Regression Results for the Second Research Sub-question

The second research sub-question seeks to determine to what extent does the level of parity between baseline (1971-1975) and the second follow-up (1987) survey account for the differences in probability of developing type 2 diabetes mellitus?

A longitudinal analysis of the 6530 women without diabetes at baseline in the NHANES I cohort and incidence of type 2 diabetes during the NHEFS 1987 using Cox proportional hazards regression model was conducted. In step 1, parity was added to the model to determine if there was an association between change in parity over time and type 2 diabetes mellitus development. In step 2, demographic characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity and BMI, and parity and race) were added. In step 3, reproductive history (miscarriages) was added. In step 4, physiological history (hypertension status and cholesterol level) variables were added. In step 5, the final step, the behavioral factors (alcohol use, smoking status, physical activity, and fat intake) were added to the model. The Relative Hazards changed as the variables were added to the model. The results indicated that having one or more children does not increase the risk of developing type 2 diabetes mellitus. Table 8 illustrates that during the follow-up analysis for 1987, there was not a statistically significant relationship between parity and type 2 diabetes mellitus development (RH=.714, 95% CI .223-.2.190, p >.05). After controlling for demographic characteristics, reproductive history, physiological factors, and interaction variables, parity was not statistically significant. There was a statistically significant relationship between age and subsequent type 2 diabetes mellitus development (RH = 1.058, 95% CI 1.032-1.084, p < .05). There was a 5% increase in hazard of developing type 2 diabetes

mellitus as the women in the study increased in age by a year. Age remained significant after controlling for demographic variables, reproductive factors, and physiological factors. There was a statistically significant relationship found between the interaction effect of parity and BMI and type 2 diabetes development (RH = 1.026, 95% CI 1.011-1.042, $p < .05$) even before adjusting for miscarriages. As the interaction effect increased, there was a 2% increase in risk of developing type 2 diabetes. The same was seen in the relationship of total miscarriages and type 2 diabetes (RH = 1.718, 95% CI 1.242-2.377, $p < .05$). As miscarriages increased, there was a 71% increase in hazard of developing type 2 diabetes. There were no other statistically significant relationships found.

Table 8

Relative Hazards for Women Who Developed Type 2 Diabetes Mellitus During the NHEFS (1987)

Variables added	β	SE	RH	95% CI
n = 4304, diabetes = 177				
Step 1- Parity				
Parity	-.337	.572	.714	(.223-2.190)
n = 810, diabetes = 25				
Step 2-Demographic characteristics				
Parity	-.216	.567	.806	(.265-2.447)
Age	.056	.013	1.058*	(1.032-1.084)
Race	-1.085	1.330	.338	(.025-4.583)
Education level	.218	.816	1.243	(.251-6.160)
Income (annual)	-.432	.568	.649	(.213-1.978)
BMI	-.011	.041	.989	(.914-1.071)
Parity and Race interaction	.168	.202	1.183	(.797-1.757)
Parity and BMI interaction	.026	.008	1.026*	(1.011-1.042)
n = 809, diabetes 25				
Step 3- Reproductive history				
Parity	-.038	.055	.963	(.865-1.071)

Table 8 *(Continued)*

Relative Hazards for Women Who Developed Type 2 Diabetes Mellitus During the NHEFS (1987)

Variables added	β	SE	RH	95% CI
Age	.056	.013	1.058*	(1.032-1.084)
Race	-1.284	.1.434	.336	(.017-4.606)
Education level	.207	.822	1.230	(.245-6.162)
Income (annual)	-.344	.567	.709	(.233-2.152)
BMI	-.014	.042	.986	(.909-1.070)
Parity and Race interaction	.136	.229	1.146	(.731-1.795)
Parity and BMI interaction	.022	.008	1.022*	(1.007-1.038)
Total miscarriages	.541	166	1.718*	(1.242-2.377)
n = 800, diabetes 23				
Step 4- Physiological history				
Parity	-.011	.041	.989	(.914-1.071)
Age	.037	.016	1.038*	(1.006-1.071)
Race	-1.272	1.447	.280	(.016-4.781)
Education level	.069	.821	1.072	(.214-5.386)
Income (annual)	-.024	.649	.976	(.273-3.484)
BMI	-.022	.047	.978	(.893-1.073)
Parity and Race interaction	.126	.236	1.134	(.714-1.803)
Parity and BMI interaction	.021	.008	1.021*	(1.005-1.038)
Total miscarriages	.486	.172	1.627*	(1.161-2.280)
Systolic Blood Pressure	.424	.317	1.528	(.821-2.847)
Diastolic Blood Pressure	.089	.287	1.093	(.622-1.919)
Cholesterol level	.105	.761	1.111	(.250-4.931)
n = 347, diabetes 2				
No other models were able to be fitted				

Note. X^2=3.693 at Step 1; Δ X^2 = 32.251 at Step 2; Δ X^2 = 14.257 at Step 3; Δ X^2 = .070 at Step 4.
* $\rho < .05$. β, the estimate of the regression coefficient; S.E., standard error of the coefficients; R.H., relative hazard.

3. Cox Proportional Hazards Regression Results for the Third Research Sub-question

The third research question seeks to determine to what extent does the level of parity between baseline (1971-1975) and the third follow-up (1992) survey account for the differences in probability of developing type 2 diabetes mellitus?

A longitudinal analysis of the 6530 women without diabetes at baseline in the NHANES I cohort and incidence of type 2 diabetes during the NHEFS 1992 using Cox proportional hazards regression model was conducted. In step 1, parity was added to the model to determine if there was an association between change in parity over time and type 2 diabetes mellitus development. In step 2, demographic characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity and BMI, and parity and race) were added. In step 3, reproductive history (miscarriages) was added. In step 4, physiological history (hypertension status and cholesterol level) variables were added. In step 5, the final step, the behavioral factors (alcohol use, smoking status, physical activity, and fat intake) were added to the model. The Relative Hazards changed as the variables were added to the model. The results indicated that having one or more children does not increase the risk of developing type 2 diabetes mellitus. Table 9 illustrates that during the follow-up analysis for 1992, there was not a statistically significant relationship between parity and type 2 diabetes mellitus development (RH=.893, 95% CI .665- 1.200, p >.05). After controlling for demographic characteristics, reproductive history, physiological factors, and interaction variables, parity was not statistically significant. There was a statistically significant relationship between age and subsequent type 2 diabetes mellitus development (RH = 1.060, 95% CI 1.033-1.087, p < .05). There was a 6% increase in hazard of developing type 2 diabetes mellitus as the women in the study increased in age by a year. Age remained significant after controlling for demographic variables, reproductive factors, and physiological factors. There was a statistically significant relationship found between the interaction effect of parity and BMI and type 2 diabetes development (RH = 1.020, 95% CI 1.002-

1.038, $p < .05$). As the interaction effect increased, there was a 2% increase in risk of developing type 2 diabetes. The same was seen in the relationship of total miscarriages and type 2 diabetes (RH = 1.876, 95% CI 1.396-2.521, $p < .05$). As miscarriages increased, there was an 87% increase in hazard of developing type 2 diabetes. There were no other statistically significant relationships found.

Table 9

Relative Hazards for Women Who Developed Type 2 Diabetes Mellitus During the NHEFS (1992)

Variables added	β	SE	RH	95% CI
n = 4386, diabetes = 180				
Parity		.	.	
Parity	-.113	151	893	(.665-1.200)
n = 720, diabetes = 24				
Step 2- Demographic characteristics				
Parity	.325	.433	1.383	(.592-3.232)
Age	.058	.013	1.060*	(1.033-1.087)
Race	1.199	1.048	3.318	(.425-25.895)
Education level	-.320	.738	.726	(.171-3.084)
Income (annual)	-.382	.573	.683	(.222-2.098)
BMI	.010	.043	1.010	(.927-1.100)
Parity and Race interaction	-.454	.277	.635	(.369-1.092)
Parity and BMI interaction	.020	.009	1.020*	(1.002-1.038)
n = 719, diabetes = 24				
Step 3- Reproductive history				
Parity	.353	.434	1.424	(.608-3.334)
Age	.056	.013	1.058*	(1.031-1.086)
Race	.965	1.106	2.624	(.300-22.927)
Education level	-.306	.809	.736	(.151-3.596)
Income (annual)	-.269	.570	.764	(.250-2.335)
BMI	-.007	.046	.993	(.909-1.086)
Parity and Race interaction	-.344	.567	.709	(.233-2.152)
Parity and BMI interaction	.022	.009	1.022*	(1.005-1.040)
Total miscarriages	.629	.151	1.876*	(1.396-2.521)
n = 710, diabetes 22				
Step 4- Physiological history				

Table 9 *(Continued)*

Relative Hazards for Women Who Developed Type 2 Diabetes Mellitus During the NHEFS (1992)

Variables added	β	SE	RH	95% CI
Parity	.606	.480	1.834	(.716-4.699)
Age	.032	.016	1.033*	(1.001-1.066)
Race	.662	1.213	1.938	(.180-20.875)
Education level	-.316	.806	.729	(.150-3.534)
Income (annual)	.188	.658	1.207	(.332-4.381)
BMI	-.014	052	.986	(.890-1.092)
Parity and Race interaction	-.543	.315	.581	(.313-1.077)
Parity and BMI interaction	.020	.010	1.020*	(1.000-1.041)
Total miscarriages	.610	.160	1.840*	(1.346-2.515)
Systolic Blood Pressure	.554	.312	1.741	(.944-3.208)
Diastolic Blood Pressure	.181	.275	1.199	(.699-2.056)
Cholesterol level	.030	.784	1.031	(.222-4.794)

n = 292, diabetes 2
No other models were able
to be fitted (non-convergence)

**Note.* X^2=1.137 at Step 1; Δ X^2 = 33.604 at Step 2; Δ X^2 = 13.075 at Step 3; Δ X^2 = 5.622 at Step 4.
* $\rho < .05$.
β, the estimate of the regression coefficient
S.E., standard error of the coefficients
R.H., relative hazard

4. Cox Proportional Hazards Regression Results for the Fourth Research Sub-question

The fourth research question seeks to determine to what extent does the interaction effect between parity and race account for the differences in the probability of developing type 2 diabetes mellitus?

A longitudinal analysis of the 6530 women without diabetes at baseline in the NHANES I cohort and incidence of type 2 diabetes during each of the NHEFS follow-up surveys using Cox proportional hazards regression model was conducted. In step 1, parity was added to the model to determine if there was an association between change in parity over time and type 2 diabetes mellitus development. In step 2, demographic

characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity and BMI, and parity and race) were added. In step 3, reproductive history (miscarriages) was added. In step 4, physiological history (hypertension status and cholesterol level) variables were added. In step 5, the final step, the behavioral factors (alcohol use, smoking status, physical activity, and fat intake) were added to the model. The Relative Hazards changed as the variables were added to the model. The results seen in tables 7, 8, and 9 indicate that there was not a statistically significant relationship found between the interaction effect of parity and race and type 2 diabetes mellitus during the follow-up surveys (RH=1.016, 95% CI .354-1.122, p >.05; RH= 1.183, 95% CI .797-1.757, p >.05; RH= .635, 95% CI .369-1.092, p >.05). These results were seen in step 2 of the model as well as in steps three, four, and five of each of the follow-up surveys.

5. Cox Proportional Hazards Regression Results for the Fifth Research Sub-question

The fifth research question seeks to determine to what extent does the interaction effect between parity and BMI account for the differences in the probability of developing type 2 diabetes mellitus?

A longitudinal analysis of the 6530 women without diabetes at baseline in the NHANES I cohort and incidence of type 2 diabetes during each of the NHEFS follow-up surveys using Cox proportional hazards regression model was conducted. In step 1, parity was added to the model to determine if there was an association between change in parity over time and type 2 diabetes mellitus development. In step 2, demographic characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity and BMI, and parity and race) were added. In step 3, reproductive history (miscarriages) was added. In step 4, physiological history (hypertension status and

cholesterol level) variables were added. In step 5, the final step, the behavioral factors (alcohol use, smoking status, physical activity, and fat intake) were added to the model. The results seen in tables 7, 8, and 9 indicate that there was a statistically significant relationship found between the interaction effect of parity and BMI and type 2 diabetes mellitus during the initial follow-up survey in step 3 (RH=1.020, 95% CI 1.003-1.037, p <.05). In addition, there was a statistically significant relationship found between the interaction effect of parity and BMI during the 1987 and 1992 follow-up surveys (RH= 1.026, 95% CI 1.011-1.042, p >.05; RH= 1.020, 95% CI 1.002-1.038, p >.05). These results were seen in step 2 of the model as well as in steps three, four, and five of each of the follow-up surveys.

In order to evaluate the change in parity at follow-ups and type 2 diabetes mellitus development, the regression results were observed. Table 10 illustrates no significant relation between change in parity and type 2 diabetes mellitus development during the 1982, 1987, 1992 follow-up surveys.

Summary

The results have indicated parity is not significantly associated with type 2 diabetes mellitus development. When variables were added to the model to determine the independent prognostic significance of the changes in parity over time and the risk of type 2 mellitus development, the results showed no significant effects. Age was statistically significant in step 2 of the model and remained significant through steps 3

and 4 of the model after controlling for reproductive and physiological factors. These results were seen in the 1982, 1987, and 1992 surveys.

There was a statistically significant relation found between the interaction of parity and BMI during the follow-up surveys. The association remained significant after adding the reproductive and physiological factors. The results of the analyses from the 1982, 1987 and 1992 surveys indicate the interaction of parity and BMI was significant during steps 2, 3, and 5. There were no statistically significant relation found between change in parity and the later development of type 2 diabetes mellitus. These findings are also seen in Table 10. The results from this study suggests change in parity is not associated with the subsequent develop of type 2 diabetes mellitus. However, the results indicate that there may be an inverse relationship between change in parity and the development of type 2 diabetes.

There was an attempt made to analyze nulliparous women without type 2 diabetes mellitus at baseline and during the 1982 follow-up survey to determine if nulliparous women at baseline had an increased risk of developing type 2 diabetes mellitus after controlling for other risk factors seen in Table 11. There were approximately 259 nulliparous women without type 2 diabetes mellitus at baseline which were used for the analyses. In step 1, the variable nulliparity was added to the model to determine if there was an association between change in parity (going from no children to 1 or more children) over time and type 2 diabetes mellitus development. In step 2, demographic characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity and BMI, and parity and race) were added. No other variables were added to model due to model non-convergence. Also, there were only 10 subjects with type 2

diabetes that were available for the analysis during step 1. The results were similar to the analyses of women with children during baseline and during the follow-ups. There was not a statistically significant relation found between nulliparity and type 2 diabetes.

The results indicate change in parity is not significantly associated with the development of type 2 diabetes mellitus. However, all of the models illustrated an insignificant inverse association between increase in parity and type 2 diabetes. When variables were added to the models to determine the independent prognostic significance of the changes in parity over time and the risk of type 2 diabetes development, the results showed no significant effects. It is proper to conclude that there is no statistically significant relation between change in parity and type 2 diabetes mellitus.

Table 10

Adjusted Relative Risk (RR) and 95% Confidence Interval (CI) of Change in Parity and Type 2 Diabetes Mellitus in NHEFS

		Cox Proportional Hazard Model		
Change in Parity	NHANES I Baseline (1971-1975)	NHEFS (1982)	NHEFS (1987)	NHEFS (1992)
	No Diabetes			
n	6530	177	177	180
	(reference)			
0 to 1	0	1.028 (.710-1.489)	1.031 (.713-1.494)	1.030 (.712-1.492)
2 to 3	0	.965 (.647-1.440)	.961 (.644-1.433)	.968 (.649-1.444)
4 to 5	0	1.374 (.908-2.080)	1.375 (.908-2.080)	1.366 (.903-2.068)
6 or greater	0	1.424 (.608-3.334)	1.383 (.592-3.232)	1.272 (.350-4.624)

Table 11

Relative Hazards for Nulliparous Women Who Developed Type 2 Diabetes Mellitus During the NHEFS (1982)

Variables added	β	SE	RH	95% CI
n = 152, diabetes 10				
Step 1- No Parity				
No Parity				
No other models were able to be fitted; no cases available for analysis	3.086	3.896	21.894	(.011-45.361)

Note. X^2=0 at Step 1. $^{*}\rho < .05$.
β, the estimate of the regression coefficient
S.E., standard error of the coefficients
R.H., relative hazard

CHAPTER 5

DISCUSSION

Overview

This chapter comprises three sections. The first section focuses on the discussion of the results with the specific purpose of explaining findings and determining their bearing on what was postulated about the influence of parity on type 2 diabetes mellitus. In the second section, the conclusions based on an evaluation of the results are made. The last section focuses on the discussion of implications of the present study to research and practice pertaining to parity and its relation to type 2 diabetes mellitus. This study took advantage of nearly 20 years follow-up experience from the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study.

Summary of the Findings

A reiteration of the goals of this research study may aid in the appreciation of the findings and the understanding of the problem as it has been approached. The purpose of this research study was to assess whether change in parity influence the development of type 2 diabetes mellitus.

A synopsis of the findings for this study is given. The research question serves to establish the influence of parity on type 2 diabetes mellitus after controlling for other risk factors such as age, race, education level, income level, total miscarriages, alcohol use,

smoking status, physical activity, fat intake, BMI, hypertension, cholesterol level, parity and race interaction, and parity and BMI interaction variable.

Research sub-question 1 asked, "To what extent does the level of parity between baseline and the initial follow-up (baseline vs. time 1) account for the differences in probability of developing type 2 diabetes mellitus?" The findings revealed parity was not associated with type 2 diabetes mellitus after controlling for age, race, education level, income level, total miscarriages, BMI, blood pressure, cholesterol level, parity and race interaction variable, and parity and BMI interaction variable.

Research sub-question 2 asked, "To what extent does the level of parity between baseline and the second follow-up (baseline vs. time 2) account for the differences in probability of developing type 2 diabetes mellitus?" The findings remained the same in that parity was not associated with type 2 diabetes mellitus after controlling for age, race, education level, income level, total miscarriages, BMI, blood pressure cholesterol level, parity and race interaction variable, and parity and BMI interaction variable.

Research sub-question 3 asked, "To what extent does the level of parity between baseline and the third follow-up (baseline vs. time 3) account for the differences in probability of developing type 2 diabetes mellitus? Parity was not associated with type 2 diabetes mellitus before or after controlling for age, race, education level, income level, total miscarriages, BMI, blood pressure, cholesterol level, parity and race interaction variable, and parity and BMI interaction variable.

Research sub-question 4 asked, "To what extent does the interaction effect between parity and race account for the differences in probability of developing type 2 diabetes mellitus?" The findings showed there was not an association between the

interaction effect of parity and race, and type 2 diabetes after controlling for age, race, education level, income level, total miscarriages, fat1 intake, BMI, blood pressure, cholesterol level, and parity and BMI interaction variable.

. Research sub-question 5 asked: To what extent does the interaction effect between parity and BMI account for the differences in probability of developing type 2 diabetes mellitus? The findings suggested an association between the interaction effect of parity and BMI, and type 2 diabetes after controlling for age, race, education level, income level, total miscarriages, BMI, blood pressure, cholesterol level, and parity and race interaction variable.

During an average follow-up of approximately 20 years, the findings for the parity measure used in the present study show parity is not associated with type 2 diabetes mellitus in the respondents during the NHEFS surveys after controlling for other risk factors. When change in parity is measured over time, it does not influence type 2 diabetes mellitus development. That is, the results show there is no association with the change in parity over time and type 2 diabetes mellitus development in the present study. However, there was a non-significant inverse relationship found between change in parity and type 2 diabetes. As parity increases, the risk of developing type 2 diabetes decreases.

There was a significant association found between the interaction effect of parity and BMI after controlling for age, race, education level, income level, BMI, blood pressure, cholesterol level, miscarriages, and parity and race interaction variable. As the product of parity and BMI increases, the risk of developing type 2 diabetes increases. The positive slope for the interaction indicates that as BMI and parity jointly increases, there is an independent and additional risk of developing diabetes beyond that which is

attributed to BMI or parity alone. In contrast, there was not a significant association between the joint effect of parity and race seen in the present study.

Significant results were found between total miscarriages and type 2 diabetes after controlling for parity, age, race, education level, income level, alcohol use, BMI, blood pressure, cholesterol level, parity and BMI interaction variable, and parity and race interaction variable. As the number of miscarriages increase, the risk of developing type 2 diabetes increases by 90%. In looking at all of the associations and their relationship with type 2 diabetes, there is a very strong effect seen among miscarriages and type 2 diabetes after controlling for parity, age, race, education level, income level, alcohol use, BMI, blood pressure, cholesterol level, parity and BMI interaction variable, and parity and race interaction variable.

There was also a significant association found between age and type 2 diabetes. Age appeared to contribute to the increased risk of developing type 2 diabetes. In the model, age remained significant after controlling for parity, race, education level, income level, BMI, total miscarriages, blood pressure, cholesterol level, parity and BMI interaction variable, and parity and race interaction variable. The effect of age is consistent with the physiological model. Age has an association with type 2 diabetes. Aging puts people at higher risk of developing diabetes. As people age, their weight increases, insulin secretion tends to decrease slightly and insulin resistance tends to increase slightly. Even if the elderly person is thin, they still may be predisposed to developing diabetes. Therefore, even older people who do not have diabetes tend to have slightly higher blood sugar levels after eating than do their younger counterparts. Scientists theorize that the pancreas ages right along with us, and does not express insulin

as efficiently as it did when we were younger (Diabetes Research Group, 2002). Also, as our cells age, they become more resistant to insulin as well. Muscle mass also decreases in older adults. Muscles use sugar for energy, so less muscle means that less sugar is consumed for energy and more sugar is converted to fat (Diabetes Research Group, 2002).

In the physiological model, a direct association between parity and type 2 diabetes was not found. However, age did show a relationship with type 2 diabetes through the various stages in the physiological model. One way was through weight gain, and the other was through pancreatic fatigue or malfunctioning which leads to subsequent type 2 diabetes.

Discussion and Conclusions

Based on the summary of findings provided above, there are important concerns that need to be discussed. First, in regard to the findings parity is not associated with the development of type 2 diabetes mellitus, the results conflict with the conclusions reached by the Atherosclerosis Risk in Communities Study researchers and others (Cheung, 2004; Kritz-Silverstein et al., Martin et al., 1984; Nicholson et al., 2006; 1989).

In the present study, the methods and the controlling variables were similar to those in the Atherosclerosis Risk in Communities Study in which age, BMI, education level, and socioeconomic status were simultaneously. However, the findings were not consistent. One reason could be population bias in the Atherosclerosis Risk in Communities Study. They only selected participants from North Carolina, Mississippi,

Maryland, and Minnesota in which two of those states have higher numbers of diagnosed diabetes and obesity. In the present study, there was representation from all fifty states in the United States which allows for a more non-biased sample selection. Also in the present study, the criteria used for diabetes diagnosis was very liberal (> 140 mg/dl) compared to (> 120mg/dl) in the Atherosclerosis Risk in Communities Study. There could have possibly been an underestimation of diagnosed diabetes cases in the present study. Boyko and others (1990) and Collins et al., (1991) controlled for age and BMI and was conducted in relatively homogeneous populations. Most previous studies have not controlled for both age and BMI (Cheung, 2004; Martin, et al., 1984). Of the studies that did control both for age and BMI, one did not control simultaneously for educational and socioeconomic variables (Kritz-Silverstein et al., 1989). Other researchers have found both higher parity and type 2 diabetes mellitus have been demonstrated to be associated with lower educational attainment, lower socioeconomic status, and minority ethnicities including Mexican Americans, Native Americans, and African Americans (Harris, Hadden, Knowler, & Bennett, 1987).

The results in the present study are in accordance with other studies (see Alderman et al., 1993; Boyko, et al., 1990; Collins et al., 1991; Manson, et al., 1992). The study of Manson and others (1992), like the present research study, was longitudinal. However, unlike the present study which is based on national data, the study of Manson and other researchers (1992) focused on a special selected population of registered nurses in the United States. On the other hand, Boyko and others (1990) also used national data to conduct his research. However, unlike the present research, their study was cross-sectional which is considered a limitation.

A study by Kritz-Silverstein and others, (1989) suggested an increased risk of type 2 diabetes mellitus predominantly among women with increased parity (six or more births), after controlling for age and obesity. The association between parity and type 2 diabetes mellitus was nonlinear. The researchers concluded parity is associated with an increased risk of type 2 diabetes mellitus and may have important implications for our understanding of both the causes of diabetes and the geographic, ethnic, and social-class differences in its prevalence among women. The finding of elevated risk only in a small sub-group, however, suggests chance rather than causality (association), may explain the researchers' results. There were 1158 women with five or more births, among whom 34 cases of type 2 diabetes were diagnosed. The confidence intervals were narrow to exclude an important elevation in risk of type 2 diabetes mellitus in this sub-group (RR= .869, CI .607-1.244; RR=1.511, CI 1.347-1.696; RR= 1.492, CI 1.330-1.674). The data in the present study suggest the change in parity over time, independent of sustained weight gain, is unlikely to have an appreciable effect on the incidence of type 2 diabetes mellitus in women.

The SEM was utilized to explain health behavior and its association with type 2 diabetes. The integration of the SEM into the established models helps to explain health behavior and its association with type 2 diabetes. There is considerable evidence that personal characteristics and behaviors are critically associated with the development of type 2 diabetes and obesity (Kaplan, Everson, and Lynch, 2000). Therefore, the SEM is an independent area along with parity and physiologic variables which incorporates factors which influence type 2 diabetes development. The SEM consists of social group effects such as culture, ethnicity, economic status, and attitudes

which have an effect on behavioral factors such as diet and exercise and obesity in which there is presently an established link between obesity and type 2 diabetes.

The demographic factors and socioecological factors helped to guide the development of the comprehensive model tested and explain the results as well. There were actually three different models combined to develop the present study. One model was an established physiological model beginning with obesity and increased weight gain and its association with subsequent type 2 diabetes. The second model incorporated physiological factors such as age, the effect of the interaction between parity and BMI, and miscarriages. The final model incorporated the SEM which consisted of behavioral and social factors to explain behavior which effects diet and exercise and obesity. There were not enough complete data on behavioral factors to test that particular component of the model. While behavioral factors did not account for significant variance in risk in the analyses, this may be due to constraints from the data rather than from an actual lack of effect.

Strengths of the Study

This study has several important strengths. First, this study was conducted on a nationally representative sample of the non-institutionalized United States population; therefore, these findings are broadly generalizable. Second, because parity was measured at baseline and participants were followed longitudinally, temporal relationships can be established with confidence. Third, the assessment of the incidence of type 2 diabetes mellitus occurred over an average of nineteen years of follow-up, with follow-up

experience available for more than 96% of participants. Fourth, the estimates of risk in this study were controlled for most major risk factors for type 2 diabetes mellitus. Such an adjustment is important to reduce potential confounding effects.

In the present study, there was a standardized method of identifying incident diabetes for up to an average of nineteen years. Because there are standardized measures of exposures, outcomes, and behavioral factors, the NHEFS provides an opportunity to examine potential mechanisms of the associations between parity and type 2 diabetes mellitus. However, the National Center for Health Statistics data, such as these, are regarded as both valid and reliable. According to Bailey (1982), the more valid and reliable are the measures, the less measurement error one encounters in the data. Examination of the conceptualization of all the variables used in this study, shows that each variable defined seems to adequately capture what the study intends to measure. In other words, the face validity of all the variables is accepted.

Limitations of the Data

The limitations of this data include its secondary nature. Because of the secondary nature of the data, selection of variables is limited to what already exists. Thus, despite the quality of the NHANES data, there is an imperfect fit between theoretical concepts and available measures. Further, although self-report on health status and personal health practices are widely used in research and widely accepted as reliable, there is always the possibility of inaccurate responses because of social desirability.

Although these data are longitudinal, it is not free of other limitations and problems that affect other longitudinal surveys. First, the effects of repeated measurements may damage the internal validity of variables. Willingness of the respondents to answer questions in a way that evokes a known response is only one threat to validity that emerges with the use of continued study of the same cases. More general unwillingness to participate in the study may also result from continued study. Yet another possibility is that respondents change as a result of participation in the survey.

The second problem that affects longitudinal surveys is respondent recall. In the present study, the participants' ages ranged between 25 and 74 when they were interviewed in the original survey. During the follow-up surveys, most of these participants were aged; some were already institutionalized. Therefore, when older people are studied, there is always a problem of recall because, as they advance in age, their memory tends to fade. In order to minimize the problem of recall in this data, there were proxies who helped to respond to any questions in case the participants were incapacitated. This procedure was also utilized if younger participants were not able to recall the information. Proxies, however, can introduce another source of error in the data.

Another problem that affects longitudinal studies is attrition rate. The fact that the participants are followed over time may cause some to be lost to follow-up. In this study, however, the attrition rate was very small since only an average of 4 percent of the participants were lost to follow-up during the follow-up surveys. Lewis-Beck (1980) noted a small attrition rate does not in most cases affect the validity of the data; it becomes problematic when the attrition rate is large, in which case, the data as well as the

results may be affected. The reliability and validity of data with a large attrition rate at follow-up can also be questionable (Lewis-Beck, 1980).

Sampling error is another problem that usually affects all surveys, including longitudinal data. The presence of sampling error in a survey decreases the chances of external validity. In the present study, to minimize the problem of sampling error, a probability, stratified, cluster sampling procedure was employed to select participants in the survey.

One other fundamental problem that affects longitudinal data is the unreliability of measurement (Nesselroade & Baltes, 1979). In longitudinal data, errors of measurement are often confounded with true individual change and, as a result, estimates of over-time relationships among variables may be seriously biased (Heise, 1969; Wiley & Wiley, 1970). Therefore, in order to study any change in individual health status, it is necessary to confront the problem of measurement of unreliability (Bohrenstedt, 1983). In this research study, the reliability of each measure has not been explicitly evaluated, although the validity of the measures, most of which are categorical, can be accepted at face value. Data with categorical single indicators do not lend themselves well to evaluating reliability or internal consistency.

Scope and Limitations of the Study

This study, like every study, has its limitations. Because of the secondary nature of the data set used, some of the variables that were ideal for the causal model were unavailable. Furthermore, the data contained errors that were not detected and specific

variables included in the causal model were difficult to operationalize due to missing data. As parity was not coded consistently in the 1982, 1987, and 1992 follow-up surveys, a default judgment was made that the parity measures of women who were older than 45 years of age during the baseline survey (1971-1975) were used during the 1982 (time 1), 1987 (time 2), and 1992 (time 2) follow-up survey analyses. The rate of birth for women 45 years of age and older was only .08% in 1971 which was the lowest compared to the younger age groups (National Center for Health Statistics, 2005). This was done to allow parity to be stable across the time periods for women for whom data were missing and for whom there was a likelihood they were beyond childbearing age.

There was an attempt made to analyze nulliparous women without type 2 diabetes mellitus at baseline and during the 1982 follow-up survey to determine if nulliparous women at baseline had an increased risk of developing type 2 diabetes mellitus after controlling for other risk factors. There were approximately 259 nulliparous women without type 2 diabetes mellitus at baseline which were used for the analyses. In step 1, the variable nulliparity was added to the model to determine if there was an association between change in parity (going from no children to 1 or more children) over time and type 2 diabetes mellitus development. In step 2, demographic characteristics, BMI, and interaction variables (age, race, income level, education level, BMI, parity and BMI, and parity and race) were added. No other variables were added to model due to model non-convergence since there were only 10 subjects with type 2 diabetes that were available for the analysis during step 1. The results were similar to the analyses of women with children during baseline and during the follow-ups. There was not a statistically significant relation found between nulliparity and type 2 diabetes.

Another limitation of the data is the age of the data. The data used was 25 years old. The baseline survey was conducted in 1971-1975. The follow-up surveys were conducted in 1982, 1987, and 1992. Using old data or out of date data for analyses may hinder the validity of the study due to analyzing time sensitive variables. That is, some variables may have an influence only for a short period of time and the results cannot be generalized which compromises the study.

Given that the median age was 47 years at baseline for the women participants in the study, the baseline sample is not representative of women in the childbearing cohort. There was a ten year age increase from baseline to the first follow-up time period which means the 47 year mean age increased by ten years. There was an accumulative 10 year increase from the first follow-up to the last follow-up. Therefore, the findings have to be interpreted. The average woman was 47 years of age and those who did not have diabetes were eliminated. This may have affected the generalizability of the study in which it may have been compromised.

Although NHANES data have been shown to be valid, all data from census, surveys or administrative records are subject to errors arising from a number of factors such as sampling variability (for statistics that are based on samples), incomplete coverage, non-response, and computing and processing errors. The data for this study is therefore, limited in these respects. Other limitations included limited generalizability to other racial groups with higher rates of diabetes, such as Native Americans and Hispanics. We did not have data on inflammatory markers and pregnancy-related variables such as history of gestational diabetes and gestational weight gain. Women with prior gestational diabetes are known to be at high risk for the development of type 2

diabetes. Information on breast-feeding practices which may affect the incidence of type 2 diabetes was also not ascertained (Stuebe et al., 2005). There were also missing data which led to an increased number of censored subjects. There were only 177 women who developed type 2 diabetes during the follow-up period which were used in the analyses. Also, in the present study, the criteria used for diabetes diagnosis was very liberal (> 140 mg/dl) compared to today's criteria of (> 126 mg/dl). Therefore, there could have possibly been an underestimation of diagnosed diabetes in the present study.

Finally, the NHEFS Sample Person Questionnaire responses were provided by one person in each household. In some instances, the respondent was the spouse of the participant in the household. This was a potential threat to the study's ecological validity because a third party may have represented the participant. There is room for bias if the individual did not accurately represent the participant's information. The fact that self-reporting of health status was used to collect data from respondents is another limitation of the study. Many people who are answering a questionnaire about their health status have been found to under-report the information requested, especially in terms of physician visits, any diagnosed chronic diseases, or hospitalizations.

Implications for Researchers

There are discrepant findings between the population studies regarding the effect of pregnancy on the development of type 2 diabetes mellitus. One possibility is that pregnancy accelerates the development of diabetes only in predisposed populations. Peter and other researchers (1996) found a relationship in women with gestational

diabetes who are ultimately predisposed to diabetes. In the present study as well as other epidemiologic studies that did not find a relation between parity (childbearing) and type 2 diabetes, the effects may have been diluted due to the vast majority of participants who did not have a genetic predisposition.

It has been postulated that a permanent decline in B-cell function is due to an increased risk of diabetes resulting from a gestational diabetes mellitus pregnancy (Peters et al., 1996). Researchers established that increased insulin resistance occurs in all pregnancies; however, in women who have gestational diabetes mellitus, there is also a reduction in B-cell function (Peters et al., 1996). It is this inability of the B-cells to compensate for increased insulin resistance which results in gestational diabetes mellitus.

Although the present study suggests parity does not influence subsequent incidence of type 2 diabetes mellitus; however, it is uncertain whether increasing parity may influence risk of type 2 diabetes in susceptible women with gestational diabetes. At the time of childbearing for most of the women in this cohort, screening for gestational diabetes was not performed and the diagnostic criteria were poorly standardized.

Recommendations for Future Research

The recommendations that are given under this subsection are for future research. It is obvious based on the results and the above discussion there are several concerns worth noting with regards to conducting research on parity and the risk factors for type 2 diabetes mellitus. As pointed out earlier, this study has some pragmatic limitations due to

the secondary nature of the data. Operationalization and conception of the variables are also issues of concern in this research.

However, despite the limitations, this study is a step forward in the improvement of research design and instrumentation. Future research should concentrate on studying those variables shown to be more important in explaining effects of parity in relation to type 2 diabetes mellitus development. From the results of this study, it can be argued there is a need for researchers to continue to examine the relationship of parity and type 2 diabetes mellitus especially the effect of miscarriage. As has already been mentioned, there are discrepancies in the results of the previous studies regarding the effects of parity on type 2 diabetes mellitus. Importantly, physicians and health education researchers should re-examine the potential long-term effects of pregnancy on type 2 diabetes mellitus. Additional longitudinal studies of young women in which specific pregnancy-related weight gain measures, lifestyle factors, and changes in socioeconomic status can be prospectively measured. Also, those studies should include laboratory measures of insulin resistance, glucose tolerance, and adiposity as women progress through their reproductive years.

The practical implications for public health would include focusing on defining more effective and specific strategies for decreasing the development of type 2 diabetes in women in the future. The findings in the present study reveal that amongst all of the risk factors associated with type 2 diabetes, there is a strong relation between miscarriage and type 2 diabetes. For every miscarriage, the relative risk of developing type 2 diabetes increases by 90%. The other risks include age and the interaction of parity and BMI.

Health education awareness programs targeting women who are at risk of developing type 2 diabetes should be developed based on the findings from the present study.

The ecological theories state that health is affected not only by the presence of environmental factors but also by the reciprocal relationship that exists among the environmental factors and health that impacts the health status of individuals. Health education awareness programs characterizing potential long-term consequences of the metabolic and lifestyle changes associated with women before pregnancy and during pregnancy to prevent miscarriages could be developed and implemented. The interventions would target lifestyle changes (behavioral factors) such as proper diet and adequate exercise. Collaborative efforts combined with strategic planning, social marketing, and media advocacy which targets multiple levels of influence could expand diabetes prevention programs in the future.

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APPENDIX

IRB APPROVAL FORM

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research
Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office for Human Research Protections (OHRP). The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56 and ICH GCP Guidelines. The Assurance became effective on November 24, 2003 and expires on February 14, 2009. The Assurance number is FWA00005960.

Principal Investigator: DOBBS, JOHNITA L

Co-Investigator(s):

Protocol Number: **E070706001**

Protocol Title: *After Controlling for Other Risk Factors, To What Extent Does the Level of Parity Account for the Differences in the Probability of Developing Diabetes Mellitus?*

The above project was reviewed on 7/6/07. The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This project qualifies as an exemption as defined in 45CF46.101, paragraph 4.

This project received EXEMPT review.

IRB Approval Date: 7/6/07

Date IRB Approval Issued: 07/06/07

Sheila Moore, CIP
Director, Office of the Institutional
Review Board for Human Use (IRB)

Investigators please note:

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

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