THESIS

EXCESSIVE WEIGHT GAIN AND GESTATIONAL DIABETES MELITUS (GDM), HYPERTENSIVE STATES, AND CESAREAN DELIVERIES AMONG WYOMING WOMEN

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ABSTRACT

EXCESSIVE WEIGHT GAIN AND GESTATIONAL DIABETES MELITUS (GDM), HYPERTENSIVE STATES, AND CESAREAN DELIVERIES AMONG WYOMING WOMEN

Background

The proportion of women gaining more weight during pregnancy has become an increasing public health issue. Recent data show that nationally, about half of pregnant women gain more weight than the current Institute of Medicine guidelines. Further, over gaining during pregnancy can lead to a number of adverse outcomes for both the mother as well as the fetus.

In this study our aim was to determine if, and to what extent, excessive gestational weight gain increased the risk of gestational diabetes mellitus, hypertensive conditions and incidence of Cesarean deliveries among Wyoming women.

Methods

Birth certificates from all Wyoming residence were collected between January 2006 and August 2010. More than 36,000 records were obtained. Logistic regression models were used, to evaluate the associations between excessive weight gain and gestational diabetes, hypertensive conditions and cesarean deliveries. Confounders and effect modifiers were also assessed.

Results

Among the entire population we found that 49% gained more weight than recommended. Further, 2% had gestational diabetes, 4.9% had a hypertensive condition and 25% had a cesarean

delivery. We found that women who were classified as having excessive weight gain were not significantly more likely to have an increased risk of gestational diabetes. Women with excessive weight gain were 2 times more likely to have a hypertensive state (OR: 2.148; 95% CI: 1.85-2.49) and were 30% more likely to have a Cesarean delivery (OR: 1.29; 95% CI: 1.22-1.37). None of our 16 potential confounders, identified a priori, were identified to significantly affect this relationship.

Several interaction variables were significantly associated. When the endpoint of interest was hypertension there were two interactions that were associated. Among women who had excessive weight gain, women who had adequate plus prenatal care, compared to women with adequate were 50% more likely to have a hypertensive condition. Among women who had excessive weight gain, women who were American Indian, compared to white were half as likely to have a hypertensive condition. When the endpoint of interest was Cesarean deliveries there were three interactions that were associated. Among women who had excessive weight gain, women who had three or more children, compared to women who had none were 20% less likely to have a Cesarean delivery. Among women who had excessive weight gain, women who were had less than a high school level of education, compared to women with a college level of education were 20% less likely to have a Cesarean delivery. Lastly, among women who had excessive weight gain, women who were classified as a race of other, compared to white women were 25% more likely to have a Cesarean delivery.

Conclusion

The results from this study show that excessive weight gain is associated with twice the risk of having a hypertensive condition and 30% increased risk in having a Cesarean delivery.

These results add to the accumulating body of evidence to help explain the risk of excessive weight gain and how optimal gain depends on maternal characteristics.

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CHAPTER ONE: INTRODUCTION

1.1 Introduction

The worldwide epidemics of overweight and obesity have become important public health issues (1-4). A 2008 study found that nearly half of women of reproductive age within the United States are either overweight or obese. This study also reported that nearly half of the women in the study were categorized as gaining too much weight during pregnancy, according to the most recent guidelines (1). In a 2015 study, among women in the US, 47% of women gained more than the recommended amount of weight during pregnancy (5).

In 1990 the Institute of Medicine (IOM) and National Research Council published the first guidelines for weight gain during pregnancy (6). Maternal and infant outcomes depend greatly on pre-pregnancy Body Mass Index (BMI). BMI is a measure of body fat based on height and weight. These weight gain recommendations differ depending on whether the woman is entering pregnancy as underweight (less than 18.5kg/m^2), healthy weight (18.5-24.9 kg/m^2), overweight (24.9-29.9kg/m^2) or obese (>30kg/m^2). The IOM guidelines were later reviewed in 2009 and revised based on a much larger body of evidence. Table 1.1 presents the 2009, most recent weight gain recommendations. Two changes were made to the original guidelines. First, the pre-pregnancy BMIs were adjusted slightly to match the World Health Organization (WHO) BMI categories. Secondly, the new guidelines include an upper limit of weight gain for obese women where previously there was none (7). Further, the 1990 standards noted that young adolescents and black women should gain towards the upper end of the interval and that women of short stature should gain toward the lower end. Due to insufficient evidence, these suggestions were not supported in the 2009 revision.

Wyoming is the least populous state in the United States with an estimated population of 586,107 in 2015 (8). Additionally, the Wyoming population is racially homogeneous. Data from the US Census Bureau in 2014 reported that 90.8% of the Wyoming population were white, compared to 73.8% for the entire US (9). A study conducted using the Maternal Outcome Monitoring System (MOMS) specific to mothers in Wyoming from 2003 to 2005 found that 42.8% of Wyoming women gained excessive weight during pregnancy (10). Stotland et al. (2006) examined Californian women and found 43.3% of women gained more than the recommended weight (11). 49.1% of women gained excessive weight in a study conducted in Quebec by Brennand (2005) (2). More recently, data from 2012 and 2013 show that Wyoming women have an incidence of excessive weight gain during pregnancy of 52.9% (12).

There are many adverse outcomes associated with excessive Gestational Weight Gain (GWG) for both the infant as well as the mother. This study will be limited to analyze the association of Gestational Diabetes Mellitus (GDM), hypertensive states and Cesarean deliveries in relation to GWG. To our knowledge, this has never been studied using the Wyoming population.

1.2 Rationale

There is still controversy on the appropriate amount of weight a woman should gain during pregnancy. The IOM recommendations have changed very little in 25 years largely due to conflicting findings and a combination of statistically significant and non-significant results. Conclusions are further complicated by non-uniformity of methodologies and definitions. For example, different authors use dissimilar weight gain or BMI cut-offs making comparisons difficult. As a result, recommendations regarding GWG remain controversial.

1.3 Study Objective

There was one primary, overarching, goal of this current study. Our aim was to identify if and to what extent excessive weight gain poses a risk to GDM, hypertensive states and Cesarean deliveries. To meet this aim our objectives were as follows:

1. Applied the 2009 IOM weight gain standards to Wyoming women of reproductive age using birth certificate data.
2. Determined which variables contained in the birth certificate are found in the literature to be associated with both GWG and one of our three outcomes (GDM, Cesarean delivery or hypertensive states).
3. Determined which of these identified possible risk factors are statistically relevant confounders, effect modifiers or interaction variables. This was accomplished by creating three different logistic regression models for each of the three outcomes, using GWG as a predictor variable and including other variables deemed to be appropriate in the model.
4. Reported results in order for the Wyoming Department of Health and other agencies to use these findings to assist them in providing and implementing appropriate programs and interventions to improve maternal health. These results will also be used for appropriate educational programs and efforts to maximize the nutritional status of pregnant women.

This study attempts to determine and explain which risk factors, in combination with GWG affects the incidence of GDM, hypertensive states and Cesarean deliveries among Wyoming women using birth certificate data. Results from this study may be used to contribute to the body of evidence to inform and guide appropriate recommendations for weight gain during pregnancy.

CHAPTER TWO: BACKGROUND AND LITERATURE REVIEW

Overweight and obesity have increased in prevalence in developed countries, including among women of child bearing years (5, 6, 12-14). Assessing nine states, one study found pre-pregnancy obesity increased from 13% in 1993 to 22% in 2002. More recently, in the US in 2014, the percentage of obesity among women of childbearing years was 27.2% (15). A related problem, excessive GWG, has also been increasing leading to concerns about potential adverse maternal and child outcomes (2, 3, 5-7, 16-19). Here, we focus on maternal outcomes, specifically GDM, hypertensive states and Cesarean deliveries.

2.1 Excessive gestational weight gain

2.1.1 Definition and prevalence

In the context of this study, and many others, excessive GWG is defined as weight gain that exceeds the 2009 IOM weight gain recommendations. The IOM recommends that underweight women (BMI of less than 18.5 kg/m^2) gain 28-40 pounds, normal weight women (BMI 18.5-24.9 kg/m^2) gain 25-35 pounds, overweight women (BMI 24.9-29.9 kg/m^2) gain 15-25 pounds and obese women (BMI greater than 30.0 kg/m^2) gain 11-20 pounds (Table 1.1) (7).

Nationally, excessive GWG has been persistent for many years. Data from the National Maternal and Infant Health Study, which includes a representative sample of women in the United States found that in 1988, 36% of women gained above the IOM recommendations (20). Ten years later in 1998, the prevalence had increased to 66% of women gaining weight above recommendations (21). In 2015 a study with a representative sample of 79% of US annual births found that 47% of women gained above the recommendations. This percentage ranged from 38.2%-54.7%, depending on the state (12). Excessive GWG prevalence for Wyoming available for 2003 to 2005 was 42.8% (10). In 2015, a study found the prevalence to be 52.9% (12).

2.1.2 Risk factors for excessive gestational weight gain

A number of risk factors have been linked to excessive GWG in the literature. These include pre-pregnancy BMI, parity, maternal age, education, race and ethnicity, and smoking. Pre-pregnancy BMI has been found to be a risk factor for excessive GWG with overweight and obese women having two to seven times the risk compared to healthy weight women (22-24). In 2015 Deputy et al. documented the prevalence of excessive GWG was 23.5% for underweight women, 37.6% for normal weight women and 61.6% for overweight (12). Parity has also been shown to be an independent risk factor for excessive GWG (25-27) with multiparous women having a 30% reduction in risk of gaining above the IOM weight guidelines (OR; 0.69; 95% CI: 0.57-0.82) (28). Women who were classified into older age categories have statistically lower risk of excessive gain compared to younger women (10, 27, 29, 30). In addition, studies have found women with a normal pre-pregnancy BMI who have less than 12 years of education are more likely to gain excessive weight (greater than 35 lbs) (27, 28, 31). In Wyoming, the risk of excessive GWG was suggested to be highest among women less than 20 years of age (OR: 1.72; 95%CI: 1.36-2.18), primiparous women (OR: 1.44; 95%CI: 1.26-1.65) and women that were enrolled in Medicaid (OR: 1.16; 95%CI: 1.01-1.33) (10). Race and ethnicity were not found to be a significant predictor in the same study. Since Wyoming has such little diversity ethnically and racially, these potential differences may be difficult to measure in this population. Other literature however, among women in the US found black women were more likely to gain weight above IOM guidelines compared to white women (31). A 2015 study found both black and Hispanic women had 16-46% lower odds of gaining weight above the recommendations (32).

Several authors suggest that a lower GWG may be more appropriate for Asian women in preventing adverse maternal consequences (30, 33, 34). Studies show more often than not that smoking during pregnancy is associated with a greater risk of lower maternal weight gain (35-38). A recent study found that ceasing smoking during gestation resulted in a 67% increase in likelihood that women would gain excessive weight during gestation (24).

2.1.3 Maternal consequences of excessive gestational weight gain

Evidence linking certain adverse maternal outcome and GWG has been inconclusive due to limited scope, non-uniformity of methodologies and definitions and limited prospectively designed studies. Based on birth certificate data, the most common maternal consequences of excessive GWG are GDM, hypertensive status and Cesarean delivery (2, 22, 39-44). These outcomes are described in detail in later sections.

Other adverse outcomes related to excessive GWG not studied here include low birth weight (less than 5 lbs. 8 ounces or 2,495 grams), preterm birth (less than 37 weeks of gestational age) (45), and large for gestational age or macrosomia (weight above the 90^{th} percentile for gestational age) (11, 41, 46). GWG has been shown to be an independent predictor of bearing a macrosomic child. Macrosomia has been a well-established risk factor for a variety of different fetal and maternal risk and consequences, including delivery by Cesarean section. These include cephalopelvic disproportion, failure to progress, shoulder dystocia (where the shoulder of the infant cannot pass through to be delivered or requires significant manipulation to be delivered), increased risk of third or fourth degree lacerations, among others. These risks greatly increase the probability that a Cesarean is required, or is the safest option. Boulet et al. (2003) reported that compared to mothers with non-macrosomic infants, mothers who had grade

3 (greater than 5000g) macrosomic children were almost five (OR: 4.68; 95% CI: 4.54-4.83) times as likely to receive a Cesarean section (47). Stotland et al. found a similar result (48).

2.2 Gestational Diabetes Mellitus (GDM)

2.2.1 Definition and prevalence

GDM is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. In the US, the incidence of GDM is estimated to occur in 4-7% of women (49, 50). In Wyoming, GDM was diagnosed in 5.9% of mothers in 2005, and increased to 6.6% in 2009 (52).

2.2.2 Diagnostic criteria and screening methods

There is no standard screening methodology for GDM and it varies between states. The Centers for Disease Control and Prevention (CDC) report that most women are screened for GDM at 24-28 weeks of gestation. The CDC recommends earlier screening for women who are at a high risk for GDM (previous pregnancy with GDM, delivery of a baby over 9 pounds, currently overweight or obese, greater than 25 years of age, family history of diabetes, are African American, Hispanic, American Indian, Alaska Native, Native Hawaiian or Pacific Islander, current treatment of Human Immunodeficiency Virus (HIV)) (53). In 2008, Wyoming published clinical practice recommendations for GDM diagnosis and criteria stating that all pregnant women should be considered for screening (54). The recommendations specify that women with high risk should be tested as soon as possible and those with average or low risk should be tested at 24-28 weeks of gestation.

The Oral Glucose Tolerance Test (OGTT) is used for clinical diagnosis and measures glucose levels in blood plasma. Concentrations of glucose load are determined depending on time since last meal. To meet the definition for GDM diagnosis, two or more plasma concentrations of glucose must meet or exceed the current clinical recommended thresholds. These criteria can be found in Table 2.1 (55, 56).

2.2.3 Risk factors for GDM

Research concerning the association between GDM and maternal weight gain has been limited and few studies have shown significant findings. A number of studies have found no statistically significant association between weight gain and GDM (39, 57-62), others have found that increased GWG increases risk of GDM (3, 63-65) and yet others have reported an inverse association between GWG and GDM (2, 66, 67). Overall the IOM concludes that there is no definitive evidence from the studies conducted that a relationship exists between high GWG and risk of developing GDM (7). Besides excessive GWG, the following risk factors have been suggested in the literature: parity, race, ethnicity, age, and smoking (3, 39, 59-61, 63, 66, 68-71). Parity has been controversial as a potential risk factor for GDM as some studies determine it to be non-significant(3, 61, 68, 71) while others find it to be a significant risk factor for GDM (59, 60, 63, 66, 69). Maternal race has been suggested to be a statistically significant risk factor with studies showing white women have an increased risk for impaired glucose tolerance (a pre-diabetic state of hyperglycemia that is associated with insulin resistance) as well as GDM compared to black women (63, 71). It has been found that older mothers are at a higher risk for GDM when assessed as either a continuous variable or a categorical variable (3, 39, 59-63, 66, 69-71). Glucose regulation appears to be adversely affected by smoking and smoking has been shown to increase insulin resistance in two studies (72, 73) but not in a third study (74). In a 2004 study, among women smoking 20 cigarettes a day or more versus women who had never smoked the odds for GDM was 3.5 (75).

2.2.4 Consequences of GDM

Adverse short and long term maternal and fetal complications can occur from GDM. Maternal complications that can arise include increased risk of gestational hypertension (3-fold) (76), cardiovascular disease (1.7-fold) (77), metabolic syndromes (2.5-fold) (78), preterm birth (Adjusted Odds Ratio(AOR): 2.1), and Cesarean delivery (AOR:2.2)(79). Further, some studies report GDM increases risk of type 2 diabetes later in life (80) while others have shown this not to be the case (81). Potential fetal complications include large for gestational age/macrosomia , shoulder dystocia and respiratory distress syndrome (a breathing disorder due to structural immaturity of the lungs)(47, 82).

2.3 Hypertensive states

2.3.1 Definition and prevalence

There are numerous different classifications for severity of gestational hypertension and many different clinical forms it presents. The three hypertensive states of interest, for this study, are gestational hypertension, preeclampsia and eclampsia. Gestational hypertension is defined as the development of hypertension (140/90 mm Hg) after 20 weeks for pregnancy, in previously normotensive (normal blood pressure) women, which returns to normal within 12 weeks postpartum (83). Preeclampsia is defined as the presence of pregnancy induced hypertension with the addition of proteinuria (presence of urinary protein at concentrations greater than 0.3 g per liter in 24 hours). Preeclampsia may be accompanied by other complications or may also present in an atypical fashion (83). Eclampsia is defined as the presence of preeclampsia with the addition of seizures (84).

Pregnancy related hypertension is the leading cause of maternal death in industrialized countries accounting for 16% of deaths (85). Hypertensive disorders occur in 5-10% of all pregnancies worldwide (86). Preeclampsia, specifically complicates 3% of pregnancies in the US (87).

2.3.2 Diagnostic criteria and screening methods

Blood pressure measurements are routinely taken upon each doctor's visit and women are classified as having a hypertensive state accordingly. Additionally urinary protein levels are screened to delineate between gestational hypertension and preeclampsia.

2.3.3 Risk factors for hypertensive states

Many studies have investigated the risk factors for hypertensive disorders of pregnancy and they are not fully understood. In many of these investigations there has been a significant positive relationship between hypertensive states during pregnancy and increased GWG. A 2015 study found women with excessive GWG had over two and a half times the risk of having gestational hypertension compared to women with appropriate GWG (OR:2.55; 95% CI:1.92-2.80) (67). Another recent study assessing Chinese women found the increase in risk to be 72% (OR:1.72; 95% CI:1.54-1.93) (88). This positive association has been supported by other evidence (16, 24, 58, 89-91). For the prevention of pregnancy associated hypertension, controlled weight gain has been hypothesized to be especially important in women who are obese prior to pregnancy. Jensen et al. (2005) found that compared to obese glucose-tolerant women gaining less than 5 kg, those gaining more than 15 kg during pregnancy had almost a fivefold increased odds of hypertension (OR: 4.8; 95% CI: 1.7-13.1) (92). Many other studies have supported this finding (2, 17, 18, 23, 64). Other authors have found non-significant or mixed results (39, 60, 62, 66).

Other risk factors for hypertension during pregnancy besides excessive GWG that have been suggested in the literature include parity, gestational age, race and maternal smoking (16, 17, 60, 62, 66, 92-95). Pre-eclampsia is two to three times as common in primigravid (a woman in her first pregnancy) women, compared to women in their subsequent pregnancies (OR: 2.42; 95% CI: 2.16-2.71) (32, 93). Gestational age has been suggested to be a risk factor in a number of studies (62, 66), although not all findings have been statistically significant (92). Racial disparities exist with the burden being the highest in black women (96, 97). Maternal smoking has consistently been shown to be a protective factor for hypertension during pregnancy (98). The 2004 Surgeon General report found sufficient evidence to infer a causal relationship between maternal smoking and decreased risk for preeclampsia (95). A comprehensive meta-analysis found a 32% risk reduction of preeclampsia among women who smoked (94).

2.3.4 Consequences of hypertensive states

Different forms of high blood pressure pose risks for the mother and fetus. Women with hypertension during pregnancy are at a higher risk for non-pregnancy hypertension, ischemic heart disease, stroke, end organ failure and for venous thromboembolism later in life (99, 100). Additionally risks of serious complications are higher for these women such as acute renal failure, pulmonary edema and placental abruption (87, 101). Further, women with preeclampsia can quickly progress to eclampsia without treatment, which may lead to seizures and coma (102, 103). The fetus is at risk for intrauterine growth retardation, prematurity and intrauterine death (104-106).

2.4 Cesarean section

2.4.1Definition and prevalence

A Cesarean section is the extraction of the fetus through an incision in the abdomen (107). In the United States in 2014, nearly one third (32.2%) of births were Cesarean deliveries. In some instances a Cesarean delivery may be necessary. Indications most commonly leading to

Cesarean delivery include a previous Cesarean delivery, failure of the fetus to progress, breech presentation (a position of a fetus in which the feet or buttocks appear first during birth), dystocia (abnormal or difficult childbirth or labor) and fetal distress. Efforts are being made to reduce rates of Cesarean sections among women with previous Cesarean sections. In 2007 the National Vital Statistics System-Natality (NVSS-N), and the CDC/National Center for Health Statistics (NCHS) found Cesarean section incidences of 26.5% and 90.7% among women without a prior Cesarean section and among women with a prior Cesarean section, respectively (108). In Wyoming, from 2000 to 2007 the proportion of births delivered via Cesarean section significantly increased from 19.6% to 27% (109). In 2013 this incidence was 28.9% (110).

2.4.2 Risk factors for Cesarean section

Stotland et al. (2004) estimated that 64,000 primary Cesarean deliveries could be prevented if no women exceeded IOM pregnancy weight gain standards (using 1990 standards). Further, they found that women who delivered via Cesarean section were 40% (OR=1.4, 95%CI: 1.22-1.59) more likely to have gained excessive weight compared to women who did not deliver via Cesarean section (46). This study as well as others found statistically significant association between Cesarean delivery and excessive GWG in underweight and healthy weight women (16, 30, 58, 64, 67, 111, 112). Other studies considering women who had normal pre-pregnancy weights (using the 1990 IOM recommendations) observed non-significant associations (60, 66).

Results are less conclusive and more mixed for women who are obese when they become pregnant. While a number of studies did not find an increased risk for Cesarean delivery among obese women with excessive GWG (39, 46, 60, 64, 111) others found that excessive GWG in obese women significantly increased the risk for Cesarean delivery (17, 18, 92).

Besides excessive GWG, risk factors for Cesarean delivery include maternal age and race (16, 17, 48, 95, 111-114). It has been suggested that women who are younger or older than ages 20-24 have increased risk for a Cesarean delivery (114). A 2007 study found American Indian or Alaskan Native women had the lowest rate of Cesarean deliveries (28%), while non-Hispanic blacks had the highest (34%) (115).

2.4.3 Consequences of Cesarean section

Adverse maternal outcomes include increased risk of infection, hemorrhage or blood loss, injury to organs, and adhesions (scar tissue development) (116, 117). Additionally, mothers who deliver via Cesarean section are less likely to breastfeed, and have increased risks of bleeding, infection, and injuries to the bladder or bowel and blood clots (118). Complications for the baby include premature birth if gestational age was calculated incorrectly, breathing and respiratory problems, lower APGAR scores and fetal injury (119, 120).

2.4 Mechanisms

2.4.1 The association between excessive gestational weight gain and GDM

Diabetes is characterized by the inability of cells to properly absorb glucose from circulation, which results in excessively high blood glucose concentrations. The proper cellular absorption and utilization of glucose is dependent on the hormone insulin. Insulin is released from β cells, located in the pancreas in response to increasing blood glucose concentrations that occurs during the postprandial period when exogenous carbohydrate availability is high from meal consumption. This allows many other cells in the body to take up glucose to produce energy. Like all forms of diabetes, GDM is characterized by elevated circulating glucose, a phenomenon that can occur for two reasons. First, cells that require insulin-stimulated glucose transport may develop resistance to insulin, which results in reduced clearance of circulating glucose into cells. This scenario is strongly correlated to excessive adiposity and obesity-related inflammation that compromises the insulin signal. Second, β cells in the pancreas may not produce enough insulin, which may be due to autoimmune-mediated destruction or excessive lipid accumulation, resulting in concentrations of insulin that are too low to effectively overcome the insulin resistance and normalize blood glucose concentrations.

The exact pathophysiology of the effect of obesity and GDM is not fully understood but the literature suggests that the mechanism is multifaceted. Increased circulating levels of leptin, the inflammatory marker TNF-α (Tumor Necrosis Factor), and decreased levels of adiponectin among women with GDM have been proposed as possible mechanistic factors.

Adipose tissues (fat tissues) in the body release a hormone called leptin that acts on the hypothalamus in the brain. Leptin is a neuroendocrine hormone that is important in appetite regulation, metabolism and fat accumulation (121-124). In addition, leptin inhibits insulin biosynthesis (125). Therefore, as adipose tissue is increased and thus leptin rises concurrently, insulin synthesis decreases, which results in less than adequate circulating insulin and increased risk for diabetes.

TNF-α induces insulin resistance and has been shown to increase with higher levels of adipose tissue (126-128). This may occur due to an alteration of signal transduction from the insulin receptor to the glucose transporter (128) and decreased expression of the glucose transporter 4 (129). Additionally, TNF-α has been shown to inhibit the synthesis of adiponectin (130, 131).

Adiponectin is an adipocyte derived polypeptide that has insulin sensitizing properties and is inversely associated with BMI. Williams et al. found decreased plasma adiponectin concentrations measured in early pregnancy were associated with a 4.6 fold increase in GDM

(132). Adiponectin is known to stimulate fatty acid oxidation, reduce plasma triglycerides and improve glucose metabolism by increasing insulin sensitivity. Of note, the diabetes susceptibility locus that has been mapped to human chromosome is also the site of adiponectin gene. The gene is thought to be expressed exclusively in adipose tissue (130, 133).

2.4.2 The association between excessive gestational weight gain and hypertensive states

Currently, the etiology of hypertensive disorders in pregnancy is not completely understood. The causes and the mechanism are multifactorial and may include insulin resistance, inflammation, and angiogenic factors (biological mechanisms to support the creation of new blood vessels). Insulin resistance is common in women with hypertension (134) and may contribute to hypertension by reduction in available nitric oxide due to oxidative stress, increase in sympathetic tone, and increased angiotensinogen by adipose tissue (135). Inflammation markers produced by adipose tissue are common in preeclampsia and hypertension. Several inflammatory mediations (C-reactive protein, TNF-α) are generated that have been shown to alter endothelial function (136-139).

Recent studies have shown associations between obesity and imbalances in angiogenic factors and anti-angiogenic factors as well as anti-angiogenic receptor antibodies (140-142). It has been suggested that the specific mechanism involves Vascular Endothelial Growth Factor (VEGF) that plays a key role in angiogenesis. VEGF has two receptors, one of which is a receptor for sFLT-1 which is an anti-angiogenic protein. In women with preeclampsia, it is hypothesized that Placental Growth Factor (PGF) binds to the VEGF where the sFLT-1 should. As a result this, sFLT-1 remains in the blood stream (143, 144).

CHAPTER THREE: METHODS

3.1 Data Source

The data used for this investigation are specific to Wyoming women and provide insight into the relationship between weight gain and adverse maternal outcomes (10). Birth certificate data were provided by Wyoming Vital Statistics Services for children born to Wyoming residents. Births to residents that occur out of state were also captured in this data set. This is important as Wyoming does not yet have a tertiary care hospital. Therefore high risk births, and possibly more women with the outcomes of interest in this study, were born out of state. Births included in this data set are those between January 2006 and August 2010. In birth certificates before 2006, weight measures were not included. Birth certificates from August 2010 were the most current data at the time of our request.

3.2 Ethical Considerations

Birth certificates are collected for all live births and are documents that are retained by state health departments. For this study, the risk to the women and infants whose data were used was minimal. Only data essential to this study were obtained (Table 3.1 and 3.2) and no personal identifiers such as name, address or date of birth were collected. Table 3.1 lists all variables of interest from the dataset and 3.2 lists all variables that were derived using the dataset. The Wyoming Department of Health's Institutional Review Board granted approval for this present project. No approval was required from Colorado State University's Human Research Committee as this study is a secondary use of data that had already been collected.

3.3 Data Verification

All variables of interest were analyzed to validate the accuracy of the data. Biologic plausibility of all variables was assessed by analyzing ranges, clusters, means, medians, and standard deviations. An example of a cluster that was problematic was a large number of women weighing 99 pounds pre-pregnancy and post pregnancy were identified. Although this could have been a biologically plausible pre-pregnancy value for some women, there were more 99 codes then would have been expected and they were inconsistent with the data when other variables were present. When the Wyoming Vital Statistical Services were consulted, they indicated that the value of 99 was used previously to indicate a missing value. The Wyoming Vital Statistics Services were consulted on a number of other occasions regarding specific suspected anomalies and, when suspect, the data were compared against the original birth certificates and corrected.

3.4 Exposure and Outcome Variables

3.4.1 Exposure Variable

The exposure of interest in this study was excessive GWG compared to appropriate GWG. Women who had gained an insufficient amount were excluded from the analysis as they are likely to have different risk factors as well as outcomes.

IOM weight gain categories (excessive, sufficient, and insufficient) were calculated based on reported height, pre-pregnancy weight, post pregnancy weight, and the IOM guidelines. First, pre-pregnancy BMI was calculated by multiplying weight (in pounds) by 703 and then dividing by height (in inches) squared. Based on this value, women were classified into the four BMI categories defined by WHO (underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (24.9-29.9 kg/m^2) or obese (>30.0 kg/m^2)). Total GWG was then calculated by subtracting pre-pregnancy weight from documented delivery weight. According to IOM guidelines, underweight women should gain 28-40 pounds, women with normal weight should gain 25-35 pounds, overweight women should gain 15-25 pounds and obese women should gain 11-20 pounds. We classified women as having gained insufficient, sufficient or excessive weight by determining for each woman whether she gained below, within or above the recommended values.

3.4.2 Outcome Variables

The three outcome variables of interest in this study were Cesarean delivery, GDM and hypertension. Cesarean delivery and GDM can be assessed based on check boxes on birth certificates.

Two check boxes on the birth certificate refer to gestational hypertension; one labeled 'Gestational (Pregnancy Induced Hypertension, preeclampsia)', and the other 'Eclampsia'. Due to the expected small number of women with eclampsia, this group was combined with women with gestational hypertension and, when either of the boxes was checked, the woman was classified as having a "hypertensive state".

3.5 Potential Confounders and Effect Modifiers

Confounders and effect modifiers included maternal age, maternal education, maternal race, maternal ethnicity, payment source for the delivery, recipient of Women Infant and Children (WIC) food, clinical gestation, parity, birth weight, prenatal care, adequacy of prenatal care utilization (APNCU) (inadequate, intermediate, adequate or adequate plus based on number of prenatal care visits and first prenatal care date according to APNCU guidelines), gender of child, and smoking status (smoking three months prior to pregnancy; smoking during the first trimester; smoking during the second and third trimester; and a categorical smoking variable with categories “never smoked”, “quit during first trimester”,” quit during second trimester”, and “smoked during the entire pregnancy”.   Data for all variables were collected from the birth certificates and can be found in Table 3.1.

3.6 Exclusions

After completing data verification the data were imported into SAS (version 9.3, Cary, North Carolina). We calculated frequencies for categorical variables and extreme values for continuous variables to detect incorrect entries. Despite our data verification efforts, implausible values remained for a number of continuous variables (child’s birth weight, pre-pregnancy weight, delivery weight, and weight gain). In these cases, we excluded subjects with observations in the top or bottom 1% of all observed values (Table 3.3). For example, child’s birth weight initially ranged from 181g to 10,007g. These extremes are highly implausible and are likely the result of incorrect data entry. When the top and bottom 1% were deleted, the range decreased to 1642g to 4366g.

We restricted maternal age to 15-45 years to meet the definition of maternal age. Women with pre-pregnancy hypertensive states or diabetes were excluded and only cases that occurred during pregnancy were used. Women without data on pre-pregnancy height and weight were also excluded from analysis as it was impossible to establish a baseline.

Finally, we excluded extreme preterm births (less than 28 weeks gestation). Extreme preterm births are at a very high risk for a number of adverse medical conditions (145). We also excluded multiple births because mothers carrying multiple children have a different expectation for weight gain as well as a different risk for Cesarean deliveries.

After all exclusions 24,885 women remained in the study. A summary of the exclusions is shown in Table 3.3.

3.7 Data Manipulation

Race was assessed based on self-report. Possible responses were White, Black of African American, American Indian or Alaska Native, Asian Indian, Chinese, Filipino, Japanese, Korean, Vietnamese, Other Asian (specify), Native Hawaiian, Guamanian or Chamorro, Samoan, Other Pacific Islander (specify), and Other (specify). Due to lack of racial diversity in our study population, these variables were collapsed based on methodology used in Wyoming for birth certificate data. These categorized variables are as follows: White, Black or African American, American Indian or Alaskan Native, Asian/Pacific Islander (includes race indicated as Asian Indian, Chinese, Filipino, Guamanian or Chamorro, Japanese, Korean, Native Hawaiian, Other Asian, Other Pacific Islander, Samoan or Vietnamese), or Other.

For results to be biologically meaningful, comparable to other Department of Health data and easily disseminated in public health reports, all continuous variables were categorized. Category boundaries were based on standard classifications of the Wyoming Department of Health, the IOM and biological importance. For example, standard classifications were applied for child birth weight which are low birth weight (less than 2500g), normal birth weight (2500g to 4000g), and macrosomic (greater than 4000g). When there was no standard classification or cut off categories that were commonly used in the literature were used. For example age was categorized into 15-19, 20-24, 25-34, and 35-45 years of age categories.

Observations coded as 99, 999, or 9999 were coded as missing. The variable with the most missing observations was APNCU (6.1% observations missing). Frequencies of missing observations for all variables are shown in Table 3.1 and 3.2.

A separate dataset was created for each outcome of interest. Due to very large sample sizes too much power was a concern because biologically meaningless associations may result in statistically significant p-values. For this reason all cases were used but controls were randomly selected to establish a 1:3 case to control ratio. A new set of controls was selected for each outcome. The resulting population sizes were 2,153 for GDM, 4,847 for hypertensive states and 24,885 for Cesarean deliveries.

3.9 Statistical Analysis

For each of our three study populations (GDM, hypertensive states and Cesarean delivery), all variables of interest were cross tabulated by the outcomes, as well as excessive weight gain status. This resulted in proportions, frequencies and chi square statistics that were evaluated to determine the strength and the significance of the associations. Cell counts were evaluated for purposes of assessing sample size.

Logistic regression was used to investigate the associations between GWG and GDM, hypertensive states, and Cesarean deliveries among Wyoming women. Three univariate models containing only GWG as the explanatory variable were created, one for each outcome variable.

Then, all potential confounders were added, one by one, to each model and their effect on the OR of GWG and their statistical significance were assessed. Multiplicative interactions between GWG and other model covariates were then tested for significance using a cut off of $p<0.10$.

CHAPTER FOUR: RESULTS

4.1 Association between Excessive Gestational Weight Gain and GDM, Hypertensive States and Cesarean Deliveries

Table 4.1 shows weight gain strata for the entire population. For the entire Wyoming population, 49.2% of women had excessive GWG, 31.4% of women gained sufficient weight, and 19.3% were found to gain insufficient weight. Additionally, within the whole population, 2.06% of women had incidence of GDM, 4.87% had a hypertensive state and 25.51% of women had a Cesarean delivery.

After the three populations were selected, using a 3:1 control to case ratio, the insufficient weight gain category was excluded. The resulting cohorts consisted of 2153, 4847, and 24,885 for GDM, hypertensive states and Cesarean delivery, respectively. A chi-square statistic was performed on each study population to determine if frequencies between the outcome of interest and excessive weight gain were associated with eachother (Table 4.2). Among women with GDM, 57.2% of women were classified as gaining excessive weight while 42.8% gained sufficient. These percentages were not found to be statistically different. Among the women with a hypertensive condition, 76.4% gained excessive weight and 23.6% gained sufficient. This resulted in a statistically significant difference (p=<0.0001). Lastly, 65.5% of women who had a Cesarean delivery in our cohort had excessive weight gain compared to 34.5% who had sufficient. This also resulted in a significant p-value of <0.0001. These frequencies can be found in Table 4.2.

For each of our three subpopulations, cell frequencies were calculated stratified by variables of interest (Table 4.3). These show the demographics and risk factors for each of our three populations of interest. The results were consistent among all three groups. Half of the women were between the ages of 25-34 and had a college degree. The majority (90%) were white and non-Hispanic (88%). Almost all women had prenatal care (99%). Most women had a term delivery (92%) and infants with a normal birth weight (90%).

Of note, 5% more women were nulliparous in our hypertensive state cohort as compared to our Cesarean delivery cohort. All other strata were extremely similar in comparison between the groups and can be found in Table 4.3.

4.2 Associations between Potential Confounders/Effect Modifiers and Gestation Weight Gain by Outcome

4.2.1 Gestational Diabetes Mellitus Subset

When variables of interest were cross tabulated against GWG there were several significant trends. Child birth weight was associated with excessive GWG and 79.5% of women who gave birth to a macrosomic infant gained excessive weight compared to 47.1% of those with a low weight baby ($p<0.0001$). Several measures of tobacco exposure were also found to have significant trends. Women that used tobacco three months prior to pregnancy were found to gain excessive weight more often than women not smoking pre-pregnancy ($p=0.0012$). Additionally, 56.7% of women that were never smokers during pregnancy gained excessive weight which was significantly lower than women who smoked during pregnancy ($p=0.0003$). See Table 4.4 for additional results of variables analyzed.

A number of risk factors were significantly associated with GDM. GDM was shown to increase with increasing maternal age with 12.3% of women ages 15-19 becoming diabetic compared to 40.3% of women 35-45 ($p<0.0001$). We also found mothers who gave birth to infants preterm were 14.6% more likely to be diagnosed with GDM ($p<0.0001$). Additional statistically significant associations were found between GWG and GDM include; maternal race, maternal ethnicity, parity, birth weight and APNCU (Table 4.5).

Regarding the association between GWG and GDM the variables that were associated with both measures that are statistically possible confounders include; clinical gestation and birth weight.

4.2.2 Hypertensive States Subset

Cross tabulation of variables by GWG category were performed and the following variables were observed to have a statistically significant chi-squared value: maternal age, parity, birth weight, prenatal care, APNCU, tobacco use during the second and third trimesters and smoking status. Women ages 15-19 had excessive weight gain of 68.6% and women 35-45 had 60.1% ($p=0.0166$). Also, within this subset, women who were smokers in the second and third trimester were less likely to be classified as excessive GWG ($p=0.0251$ and $p=0.0346$, respectively). Table 4.4 has all estimates and intervals for all variables of interest.

Cross tabulation of variables by hypertension resulted in a statistically significant p-values of the following variables: clinical gestation, previous living births, birth weight, prenatal care, APNCU, tobacco use three months prior to pregnancy, during the first trimester, during the second and third trimester as well as smoking status. Women who delivered preterm had a 23.7% higher percentage of having a hypertensive condition ($p<0.0001$). Additionally, women that were at a higher risk for being diagnosed with a hypertensive condition were those that were primiparous ($p<0.0001$), had a low birth weight infant ($p<0.0001$), had adequate plus prenatal care ($p<0.0001$), and were not smokers during pregnancy ($p=0.0005$). Women that were never smokers during pregnancy had a 25.9% incidence of a hypertensive condition. Among women who smoked during the entire pregnancy, incidence of a hypertensive state was 17.8%

(p=0.00005). The finding that smoking is protective against hypertensive conditions is consistent with the literature. See Table 4.5 for percentages and chi-squares.

Variables significantly associated with GWG and hypertensive states include; previous living birth, birth weight, prenatal care, APNCU, tobacco use during the second trimester, tobacco use during the third trimester and smoking status.

4.2.3 Cesarean Delivery Subset

When variables were cross tabulated by GWG for the Cesarean cohort, 12 of them were statistically significant. These include maternal age, maternal race, payment source for the delivery, WIC food, clinical gestation, previous living births, birth weight, prenatal care, APNCU, tobacco use three months prior to pregnancy, tobacco use during the first trimester and smoking status. All frequencies and percentages can be found on Table 4.4. A strong trend was observed between increasing maternal age and decreased weight gain ($p<0.0001$). Variables that were used in this study as proxies for socioeconomic status were significant with GWG where they were not in the previous two cohorts. Women that received WIC food during gestation were more likely to gain excessive weight ($p<0.0001$) as were women that paid for their delivery by Medicaid versus self-pay (p=0.00036).

Most of the variables of interest were also associated with Cesarean delivery including; maternal age, maternal education, maternal race, maternal ethnicity, payment source for the delivery, clinical gestation, previous living births, birth weight, APNCU, gender of child. None of the smoking measures were associated with increased frequency of Cesarean. Incidence of Cesarean delivery increased with higher maternal age ($p<0.0001$) as well as education (p=0.0423). Women that had 1-2 previous living births were found to have the highest incidence of a Cesarean delivery (26.8%) and women with the lowest percentage were those that had three or more children (22.2%). These results are found in Table 4.5.

Regarding the association between GWG and Cesarean delivery the variables that were associated with both measures that are possible confounders include; maternal age maternal race, payment source for the delivery, clinical gestation, previous living birth, birth weight, and APNCU.

4.4 Potential Confounders in a Bivariate Analysis

4.4.1 Gestational Diabetes Mellitus Subset

Before investigating any potential confounders, the effect of GWG was independently assessed on GDM. We found the odds ratio of excessive weight gain on incidence of GDM to be 0.912. The 95% confidence interval for this OR included 1 (95% CI: 0.746-1.11) so the resulting p-value was non-significant. None of the variables that were tested in the bivariate analysis resulted in a change of this unadjusted odds ratio by 10% or greater. Therefore, none of these variables are considered confounders in the bivariate model. Table 4.6 has all odds ratios and confidence intervals for these variables.

4.4.2 Hypertensive States Subset

The univariate odds ratio when GWG was modeled to predict hypertensive states was 2.148 (95%CI: 1.852-2.491) indicating women who had excessive gestational weight gain, compared to those who did not had greater than twice the risk of developing a hypertensive condition. When variables of interest were included bivariately none of them changed this odds ratio by 10% or more, so no variables were included as covariates (Table 4.7).

4.4.3 Cesarean Delivery Subset

GWG was tested univariately with Cesarean delivery as the unadjusted model. People with excessive gestation weight gain had a 30% increased risk of having a Cesarean delivery (OR: 1.292, 95%CI: 1.217-1.371). When the potential confounders were entered into the model bivariately, no change was observed by 10% or more therefore none of the variables were included as confounders. Table 4.8 has the results of these analyses.

4.5 Interactions between GWG and other risk factors by Outcome

4.5.1 Gestational Diabetes Mellitus Subset

We found no association between GWG and GDM and no confounders. Therefore we did not investigate potential interactions.

4.5.2 Hypertensive States Subset

Two interaction variables were found to be statistically significant at the 0.1 level of significance. Women who had excessive GWG were more likely to have a hypertensive condition if they had adequate plus prenatal care (OR: 2.56, 95%CI: 1.93-3.39) compared to an adequate prenatal care (OR: 1.70, 95%CI: 1.36-2.12) (p=0.0252). Additionally women who had excessive weight gain were less likely to be hypertensive if they were American Indian compared to white (p=0.0950). Although not statistically significant, the point estimate of a black women, compared to white, with excessive gain (compared to adequate) was lower at 1.440 compared to the unadjusted model of 2.148. This finding was likely not significantly different due to small sample size.

Another observation of note is that compared to 20-24 year olds, women 15-19 years of age had an odds of 2.5 (95% CI:1.510- 4.145) for hypertension if they were excessive gainers. Conversely compared to 20-24 year olds, the odds of a woman 35-45 years of age had an odds of

1.7 (95%CI:1.092-2.643) for hypertension if they were excessive gainers. Additional point estimates and confidence intervals are in Table 4.9.

4.5.3 Cesarean Delivery Subset

Three interaction terms were found to reduce incidence of Cesarean delivery. Women who had excessive weight gain were less likely to have a Cesarean delivery among women who had greater than three children compared to those who had none (p=0.0438). Additionally women with less than a high school degree, compared to a college degree had less risk of a Cesarean delivery among excessive gainers (p=0.0321). Compared to being white, women who were classified as other had an increase in odds of 34% for a Cesarean among women who gained excessive weight (p=0.07333).

There were other observations of note that were likely insignificant due to small sample size. Women who reported they had no prenatal care had a greater than 20% reduction in odds for a Cesarean among women who gained excessive weight. Additionally, compared to white women, American Indian women were observed to have 20% lower odds of Cesarean among women who were in the excessive weight gain category. Table 4.10 contains additional detail on these analyses.

4.6 Summary

We found statistically significant associations between GWG and hypertensive states and Cesarean delivery. Excessive GWG, compared to appropriate weight gain, more than doubled the risk of hypertensive states (OR: 2.148, 95% CI: 1.852-2.491) and increased risk of a Cesarean delivery by 30% (OR: 1.292, 95%CI: 1.217-1.371). Of the sixteen a priori risk factors for the outcomes of interest, none were significant confounders in any of the three models. This was in part due to uneven distributions and low cell counts among our variable strata.

Among our hypertensive model we found that adequate plus prenatal care classification (compared to adequate) among women with excessive GWG increased risk. Additionally, women that were classified as American Indian (compared to white) and had excessive GWG were less likely to have a hypertensive condition.

Among the Cesarean delivery model, three variables modified the effect of excessive GWG on risk of Cesarean deliveries. First, women with excessive GWG that had three or more children (compared to women who were primiparous) had a lower risk of a Cesarean delivery. Next, among women that had excessive GWG, women that had less than a high school education, compared to women with a college education also had a lower risk. Lastly women that were categorized as a race of other compared to white women had a higher risk of Cesarean delivery.

CHAPTER FIVE: DISCUSSION

5.1 Study Summary

In this study, our aim was to investigate if and to what extent excessive gestational weight gain, as defined by the IOM, increased the risk of GDM, hypertensive states, and Cesarean deliveries. We identified potential confounders and effect modifiers from the literature and obtained this data from birth certificate records. Logistic regression was used to investigate the associations, potential confounders and effect modifiers.

5.2 GWG and Outcomes of Interest

The high prevalence of excessive GWG (49.2%) is concerning, but consistent with previous literature (10, 12). Incidence of GDM in this study (2.06%) was lower than reported previously in Wyoming (5.9% in 2005 and 6.6% in 2009) (51, 52). Hypertension was also lower than previously reported at 4.87% compared to 5-10% in the US (86). These differences could be due to exclusion criteria applied in this study (pre-pregnancy diabetes or hypertension, pre-pregnancy BMI, total weight gain, and delivery weight).

5.3 GDM Subset

Excessive GWG had no effect of GDM in this population using this study design (OR:0.912; 95%CI:0.746-1.11). This finding is inconsistent with the mechanisms discussed above relating increased weight and increased risk for hypertension (121, 125, 126, 129-131). No confounders were identified when assessed bivariately and no further analysis was performed. Literature suggests that when assessing the effect of GWG on GDM it may be more appropriate to use weight gain at time of diagnosis as weight intervention is common among women with

GDM and thus weight gain may be attenuated. Weight gain at time of diagnosis was not available from the birth certificate. See limitations below for additional detail.

5.4 Hypertensive States Subset

In our bivariate unadjusted model we found that women with excessive GWG were twice as likely to have a hypertensive condition (OR:2.15; 95% CI: 1.85-2.49, p=<0.0001). This finding supports the biological mechanisms described above between excessive weight and hypertension. No confounders were identified as significantly affecting this relationship. However, several variables were identified as effect modifiers. These are discussed below.

5.4.1 Significant Variables

5.4.1.1 APNCU

Women who had excessive GWG were more likely to have a hypertensive condition among women who had adequate plus prenatal care compared to adequate prenatal care (p=0.0252). Other studies have cited prenatal care as a confounder, but to our knowledge no other author has found it to be an effect modifier. U-shaped trends have been found with highest risk in the inadequate and adequate plus groups(146). Inadequate prenatal care was not found to be a statistically significant effect modifier. It has been hypothesized that women with adequate plus rating have a higher risk of worse outcome leading to the need for a higher number of visits (147, 148).

5.4.1.2 Race (American Indian)

American Indian women, compared to white women who experienced excessive GWG were less likely to have a hypertensive condition (p=0.095). The odds for American Indian women were half (OR:1.107; 95%CI: 0.502-2.444) of the odds for white women (OR:2.202; 95%CI: 1.884-2.572). Other studies have found race to be a confounder related to hypertension

(16, 17, 39, 60) but to our knowledge, no studies have effect modification for race and GWG. Family history has been understood to be a risk factor for gestational hypertension suggesting a genetic link (149, 150). Recently, specific genetics involved in the pathogenesis have been identified, some of which increased risk, others decreased risk. A recent study performed on American Indian women found that 46.1% of women had genetic variants that decreased odds of preeclampsia by 75% (OR-0.259 95% CI: 0.08-0.81, p=0.020) (151). The significance of race may be a proxy for protective genetics in this population.

The 2009 IOM guidelines determined there was insufficient evidence to suggest that a women's race warrants modification of weight gain guidelines. Further, they recommended that future studies investigate the extent to which optimal GWG differs by race (7). Our findings here suggest that among American Indian women, excessive GWG might not be as an important factor in increasing risk of hypertensive states as compared to other races.

5.4.2 Nonsignificant Variables

All other variables analyzed bivariately and as an effect modifier were nonsignificant. A number of these variables were likely nonsignificant due to small sample size and uneven distributions. These are discussed below.

5.4.2.1 Child's Birth Weight

Women who had excessive GWG that gave birth to a low birth weight infant, compared to normal weight appear to have a lower risk of hypertensive states. Odds for women that had low birth weight infants were 70% lower than women that gave birth to normal weight children.

5.4.2.2 Parity

Women that had 3 or more children, compared to women that were nulliparous, who had excessive GWG status had a point estimate for hypertensive states that was 60% higher. This finding was nonsignificant likely to the small number of women with 3 or more children, compared to those who were nulliparous.

5.4.2.3 Race (Black)

The non-significant association of hypertension among black women who had excessive GWG was likely due to the small sample size among the homogenous population. Black women that had excessive weight gain were 60% less likely to have a hypertensive state compared to White women.

5.4.2.5 Smoking Status

In this study it was found that women who did not quit smoking during pregnancy had an 18% incidence of being hypertensive compared to 26% of women that never smoked (among our hypertensive subset data(Table 4.5)). Women that quit smoking during the third trimester compared to never smokers that gained excessive weight had over twice the risk of hypertension (Table 4.9). The observation that smoking is protective is consistent with the literature. Literature has been substantial linking the protective effect of smoking to hypertension and has even been referred to as causal (94, 95). Although our results and other results show smoking is protective for hypertension, the public health message should remain that women should not smoke at all during pregnancy. A woman who does smoke should quit immediately. Smoking during pregnancy is harmful to reproduction affecting aspects from fertility to fetal and child development and pregnancy outcomes. The consequences of smoking during pregnancy are many and may be severe

5.5 Cesarean Subset

In our unadjusted, bivariate analysis we found that women with excessive GWG were 30% more likely to have a Cesarean delivery compared to women with sufficient weight gain

(OR-1.29 95% CI: 1.21-1.37, p<0.0001). None of the variables analyzed were found to be significant confounders. Parity, education, and race (other) were found to be significant effect modifiers (Table 4.10).

5.5.1 Significant Variables

5.5.1.1 Parity

Among women that had excessive GWG status, women who were primiparous had a significantly increased risk of a Cesarean delivery compared to women who had greater than 3 children (p=0.044). Many other studies find parity to be a confounder when assessing the effect of GWG on Cesarean deliveries (16, 17, 60, 66, 111, 112, 152). A recent study found women with high GWG (as measured as a ratio of actual/expected) that were primiparous had a greater than additive risk for a Cesarean delivery (153).

Parity was another maternal factor in which the IOM called for additional research (7). Our findings here suggest in relation to risk of Cesarean delivery it may be beneficial for primiparous women to gain less weight than multiparous women.

5.5.1.2 Education

Among women that had excessive weight gain, women that had less than a high school level of education were 25% less likely to deliver via Cesarean compared to women with a college degree or greater (p=0.0321). Although other authors have found education to be a confounder (16, 17), we are the first to our knowledge to find it to be a significant effect modifier.

Education in this investigation may serve as an indicator of socioeconomic status which the IOM calls for additional research regarding modification of weight gain (7). This analysis suggests that the effect of weight gain on women with less than a high school degree may be less important than women with higher education when assessing Cesarean deliveries.

5.5.1.3 Race (Other)

Our findings here suggest that among women classified in a race of other, excessive GWG might not be as an important factor in predicting Cesarean deliveries as compared to different races. The other category was a self-reported category when no other category was appropriate.

5.5.2 Nonsignificant Variables

All other variables analyzed bivariately and as an effect modifier were nonsignificant. Smoking status and race both appeared to have point estimates that looked different from their comparison group but were likely nonsignificant due to small sample sizes (Table4.10).

5.5.2.1 Race (American Indian, Black)

American Indian women had a point estimate that was 20% less for risk of Cesarean delivery compared to white women among excessive GWG women. Additionally black women had a point estimate that was 20% greater for risk of Cesarean delivery compared to white women among excessive GWG women. Although nonsignificant, this suggests that it may be appropriate to modify weight gain by race when Cesarean deliveries are the outcome of concern.

5.5.2.2 Smoking Status

Compared to never smokers, women that quit during the first trimester among those that gained excessive GWG had a greater than 30% increased risk of a Cesarean delivery. Due to small sample sizes and misclassification bias, this may not be a true association.

5.6 Limitations

Reporting and recall bias are of concern when using birth certificates. Pre-pregnancy BMI was calculated using self-reported weight before pregnancy. Although is possible that some women would misreport their weight, a handful of studies have shown a highly significant association between stated and actual pre-pregnancy weight (154-158). A recent study found the only significant difference between clinical measurement and reported weight was an over reporting of 2.4 lbs. by underweight women (158). Based on these results, this study will assume that the effect of reporting bias relevant to weight has little effect on the results.

Smoking status of women may also be subject to reporting bias leading to misclassification. Studies evaluating responses of pregnant women found that of self-reported quitters 20%- 24% had biological evidence of active smoking (159-161). Women reported as quitters during pregnancy were more likely to be reclassified as smokers compared to women reporting quitting before pregnancy ($p<0.001$). For this reason, the authors found that the bias among women with hypertension that reported they were quitters was skewed 11% away from the null, and 7% towards the null among women that reported they were smokers (162).

Weight gain in relation to GDM presents temporality limitations that could not be avoided. Women with GDM are more likely to have an intervention to control weight. Since weight gain is likely to be managed more closely for these women, it is possible that intervention is a confounder in this association. It would be more appropriate to use weight gain at the time of or before diagnosis. Several recent studies have examined the association of GWG on GDM before diagnosis. These studies found mixed results (57, 63, 71). This bias would minimize our observed results, resulting in skewing towards the null. It is possible that the studies that found an inverse association between excessive GWG and GDM could be measuring the effect of treatment.

There is currently no standardized protocol for diagnosing GDM. Although there are recommendations for Wyoming, the methods used for diagnosis will vary by hospital as well as by clinician. Diagnosis of GDM is based on the individual's risk factors and history. If overweight women have GDM and are more likely to be tested, the results will be biased away from the null. Also, if symptoms are moderate it is possible for GDM to go undiagnosed. Therefore, diagnosis and treatment are difficult to standardize.

Using the birth certificate it was impossible to accurately differentiate between necessary and elective Cesarean section. Without this information the observed effect between weight gain and outcome will be decreased and the association biased towards the null. Elective Cesareans are not likely to occur in large percentages and therefore will have minimal impact on the results.

Hypertensive disorders of pregnancy consist of a broad spectrum of conditions. This study combined multiple different manifestations of one disease process and classified pregnancy induced hypertension, preeclampsia, and eclampsia into one category named "hypertensive states". There is evidence that these conditions may be pathophysiologically distinct (163). By combining these various forms of hypertension we lost the ability to discern differences there may exist between them.

These results reflect the outcomes of Wyoming women. The state is unique in that it is rural and racially homogeneous and thus these results may not be applicable to other populations.

5.7 Strengths

Birth certificate completion is required for every birth allowing these results to be entirely representative and have a high external validity. Total number of birth certificates in the analysis was approximately 36,000 resulting in a high power. Birth certificate data are reliable and consistent especially so among clinical sections completed by physicians.

Use of clinical estimation of gestation in this study compared use of last menstrual period (LMP) results in several strengths. Clinical estimation does not rely on the mothers recall, the estimation is ideally based on use of early ultrasound, and there were almost no missing values of clinical estimation of gestation whereas 10% of gestation values based on LMP were missing.

The results of this study address research recommendations suggested by the IOM. Specifically, we addressed the extent to which optimal GWG differs by parity, race and socioeconomic factors. To our knowledge we are the first to find significant interactions between GWG, APNCU and race on the outcome of hypertensive states.

5.8 Public Health Implications

Because excessive GWG has been associated to both adverse maternal and infant outcomes, it is of concern that half of the Wyoming population studied here had excessive GWG. These findings suggest that it is important to educate women on nutrition and appropriate GWG. Additionally the risk factors identified in this study may help target education programs for women at highest risk if excessive weight is gained. Understanding these risk factors may help the Wyoming Department of Health to decrease risk of Cesarean delivery and hypertensive states among these high risk women to improve the health of their population. Additionally these findings may be added to accumulating research regarding the appropriateness of weight gain differs by maternal characteristics.

5.9 Future Research

Our study can only suggest associations and should not be used to infer causality. Future research is necessary to further explore the effect of GWG on these three outcomes of interest. It remains unclear if GWG increases risk of GDM due to inherent limitations. Future studies should not only collect weight gain at delivery but also throughout pregnancy.

Future studies that used reported maternal smoking as an exposure should interpret results with caution. Misclassification bias has been found to be large and biological measures should be used as a more accurate evaluation of exposure. Since fewer than half of the women in this study met the guidelines for adequate weight gain future research should also be warranted to investigate what interventions and educational programs are effective strategies for women to meet weight gain recommendations. When possible, research should assess the effect of GWG on the various manifestations of the hypertensive spectrum.

TABLES

Table 1. 1: 2009 Institute of Medicine's Recommendations for Weight Gain during Pregnancy, by Pre-pregnancy BMI

	Total Weight Gain	
Pre-pregnancy BMI	Range in kg	Range in lbs
Underweight (<18.5 kg/m^2)	12.8-18	28-40
Normal Weight (18.5-24.9 kg/m^2)	11.5-16	25-35
Overweight (24.9-29.9 kg/m^2)	7-11.5	15-25
Obese (>30.0 kg/m^2)	5-9	11-20

Table 2. 1: Clinical Criteria for a Positive Diagnosis for Gestational Diabetes Mellitus Using Oral Glucose Load

	100 gm		75 gm	
	Mg/dL	mmol/l	mg/L	mmol/l
Fasting	≥95	≥5.3	≥95	≥5.3
1 hr	≥180	≥10.0	≥180	≥10.0
2 hr	≥155	≥8.6	≥155	≥8.6
3 hr	≥140	≥7.8		

Table 3. 1: Variables of Interest in Dataset

Variable Name	Description	Value	Number of Missing (% of Total)	Notes
BIRTH_SEQ	Birth Number	Continuous	0	Not used for modeling
SEX	Childs Sex	0=Female 1=Male	0	
CHILD_BIRTH_ WT	Birth weight	0=Low Birth Weight (Less than 2500g) 1=Normal Birth Weight (2500g to 4000g) 2=Macrosomia (Greater than 4000g)	24 (0.065%)	Categorized from continuous
M_AGE	Mothers Age	1= 15-19 2=20-24 3=25-34 4=35-45	1 (0.003%)	Categorized from continuous
EDU	Mothers Education	0= Less than High school 1=High school graduate, GED or some college credit 2= College degree	916 (2.466%)	Levels collapsed based on common definitions used by the Wyoming Department of Health.
MOTHER_HISPANIC	Mother of Hispanic Origin?	0= No 1=Yes	0	
M_RACE	Mothers Race	1=American Indian or Alaskan Native 2=Black or African American 3=White 4=Asian/Pacific Islander (Asian Indian, Other Asian, Other Pacific Islander, Samoan, Vietnamese 5=Other	567 (1.526%)	Levels collapsed based on common definitions used by the Wyoming Department of Health
PRENATAL_CARE	Prenatal care	0=No prenatal care 1=Had prenatal care	343 (0.923%)	

Variable Name	Description	Value	Number of Missing (% of Total)	Notes
APNCU	Adequacy of Prenatal Care Utilization Index	1=Inadequate 2=Intermediate 3=Adequate 4=Adequate Plus	2260 (6.084%)	
GESTATION	Obstetric estimate of gestation	0=Preterm (Less than 37 weeks) 1=Term (37 weeks or greater)	18 (0.0484%)	Categorized from continuous
M_HEIGHT	Mothers height	Continuous	1194 (3.214%)	Used to calculate pre-pregnancy BMI, and weight gain category
M_PRE_PREG_WT	Pre-pregnancy weight	Continuous	1896 (5.104%)	Used to calculate pre-pregnancy BMI, and weight gain variable
M_DELIVERY_WT	Delivery weight	Continuous	1852 (4.986%)	Used to calculate weight gain variable
M_WIC_FOOD	Did mother get WIC food for herself during this pregnancy?	0=No 1=Yes	1039 (2.797%)	
PREV_birth	Previous living birth	0=0 1=1-2 2=3 or more	101 (0.272%)	Categorized from continuous
TOBACCOTHREEMONTHSBEFOREUNKNOWN	Tobacco use 3 months before pregnancy unknown	0=No 1=Yes	1865 (5.021%)	
TOBACCO_USE_3_MONTH_PRIOR	Tobacco use 3 months before pregnancy	0=No 1=Yes	0	

Variable Name	Description	Value	Number of Missing (% of Total)	Notes
TOBACCO_USE_3_ MONTH_PRIOR	Tobacco use 3 months before pregnancy-amount	0=Less than 20 Cigarettes 1=20-39 Cigarettes 2=Greater than 40	0	Categorized from continuous, among women who reported smoking
TOBACCOFIRSTTRI MESTERUNKNOWN	Tobacco use first 3 months of pregnancy unknown	0=No 1=Yes	1906 (5.131%)	
TOBACCO_USE_1ST _TRI	Tobacco use first 3 months of pregnancy	0=No 1=Yes	0	
TOBACCO_USE_1ST _TRI	Tobacco use first 3 months of pregnancy-amount	0=Less than 20 Cigarettes 1=20-39 Cigarettes 2=Greater than 40	0	Categorized from continuous, among women who reported smoking
TOBACCOSECONDT RIMESTERUNKNO WN	Tobacco use second 3 months of pregnancy unknown	0=No 1=Yes	1921 (5.172%)	
TOBACCO_USE_2ND _TRI	Tobacco use second 3 months of pregnancy	0=No 1=Yes	0	
TOBACCO_USE_2ND _TRI	Tobacco use second 3 months of pregnancy-amount	0=Less than 20 Cigarettes 1=20-39 Cigarettes 2=Greater than 40	0	Categorized from continuous, among women who reported smoking

Variable Name	Description	Value	Number of Missing (% of Total)	Notes
TOBACCOTHIRDTRIMESTERUNKNOWN	Tobacco use last 3 months of pregnancy unknown	0=No 1=Yes	1910 (3.342%)	
TOBACCO_USE_3RD_TRI	Tobacco use last 3 months of pregnancy	0=No 1=Yes	0	
TOBACCO_USE_3RD_TRI	Tobacco use last 3 months of pregnancy-amount	0=Less than 20 Cigarettes 1=20-39 Cigarettes 2=Greater than 40	0	Categorized from continuous, among women who reported smoking
P_SOURCE	Principal source of payment for this delivery	0=Other 1=Medicaid 2=Self-Pay	1576 (4.243%)	Collapsed based on cross tabulations with other variables. See methodology section
DIABETES_PRE_PREG	Pre-pregnancy diabetes	0=No 1=Yes	0	Used as exclusion criteria in GDM model
DIABETES_GESTATIONAL	Gestational diabetes	0=No 1=Yes	0	Used to make GDM variable
HYPERTENSION_PREPREGNANACY	Pre-pregnancy hypertension	0=No 1=Yes	0	Used as exclusion criteria in Hypertensive states model
HYPERTENSION_GESTATIONAL	Gestational Hypertension	0=No 1=Yes	0	Used to create hypertensive states variable
ECLAMPSIA	Eclampsia	0=No 1=Yes	0	Used to create Hypertensive states variable

Table 3. 2:Variables Calculated and Categorized from Dataset

Variable Name	Description	Value	Number of Missing (% of Total)	Notes
Hypertensivestates	Women who experienced any hypertensive state, preeclampsia or eclampsia during pregnancy	0=No 1=Yes	0	Excludes women with pre-pregnancy hypertension
WeightGain	Total weight gain	Continuous	3349 (9.016%)	Used to create pre-pregnancy BMI category
PrepregBMI	Pre-pregnancy BMI	Continuous	2454 (6.606%)	Used to create pre-pregnancy BMI categories
BMIcat	Pre-pregnancy BMI category	1= Underweight (BMI less than 18.5) 2=Normal weight (BMI between 18.5 and 24.9) 3=Overweight (BMI greater than 24.9 and less than or equal to 29.9) 4=Obese (BMI greater than 30)	139 (0.374%)	Used to create IOM weight gain category
IOMcat	Weight gain category based on 2009 IOM	1=Insufficient 2=Sufficient 3=Excessive	139 (0.374%)	Categories based on pre-pregnancy BMI and total weight gain
Smoking_Status	Change of smoking through pregnancy	0=Never Smoker 1=Quit in 1st Trimester 2=Quit in 2nd Trimester 3=Quit in 3rd Trimester 4=Did not quit	2337 (6.292%)	

Variable Name	Description	Value	Number of Missing (% of Total)	Notes
PREV_C_SECTION	Previous Cesarean	0=No 1=Yes	0	Used to investigate medical indication for Cesarean variable
PREV_C_SECTION_COUNT	Total number of previous Cesarean	0=No 1=Yes	2 (0.005%)	Used for additional information for medical indication for Cesarean variable
PROLONGED_LABOR	Prolonged labor (≥20 hrs)	0=No 1=Yes	0	May be used to investigate medical indication for Cesarean variable
CEPHALIC_PRESENTATION	Cephalic fetal presentation	0=No 1=Yes	0	May be used to investigate medical indication for Cesarean variable
BREECH_PRESENTATION	Breech fetal presentation	0=No 1=Yes	0	May be used to investigate medical indication for Cesarean variable
OTHER_PRESENTATION	Other fetal presentation	0=No 1=Yes	0	May be used to investigate medical indication for Cesarean variable
CESAREAN	Cesarean delivery	0=No 1=Yes	0	May be used to investigate medical indication for Cesarean variable
LABOR_ATTEMPTED	If Cesarean was labor attempted?	0=No 1=Yes	490 (1.319%)	May be used to investigate medical indication for Cesarean variable

Table 3. 3: Exclusion Criteria Applied to Select Variables

Variable name	Variable Description	Range before restriction	Restriction criteria applied	Range after restriction	Number of women outside restriction range
Birth_wt	Childs Birth Weight	181g-10007g	Removed highest and lowest 1%	1642g-4366g	732
Mother_age	Mothers Age at time of delivery	11-48	Definition for maternal age	15-45	36
Gestation	Obstetric estimation of gestation	18-44	Removed all births with less than 28 weeks gestation	28-44	152
Mother_ pre_preg_ wt	Mothers self-reported pre-pregnancy weight	75 lbs.- 400 lbs.	Removed highest and lowest 1%	97 lbs.-275 lbs.	650
Mother_delivery_wt	Mothers weight a time of delivery	81 lbs.-425 lbs.	Removed highest and lowest 1%	120 lbs.-300 lbs.	640

Table 4. 1: Weight Gain Strata for the Entire population, before Subset Selection

IOM Weight Gain Category	N	%
Insufficient	5970	19.35%
Sufficient	9700	31.44%
Excessive	15185	49.21%
Total	30855	100.0%

Table 4. 2: Table of GDM, Hypertensive States and Cesarean Delivery by two Level Weight Gain Categories, among the Subset Population of Interest

	GDM			Hypertensive States			Cesarean Delivery		
IOM Weight Gain Category	**Yes (%)**	**No (%)**	**Total**	**Yes (%)**	**No (%)**	**Total**	**Yes (%)**	**No (%)**	**Total**
Excessive	293 (57.2)	976 (59.5)	1269	927 (76.4)	2182 (60.0)	3109	4149 (65.5)	11036 (61.0)	15185
Sufficient	219 (42.8)	665 (40.5)	884	287 (23.6)	1451 (40.0)	1738	2187 (34.5)	7513 (39.0)	9700
Total	512 (100.0)	1641 (100.0)	2153	1214 (100.0)	3633 (100.0)	4847	6336 (100.0)	18549 (100.0)	24885
p-value (Chi-Square)	**0.3664**			**<0.0001**			**<0.0001**		

Table 4. 3: Population Statistics, by Variables of Interest, among GDM, Hypertensive States, and Cesarean Delivery Population Subset

Variable	Level	GDM	Hypertensive States	Cesarean Deliveries
		N (%)	N (%)	N (%)
Maternal Age	15-19	220 (10.1)	522 (10.7)	3321 (10.7)
	20-24	613 (28.3)	1460 (30.0)	9672 (32.2)
	25-34	1093 (50.5)	2464 (50.6)	15334 (49.5)
	35-45	238 (11.0)	426 (8.7)	2644 (8.5)
	Missing	0	0	0
Maternal Education	Less than High school	314 (14.9)	586 (12.4)	4414 (14.6)
	High school graduate, GED or some college credit	745 (35.5)	1717 (36.3)	11016 (36.4)
	College degree	1041 (49.6)	2424 (51.3)	14857 (49.1)
	Missing	64	145	684
Maternal Race	American Indian	70 (3.2)	143 (3.0)	964 (3.1)
	Black	13 (0.6)	44 (0.9)	246 (0.8)
	White	1930 (89.2)	4395 (91.3)	27718 (89.5)
	Asian/Pacific Islander	24 (1.1)	45 (0.9)	328 (1.1)
	Other	127 (5.9)	188 (3.9)	1715 (5.5)
	Missing	0	57	0
Maternal Ethnicity	Non-Hispanic	1898 (87.7)	4335 (89.0)	27225 (87.9)
	Hispanic	266 (12.3)	537 (11.0)	3746 (12.1)
	Missing	0	0	0
Payment Source for the Delivery	Medicaid	823 (39.1)	1797 (38.0)	12203 (40.6)
	Self-pay	126 (6.0)	280 (5.9)	1792 (6.0)
	Other	1153 (54.8)	2650 (56.1)	16091 (53.5)
	Missing	62	145	885
Did Mother Receive WIC Food?	Yes	719 (33.8)	1523 (31.6)	10521 (34.4)
	No	1406 (66.1)	3292 (68.4)	20025 (65.6)
	Missing	39	57	425

Variable	Level	GDM N (%)	Hypertensive States N (%)	Cesarean Deliveries N (%)
Clinical Gestation	Preterm	164 (7.6)	413 (8.5)	2211 (7.1)
	Term	2000 (92.4)	4459 (91.5)	28760 (92.9)
	Missing	0	0	0
Previous Living Births	0	903 (50.8)	2221 (53.4)	12537 (48.5)
	1-2	636 (35.8)	1448 (34.9)	9902 (38.3)
	3 or more	237 (13.3)	486 (11.7)	3417 (13.2)
	Missing	388	717	5115
Birth Weight	Low Birth Weight	104 (4.8)	296 (6.1)	1699 (5.5)
	Normal Birth Weight	1972 (91.1)	4378 (89.9)	28041 (90.5)
	Macrosomia	88 (4.1)	198 (4.1)	1231 (4.0)
	Missing	0	0	0
Prenatal Care	Had No Prenatal Care	11 (0.5)	27 (0.5)	226 (0.7)
	Had Prenatal Care	2141 (98.9)	4816 (98.9)	30574 (99.3)
	Missing	12	29	171
APNCU	Inadequate	302 (14.7)	648 (14.0)	4751 (16.1)
	Intermediate	209 (10.2)	511 (11.0)	3434 (11.6)
	Adequate	802 (39.1)	1766 (38.1)	11797 (39.9)
	Adequate Plus	736 (35.9)	1714 (36.9)	9614 (32.5)
	Missing	115	233	1375
Gender of Child	Female	1020 (47.1)	2376 (48.8)	15190 (49.0)
	Male	1144 (52.9)	2496 (51.2)	15781 (50.1)
	Missing	0	0	0
Tobacco Use Three Months Prior to Pregnancy	No	1530 (73.9)	3677 (75.5)	21682 (73.5)
	Yes	541 (26.1)	1195 (24.3)	7803 (26.5)
	Amount:	N (%)	N (%)	N (%)
	Less than 10 Cigarettes	134 (6.5)	293 (3.0)	1825 (6.2)
	10-19 Cigarettes	153 (7.4)	320 (6.6)	2236 (7.6)
	20-39 Cigarettes	214 (10.3)	503(10.3)	3204 (10.9)
	Greater Than 40	10 (1.9)	79 (1.6)	538 (1.8)
	Missing	0	1495	

Variable	Level	GDM		Hypertensive States		Cesarean Deliveries	
			N (%)		N (%)		N (%)
Tobacco During the First Trimester	No		1758 (84.8)		4028 (85.5)		24861 (84.3)
	Yes		317 (15.3)		685 (14.5)		4615 (15.7)
	Amount:	N (%)		N (%)		N (%)	
	Less than 10 Cigarettes	134 (6.5)		318 (6.7)		2069 (7.0)	
	10-19 Cigarettes	73 (3.5)		131 (2.8)		1004 (3.4)	
	20-39 Cigarettes	99 (4.8)		216 (4.6)		1416 (4.8)	
	Greater Than 40	9 (0.4)		20 (0.4)		126 (0.4)	
	Missing		91		159		1486
Tobacco During the Second Trimester	No		1843 (88.9)		4187 (89.3)		25923 (88.0)
	Yes		229 (11.1)		499 (10.7)		3544 (12.0)
	Amount:	N (%)		N (%)		N (%)	
	Less than 10 Cigarettes	133 (6.4)		307 (6.5)		2106 (7.1)	
	10-19 Cigarettes	46 (2.2)		72 (1.5)		651 (2.2)	
	20-39 Cigarettes	45 (2.2)		108 (2.3)		733 (2.5)	
	Greater Than 40	5 (0.2)		12 (0.3)		54 (0.2)	
	Missing		92		186		1495
Tobacco During the Third Trimester	No		1844 (88.9)		4224 (89.3)		25874 (87.8)
	Yes		229 (11.1)		503 (10.6)		3596 (12.2)
	Amount:	N (%)		N (%)		N (%)	
	Less than 10 Cigarettes	144 (6.9)		355 (7.5)		2371 (8.0)	
	10-19 Cigarettes	44 (2.1)		65 (1.4)		580 (2.0)	
	20-39 Cigarettes	37 (1.8)		75 (1.6)		602 (2.0)	
	Greater Than 40	4 (0.2)		8 (0.2)		43 (0.2)	
	Missing		91		145		1501
Smoking Status	Never Smoker		1529 (74.8)		3660 (76.0)		21592 (74.3)
	Quit in First Trimester		154 (7.5)		331 (6.9)		1950 (6.7)
	Quit in Second Trimester		71 (3.5)		163 (3.4)		919 (3.2)
	Quit in Third Trimester		23 (1.1)		59 (1.2)		343(1.2)
	Did not Quit		268 (13.1)		600 (12.5)		4256 (14.7)
	Missing		119		59		1911

Table 4. 4: Cross Tabulations of Excessive Weight Gain Categories, by Variables of Interest

		GDM Subset			Hypertensive State Subset			Cesarean Delivery Subset		
Variable	Level	Weight Gain Category		Chi-Square	Weight Gain Category		Chi-Square	Weight Gain Category		Chi-Square
		Excessive	Sufficient		Excessive	Sufficient		Excessive	Sufficient	
		N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Maternal Age	15-19	135 (61.4)	85 (38.6)	0.2703	358 (68.6)	164 (31.4)	0.0166	1745 (64.9)	943 (35.1)	<0.0001
	20-24	376 (61.6)	234 (38.5)		951 (65.6)	498 (34.4)		4791 (62.2)	2914 (37.8)	
	25-34	624 (57.5)	462 (42.5)		1544 (63.0)	906 (37.0)		7468 (60.2)	4933 (39.8)	
	35-45	134 (56.5)	103 (43.5)		256 (60.0)	170 (39.9)		1177 (56.4)	909 (43.6)	
Maternal Education	Less than High school	190 (61.9)	121 (38.9)	0.7311	373 (64.0)	210 (36.0)	0.9659	2125 (62.1)	1294 (37.9)	0.1140
	High school, GED or some college credit	443 (59.6)	300 (40.4)		1090 (63.8)	619 (36.2)		5362 (62.2)	3390 (38.7)	
	College degree	607 (58.6)	428 (41.4)		1548 (64.2)	864 (35.4)		7319 (60.3)	4813 (39.7)	
Maternal Race	American Indian	38 (54.3)	32 (45.7)	0.1821	100 (69.9)	43 (30.1)	0.0784	539 (68.2)	251 (31.8)	<0.0001
	Black	11 (84.6)	2 (15.4)		33 (75.0)	11 (25.0)		113 62.8)	67 (37.2)	
	White	1132 (58.9)	789 (41.1)		2799 (64.1)	1571 (35.9)		13598 (60.9)	8736 (39.1)	
	Asian/Pacific Islander	11 (45.8)	13 (54.2)		23 (51.1)	22 (48.9)		122 (48.6)	129 (51.4)	
	Other	77 (61.6)	48 (38.4)		115 (61.2)	73 (38.8)		641 (61.9)	394 (38.1)	
Maternal Ethnicity	Non-Hispanic	1101 (58.2)	790 (41.8)	0.0689	2775 (64.4)	1537 (35.6)	0.3811	13428 (61.2)	8528 (38.8)	0.2098
	Hispanic	168 (64.1)	94 (35.9)		334 (62.4)	201 (37.6)		1753 (59.9)	1171 (40.1)	
Payment Source for the Delivery	Medicaid	487 (59.5)	332 (40.5)	0.2236	1151 (64.3)	640 (35.7)	0.3660	5987 (62.3)	3627 (37.7)	0.0036
	Self pay	82 (65.6)	43 (34.4)		168 (60.2)	111 (39.8)		867 (61.5)	542 (38.5)	
	Other	663 (57.8)	484 (43.2)		1697 (64.5)	935 (35.5)		7903 (60.1)	5248 (39.9)	
Did Mother Receive WIC Food?	Yes	433 (60.5)	283 (39.5)	0.3419	994 (65.5)	524 (34.5)	0.1723	5211 (62.8)	3080 (37.2)	<0.0001
	No	816 (58.3)	583 (41.7)		2076 (63.4)	1196 (36.6)		9775 (60.1)	6483 (39.9)	

		GDM Subset			Hypertensive State Subset			Cesarean Delivery Subset		
Variable	**Level**	**Weight Gain Category**		**Chi-Square**	**Weight Gain Category**		**Chi-Square**	**Weight Gain Category**		**Chi-Square**
		Excessive N (%)	**Sufficient N (%)**		**Excessive N (%)**	**Sufficient N (%)**		**Excessive N (%)**	**Sufficient N (%)**	
Clinical Gestation	Preterm	84 (51.2)	80 (48.8)	0.0365	226 (64.4)	147 (35.6)	0.9069	885 (55.8)	701 (44.2)	<0.0001
	Term	1185 (59.6)	804 (40.4)		2843 (64.1)	5191 (35.9)		14296 (61.4)	8998 (38.6)	
Previous Living Births	0	564 (62.8)	334 (37.2)	0.1316	1530 (69.1)	684 (30.9)	<0.0001	6803 (65.1)	3651 (34.9)	<0.0001
	1-2	366 (57.7)	268 (42.3)		873 (60.8)	563 (39.2)		4553 (58.3)	3256 (41.7)	
	3 or more	141 (60.0)	94 (40.0)		302 (62.4)	182 (37.6)		1553 (58.8)	1089 (41.2)	
Birth Weight	Low Birth Weight	49 (47.1)	55 (52.9)	<0.0001	171 (57.8)	125 (42.5)	<0.0001	562 (50.5)	550 (49.5)	<0.0001
	Normal Birth Weight	1150 (58.6)	811 (41.4)		2788 (64.0)	1568 (36.0)		13779 (60.8)	882 (39.2)	
	Macrosomia	70 (79.5)	18 (20.5)		150 (76.9)	45 (23.1)		840 (75.9)	267 (24.1)	
Prenatal Care	Had No Prenatal Care	5 (50.0)	5 (50.0)	0.5593	12 (44.4)	15 (55.6)	0.0312	72 (47.4)	80 (52.6)	0.0005
	Had Prenatal Care	1260 (59.1)	872 (40.9)		3084 (64.4)	1707 (35.6)		15031 (61.1)	9557 (38.9)	
APNCU	Inadequate	189 (63.0)	111 (37.0)	0.2378	372 (57.6)	274 (42.4)	<0.0001	2002 (58.4)	1425 (41.6)	<0.0001
	Intermediate	130 (62.5)	78 (38.5)		304 (59.6)	206 (40.4)		1616 (59.1)	1118 (40.9)	
	Adequate	456 (57.1)	343 (42.9)		1116 (63.5)	640 (36.5)		5845 (60.1)	3878 (39.9)	
	Adequate Plus	434 (59.3)	298 (40.7)		1163 (68.2)	541 (31.8)		5018 (63.8)	2851 (36.2)	
Gender of Child	Female	599 (59.1)	415 (40.9)	0.9065	1518 (64.2)	847 (35.8)	0.9511	7273 (60.5)	4746 (39.5)	0.1144
	Male	670 (58.8)	469 (41.2)		1591 (64.1)	891 (35.9)		7908 (61.5)	4953 (38.5)	
Tobacco Use Three Months Prior to Pregnancy	No	863(56.7)	658 (43.3)	0.0012	2337 (63.9)	1321 (36.1)	0.2418	11164 (59.6)	7553 (40.4)	<0.0001
	Yes	349 (64.7)	190 (35.3)		772 (64.9)	417 (35.1)		4017 (65.2)	2650 (34.8)	

Variable	Level	Weight Gain Category		Chi-Square	Weight Gain Category		Chi-Square	Weight Gain Category		Chi-Square
		Excessive	Sufficient		Excessive	Sufficient		Excessive	Sufficient	
		N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Tobacco Use during the First Trimester	No	981 (58.1)	706 (41.9)	0.1984	2594 (64.7)	1414 (35.3)	0.2660	12411 (60.5)	8090 (39.5)	0.0002
	Yes	228 (61.8)	141 (38.2)		422 (61.9)	360 (38.1)		2269 (63.6)	1300 (36.4)	
Tobacco Use during the Second Trimester	No	1029 (58.7)	725 (41.3)	0.7938	2720 (65.3)	1446 (34.7)	0.0251	13017 (61.1)	8308 (38.9)	0.1872
	Yes	179 (59.5)	122 (40.5)		293 (59.2)	202 (40.8)		1612 (61.3)	1017 (38.7)	
Tobacco Use during the Third Trimester	No	1041 (58.8)	728 (41.2)	0.8696	2741 (65.2)	1461 (34.8)	0.0346	13099 (61.1)	8349 (38.9)	0.2923
	Yes	168 (58.3)	120 (41.7)		293 (57.8)	207 (42.2)		1656 (61.9)	1020 (38.1)	
Smoking Status	Never Smoker	862 (56.7)	658 (43.3)	0.0003	2325 (63.9)	1316 (36.1)	<0.0001	11107 (59.6)	7523 (40.4)	<0.0001
	Quit During the First Trimester	112 (73.7)	40 (26.3)		248 (75.1)	82 (24.9)		2283 (70.8)	487 (29.2)	
	Quit During the Second Trimester	50 (70.4)	21 (29.6)		37 (63.8)	21 (36.2)		589 (71.8)	231 (28.2)	
	Quit During the Third Trimester	15 (65.2)	8 (34.8)		339 (56.8)	258 (43.2)		192 (68.8)	87 (31.2)	
	Did not Quit	160 (59.7)	108 (40.3)					1905(60.3)	1256 (39.7)	

Table 4. 5: Cross Tabulations of GDM, Hypertensive State and Cesarean Delivery by Variables of Interest among cohorts

Variable	Level	Diabetes Mellitus		Chi-Square	Hypertensive States		Chi-Square	Cesarean Delivery		Chi-Square
		Yes	No		Yes	No		Yes	No	
		N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Maternal Age	15-19	27 (12.3)	193 (87.7)	<0.0001	122 (23.4)	400 (76.6)	0.1599	492 (18.2)	2206 (81.8)	<0.0001
	20-24	119 (19.4)	494 (80.6)		360 (24.7)	1100 (75.3)		1850 (23.9)	5892 (76.1)	
	25-34	272 (24.9)	821 (75.1)		611 (24.8)	1853 (75.2)		3355 (26.9)	9118 (73.1)	
	35-45	96 (40.3)	142 (59.7)		125 (29.3)	301 (70.7)		681 (32.6)	1409 (67.4)	
Maternal Education	Less than High school	83 (26.4)	231 (73.6)	0.3946	135 (23.0)	451 (77.0)	0.1315	837 (24.3)	2600 (75.6)	0.0423
	High school, GED or some college credit	171 (22.9)	574 (77.1)		408 (23.8)	1309 (76.2)		2204 (25.1)	6593 (74.9)	
	College degree	238 (22.9)	803 (77.1)		632 (26.1)	1792 (73.9)		3192 (26.2)	8997 (73.8)	
Maternal Race	American Indian	24 (35.7)	45 (64.3)	0.0158	42 (39.4)	101 (70.6)	0.0805	221 (27.8)	573 (72.2)	0.0005
	Black	1 (7.7)	12 (92.3)		10 (22.7)	34 (77.3)		43 (23.8)	138 (76.2)	
	White	446 (23.1)	1484 (76.9)		1111 (25.3)	3284 (74.7)		5644 (25.1)	16802 (74.9)	
	Asian/Pacific Islander	10 (41.7)	14 (58.3)		10 (22.2)	35 (77.8)		85 (33.7)	167 (66.3)	
	Other	32 (25.2)	95 (74.8)		32 (17.0)	156 (83.0)		302 (29.0)	738 (71.0)	
Maternal Ethnicity	Non-Hispanic	438 (23.1)	1460 (76.9)	0.0486	1101 (25.4)	3234 (74.6)	0.0684	5542 (25.1)	16521 (74.9)	0.0001
	Hispanic	76 (28.6)	190 (71.4)		117 (21.8)	420 (78.2)		836 (28.4)	2104 (71.6)	
Payment Source for the Delivery	Medicaid	187 (22.7)	636 (77.3)	0.5518	697 (26.3)	1953 (73.7)	0.0608	2471 (25.6)	7184 (74.4)	<0.0001
	Self-pay	33 (26.2)	93 (73.8)		418 (23.3)	1379 (76.7)		297 (21.0)	1117 (79.0)	
	Other	282 (24.5)	871 (75.5)		66 (23.6)	214 (76.4)		3476 (26.3)	9747 (29.3)	
Did Mother Receive WIC Food?	Yes	188 (26.1)	531 (73.9)	0.0650	358 (23.5)	1165 (76.5)	0.1071	2181 (26.2)	6154 (73.8)	0.2362
	No	317 (22.5)	1089 (77.5)		845 (25.7)	2447 (74.3)		4160 (25.5)	12173 (74.5)	
Clinical Gestation	Preterm	61 (37.2)	103 (62.8)	<0.0001	193 (46.7)	220 (53.3)	<0.0001	559 (35.2)	1031 (64.8)	<0.0001
	Term	453 (22.6)	1547		1025 (23.0)	3434 (77.0)		5819 (24.8)	17594 (75.2)	

Variable	Level	Diabetes Mellitus		Chi-Square	Hypertensive States		Chi-Square	Cesarean Delivery		Chi-Square
		Yes	No		Yes	No		Yes	No	
		N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Previous Living Births	0	187 (20.7)	716 (79.3)	0.0006	724 (32.6)	1497 (67.4)	<0.0001	2623 (25.0)	7872 (75.0)	<0.0001
	1-2	156 (24.5)	480 (75.5)		275 (19.0)	1173 (81.0)		2108 (26.8)	5749 (73.2)	
	3 or more	77 (32.5)	160 (67.5)		86 (17.7)	400 (82.3)		589 (22.2)	2066 (77.8)	
Birth Weight	Low Birth Weight	36 (34.6)	68 (65.4)	0.0025	132 (44.6)	164 (55.4)	<0.0001	406 (36.3)	711 (63.7)	<0.0001
	Normal Birth Weight	449 (22.8)	1523 (77.2)		1050 (24.0)	3328 (76.0)		5648 (24.8)	17120 (75.2)	
	Macrosomia	29 (32.9)	59 (67.1)		36 (18.2)	162 (81.8)		324 (29.0)	794 (71.0)	
Prenatal Care	Had No Prenatal Care	3 (27.3)	8 (72.7)	0.7828	1 (3.7)	26 (96.3)	0.0102	36 (23.2)	119 (76.8)	0.5159
	Had Prenatal Care	508 (23.7)	16.33 (76.3)		1213 (25.2)	3603 (74.8)		6302 (25.5)	18405 (74.5)	
APNCU	Inadequate	71 (23.5)	231 (76.5)	<0.0001	127 (19.6)	521 (80.4)	<0.0001	849 (24.6)	2596 (75.4)	<0.0001
	Intermediate	35 (16.7)	174 (83.3)		86 (16.8)	425 (83.2)		687 (25.0)	2060 (75.0)	
	Adequate	136 (17.0)	666 (83.0)		341 (19.3)	1425 (80.7)		2350 (24.0)	7421 (76.0)	
	Adequate Plus	243 (33.0)	493 (67.0)		608 (35.5)	1106 (64.5)		2206 (27.9)	5701 (72.1)	
Gender	Female	249 (24.4)	71 (75.6)	0.4961	576 (24.2)	1800 (75.8)	0.2335	2946 (24.4)	9129 (75.6)	<0.0001
	Male	265 (23.2)	879 (76.8)		642 (25.7)	1854 (74.3)		3432 (26.5)	9496 (73.5)	
Tobacco Use Three Months Prior to Pregnancy	No	361 (23.6)	1169 (76.4)	0.6870	949 (25.8)	2728 (74.2)	0.0279	4736 (25.2)	14073 (74.8)	0.1522
	Yes	129 (23.8)	412 (76.2)		269 (22.5)	926 (77.5)		1642 (26.5)	4552 (73.5)	

Variable	Level	Diabetes Mellitus		Chi-Square	Hypertensive States		Chi-Square	Cesarean Delivery		Chi-Square
		Yes	No		Yes	No		Yes	No	
		N (%)	N (%)		N (%)	N (%)		N (%)	N (%)	
Tobacco Use During the First Trimester	No	402 (23.7)	1296 (76.3)	0.9434	1048 (26.0)	2980 (74.0)	0.0033	5219 (25.3)	15382 (74.7)	0.0589
	Yes	88 (23.8)	281 (76.2)		140 (20.4)	545 (79.6)		957 (26.7)	2632 (73.3)	
Tobacco Use During the Second Trimester	No	421 (23.8)	1344 (76.2)	0.7261	1090 (26.0)	3097 (74.0)	0.0103	5440 (25.4)	15985 (74.6)	0.1946
	Yes	69 (22.9)	232 (77.1)		98 (19.6)	401 (80.5)		692 (26.2)	1952 (73.8)	
Tobacco Use During the Third Trimester	No	421 (23.6)	1359 (76.4)	0.9096	1101 (26.1)	3123 (73.9)	0.0011	5457 (25.3)	16098 (74.7)	0.1143
	Yes	69 (24.0)	219 (76.0)		91 (19.1)	412 (81.9)		722 (26.8)	1969 (73.2)	
Smoking Status	Never Smoker	361 (23.6)	1168 (76.4)	0.8008	947 (25.9)	2713 (74.1)	0.0005	4711 (24.1)	14011 (74.8)	0.4099
	Quit During the First Trimester	38 (24.7)	116 (75.3)		93 (28.1)	238 (71.9)		447 (26.6)	1231 (73.4)	
	Quit During the Second Trimester	18 (25.3)	53 (74.7)		43 (26.4)	120 (73.6)		211 (25.6)	613 (73.1)	
	Quit During the Third Trimester	3 (13.0)	20 (87.0)		16 (27.1)	43 (72.9)		76 (26.9)	206 (73.1)	
	Did not Quit	64 (23.9)	204 (76.1)		107 (17.8)	493 (82.2)		839 (26.4)	2337 (73.6)	

Table 4. 6: Bivariate Analysis of Risk Factors with Excessive Gestational Weight Gain on DM

	OR	95% CI		p-value	Change in OR of More than 10%
Unadjusted Model	**0.912**	**0.746**	**1.11**	**0.4006**	
Confounder Included Bivariately					
Maternal Ethnicity	0.905	0.740	1.106	0.3291	No
Did mother receive WIC food?	0.894	0.730	1.095	0.2785	No
Clinical Gestation	0.929	0.759	1.137	0.4732	No
Childs sex	0.911	0.746	1.114	0.3656	No
Prenatal Care	0.913	0.747	1.117	0.3778	No
Childs birth weight	0.906	0.740	1.110	0.3412	No
Parity	0.999	0.797	1.252	0.9932	No
Education	0.935	0.762	1.149	0.5237	No
Maternal Age	0.934	0.761	1.145	0.5087	No
APNCU	0.900	0.729	1.110	0.3250	No
Maternal race	0.925	0.756	1.668	0.3051	No
Tobacco use Three Months Before	0.976	0.793	1.200	0.8145	No
Tobacco use during the first trimester	0.968	0.787	1.189	0.7535	No
Tobacco use during the second trimester	0.969	0.788	1.191	0.7176	No
Tobacco use during the third trimester	0.969	0.789	1.191	0.7646	No
Smoking status	0.962	0.781	1.185	0.7144	No

Table 4. 7: Bivariate Analysis of Risk Factors with Excessive Gestational Weight Gain on Hypertensive States

	OR	95% CI		p-value	Change in OR of More than 10%
Unadjusted Model	**2.148**	**1.852**	**2.491**	**<0.0001**	
Confounder Included Bivariately					
Maternal Ethnicity	2.146	1.850	2.488	<0.0001	No
Did mother receive WIC food?	2.154	1.855	2.500	<0.0001	No
Clinical Gestation	2.186	1.881	2.539	<0.0001	No
Childs sex	2.149	1.853	2.492	<0.0001	No
Prenatal Care	2.115	1.823	2.453	<0.0001	No
Childs birth weight	2.241	1.929	2.604	<0.0001	No
Parity	2.059	1.752	2.419	<0.0001	No
Education	2.100	1.807	2.440	<0.0001	No
Maternal Age	2.166	1.867	2.512	<0.0001	No
APNCU	1.988	1.706	2.316	<0.0001	No
Maternal race	2.146	1.850	2.489	<0.0001	No
Tobacco use Three Months Before	2.153	1.857	2.497	<0.0001	No
Tobacco use during the first trimester	2.138	1.844	2.480	<0.0001	No
Tobacco use during the second trimester	2.120	1.828	2.459	<0.0001	No
Tobacco use during the third trimester	2.119	1.827	2.458	<0.0001	No
Smoking status	2.136	1.865	2.447	<0.0001	No

Table 4. 8: Bivariate Analysis of Risk Factors with Excessive Gestational Weight Gain on Cesarean Delivery

	OR	95% CI		p-value	Change in OR of More than 10%
Unadjusted Model	**1.292**	**1.217**	**1.371**	**<0.0001**	
Confounder Included Bivariately					
Maternal Ethnicity	1.293	1.218	1.373	<0.0001	No
Did mother receive WIC food?	1.291	1.216	1.371	<0.0001	No
Clinical Gestation	1.303	1.228	1.383	<0.0001	No
Childs sex	1.291	1.216	1.370	<0.0001	No
Prenatal Care	1.289	1.215	1.369	<0.0001	No
Childs birth weight	1.303	1.227	1.383	<0.0001	No
Parity	1.285	1.203	1.372	<0.0001	No
Education	1.291	1.215	1.371	<0.0001	No
Maternal Age	1.315	1.239	1.396	<0.0001	No
APNCU	1.293	1.217	1.375	<0.0001	No
Maternal race	1.294	1.219	1.374	<0.0001	No
Tobacco use Three Months Before (Yes vs. No)	1.289	1.214	1.129	<0.0001	No
Tobacco use during the first trimester (Yes vs. No)	1.291	1.216	1.370	<0.0001	No
Tobacco use during the second trimester (Yes vs. No)	1.292	1.217	1.371	<0.0001	No
Tobacco use during the third trimester (Yes vs. No)	1.292	1.217	1.371	<0.0001	No
Smoking status	1.302	1.226	1.382	<0.0001	No

Table 4. 9: Testing Effect Modification of Variables of Interest on Excessive GWG for the outcome Hypertensive States

Variable added to Weight gain variable	Level	OR	95% CI		p-value	p-value for interaction with excessive GWG
Maternal Ethnicity	Non-Hispanic	2.1484	1.8373	2.5120	<0.0001	0.9600
	Hispanic	2.1217	1.3358	3.3699	0.0014	
Did mother receive WIC food?	Yes	2.2857	1.9114	2.7333	<0.0001	0.2275
	No	1.8732	1.4311	2.4519	<0.0001	
Clinical Gestation	Term	2.2048	1.8769	2.5901	<0.0001	0.7661
	Preterm	2.0608	1.3607	3.1210	0.0006	
Childs sex	Female	2.2180	1.7867	2.7533	<0.0001	0.6912
	Male	2.0884	1.7040	2.5596	<0.0001	
Prenatal Care	Yes	2.1100	1.8189	2.4476	<0.0001	0.9635
	No	70590.4	0	3.3E198	0.9609	
Childs birth weight	Normal Birth Weight	2.3269	1.9809	2.7332	<0.001	Low birth weight vs. normal birth weight=0.1677
	Low Birth Weight	1.6403	1.0252	2.6243	0.0390	Macosomia vs. normal birth weight=0.8325
	Macrosomia	2.0837	0.7588	5.7219	0.1543	
Parity	0 Children	1.9872	1.6164	2.4432	<0.0001	1-2 children vs. 0 children=0.8591
	1-2 children	2.0528	1.5313	2.7520	<0.0001	
	3 or more children	2.6462	1.5169	4.6162	0.0006	3 or more children vs. 0 children=0.3444
Education	College Degree	2.0534	1.6729	2.5204	<0.001	Less than high school vs. college degree=0.6275
	Less than High school	2.3197	1.4822	3.6303	0.0002	High school graduate vs. college degree=0.8848
	High school graduate, GED or some college credit	2.1034	1.6335	2.7084	<0.0004	
Maternal Age	20-24	2.0340	1.5462	2.6757	<0.0001	15-19 vs. 20-24=0.4802
	15-19	2.5017	1.5099	4.1451	0.0004	25-34 vs. 20-24=0.4749
	25-34	2.3065	1.8714	2.8428	<0.0001	
	35-45	1.6992	1.0925	2.6429	0.0186	35-45 vs. 20-24=0.4978

Table 4. 10: Testing Effect Modification of Variables of Interest on Excessive GWG for the Outcome Cesarean Delivery

Interaction Variable added to GWG	Level	OR	95% CI		p-value	p-value for interaction with excessive GWG
Maternal Ethnicity	Non-Hispanic	1.3044	1.2238	1.3904	<0.0001	0.4568
	Hispanic	1.2193	1.0330	1.4393	0.0191	
Did mother receive WIC food?	Yes	1.3220	1.2285	1.4227	<0.0001	0.2757
	No	1.2322	1.1116	1.3660	<0.0001	
Clinical Gestation	Term	1.2957	1.2176	1.3789	<0.0001	0.5196
	Preterm	1.3923	1.1289	1.7172	0.0020	
Childs sex	Female	1.3369	1.2256	1.4584	<0.0001	0.2730
	Male	1.2507	1.1526	1.3571	<0.0001	
Prenatal Care	Yes	1.2909	1.2158	1.3706	<0.0001	0.6183
	No	1.0646	0.5000	2.2669	0.8710	
Childs birth weight	normal birth weight	1.3086	1.2287	1.3936	<0.0001	Low birth weight vs. normal birth weight =0.6381
	Low Birth weight	1.2315	0.9639	1.5734	0.0958	
	Macrosomia	1.2866	0.9404	1.7603	0.1151	Macrosomia vs. normal birth weight =0.9174
Parity	0 children	1.3588	1.2349	1.4952	<0.0001	1-2 children vs. 0 children =0.3053
	1-2 children	1.2626	1.1393	1.3993	<0.0001	3 or more children vs. 0 children =0.0438
	3 or more children	1.0946	0.9077	1.3200	0.3442	
Education	College Degree	1.3118	1.2059	1.4271	<0.0001	Less than high school vs. college degree =0.0321
	Less than High school	1.0748	0.9143	1.2634	0.3821	
	High school graduate, GED or some college credit	1.3533	1.225	1.4980	<0.0001	High school graduate vs. college degree =0.6439
Maternal Age	20-24	1.2546	1.1239	1.4004	<0.0001	15-19 vs. 20-24=0.6987
	15-19	1.3152	1.0639	1.6258	0.0113	
	25-34	1.3426	1.2361	1.4583	<0.0001	25-34 vs. 20-24=0.3340
	35-45	1.3527	1.1225	1.6302	0.0015	35-45 vs. 20-24=0.4953

Interaction Variable added to GWG	Level	OR	95% CI		p-value	p-value for Interaction with excessive GWG
APNCU	Adequate	1.3172	1.1956	1.4512	<0.0001	Inadequate vs. Adequate =0.6316
	Inadequate	1.3792	1.1741	1.6201	<0.0001	Intermediate vs. Adequate =0.2775
	Intermediate	1.1776	0.9860	1.4063	0.0711	Adequate plus vs. Adequate =0.6328
	Adequate Plus	1.2723	1.1462	1.4122	<0.0001	
Maternal race	White	1.2819	1.2035	1.3653	<0.0001	American Indian vs. white =0.3234
	American Indian	1.0786	0.7702	1.5105	0.6595	Black vs. white =0.6752 Asian Pacific Islander vs. white =0.9563
	Black	1.5010	0.7194	3.1317	0.2791	
	Asian/Pacific Islander	1.3009	0.7704	2.1966	0.3250	Other vs. white =0.0733
	Other	1.6254	0.2633	2.0912	0.0002	
Tobacco use Three Months Before	Yes	1.3202	1.1689	1.4911	<0.0001	0.6549
	No	1.2789	1.1944	1.3693	<0.0001	
Tobacco use during the first trimester	Yes	1.3360	1.1582	1.5410	<0.0001	0.6037
	No	1.2815	1.2003	1.3682	<0.0001	
Tobacco use during the second trimester	Yes	1.3320	1.1397	1.5567	0.0003	0.6775
	No	1.2852	1.2050	1.3706	<0.0001	
Tobacco use during the third trimester	Yes	1.2641	1.0804	1.4790	0.0034	0.7682
	No	1.2968	1.2160	1.3829	<0.0001	
Smoking status	never smoker	1.2760	1.1916	1.3665	<0.0001	Quit during first trimester vs. never smoker =0.1656
	Quit during the first trimester	1.5348	1.1931	1.9745	0.0009	Quit during second trimester vs. never smoker =0.8622
	Quit during the second trimester	1.3449	0.7460	2.4245	0.3244	
	Quit during the third trimester	1.2760	1.1916	1.3665	<0.0001	Quit during third trimester vs. never smoker =.
	Did not quit	1.3670	1.1592	1.6120	0.0002	Quit during third trimester vs. never smoker =0.4499

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LIST OF ACRONYMS

IOM- Institute of Medicine

BMI-Body Mass Index

WHO-World Health Organization

MOMS- Maternal Outcome Monitoring System

GWG- Gestational Weight Gain

GDM- Gestational Diabetes Mellitus

CDC- Centers for Disease Control and Prevention

HIV- Human Immunodeficiency Virus

OGTT-Oral Glucose Tolerance Test

AOR- Adjusted Odds Ratio

OR- Odds Ratio

CI- Confidence Interval

NVSS-N- National Vital Statistics System – Natality

NCHS- National Center for Health Statistics

VEGF- Vascular Endothelial Growth Factor

PGF- Placental Growth Factor

WIC-Woman Infant and Children

APNCU-Adequacy of Prenatal Care Utilization

TNF - Tumor Necrosis Factor