Abstract

Title of dissertation: THE ASSOCIATION BETWEEN INADEQUATE GESTATIONAL WEIGHT GAIN AND INFANT DEATH AMONG U.S. INFANTS BORN 2004-2008

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Infant mortality is of great public health importance and its prevalence is often used as a summary indicator of a population's reproductive health status. Programmatic and policy focus on prematurity and birth weight stems largely from their known relationship to infant mortality and morbidity. A large body of literature exists linking poor gestational weight gain to prematurity and low birth weight, but its association with infant mortality is less well understood. Few nationally representative studies have examined infant death as an important pregnancy outcome of inadequate gestational weight gain and even fewer have explored its psychosocial and demographic correlates.

As a measure of healthy gestational weight gain, the Institute of Medicine (IOM) published guidelines which provide a recommended weight gain for each category of pre-pregnancy Body Mass Index (BMI). Informed by the Biomedical and Biopsychosocial models, this study examined the association between the IOM measure of inadequate gestational weight gain and risk of infant mortality by conducting secondary analyses of the 2005 Birth Cohort Linked Birth-Infant Death Data File (Cohort Linked File) and Phase 5 of the Pregnancy Risk Assessment Monitoring System (PRAMS). An analysis of

160,011 women who participated in PRAMS between 2004 and 2008 was used to replicate the IOM guidelines and examine the link between gestational weight gain and risks of infant mortality within four months of birth. The PRAMS dataset was also used to analyze the association between maternal pre-pregnancy BMI, weight gain, and infant death, as well as the influence of maternal stress on gestational weight gain. A separate analysis of 2,046,725 infants in the 2005 cohort linked file was conducted to quantify the risk of infant death associated with inadequate gestational weight gain as well as cause-specific mortality. Results from logistic and proportional hazards regression analyses suggest there is a substantial and significant association between inadequate gestational weight gain and infant death; however weight gain beyond the recommended amount may be protective. Inadequate gestational weight gain was associated with infant death from disorders relating to short gestation, fetal malnutrition, respiratory conditions, and birth defects. Receipt of adequate prenatal care was protective against inadequate gestational weight gain, but a positive association was not found between inadequate gestational weight gain and maternal stress. Implications for public health programs, policy, and future research are presented.

THE ASSOCIATION BETWEEN INADEQUATE GESTATIONAL WEIGHT GAIN AND INFANT MORTALITY AMONG U.S. INFANTS BORN 2004-2008

By

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Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, College Park in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
2012

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Dedication

I dedicate this dissertation to my mother, Delphynne J. Davis, and all the other strong women in my family. You have been exemplars of excellence, pride, elegance, and perseverance and will never know how profoundly you have touched me. I can reach farther today than ever imagined possible because I stand on your shoulders.

Acknowledgments

From an outside observation, a doctoral dissertation may appear to be a solitary project. However, an undertaking of this magnitude required a network of support and I would like to acknowledge those who assisted me. Foremost among these are my dissertation chairs**, Dr. Sandra Hofferth** who pushed and invested in me and **Dr. Edmond Shenassa** who always challenged me to substantiate and refine my theories. Words are not enough to thank them for all of their support throughout this journey in spite of their unbelievably busy schedules. Their contributions were critical to any research that hoped to show public health professionals how critical appropriate gestational weight gain could be for improving infant outcomes.

I am also especially grateful to my dissertation committee members for their belief in me and my research topic:

Dr. Sharon Desmond for her continued encouragement and who always offered suggestions to clarify and strengthen my writing;

Dr. Tong Tong Wu for her extensive knowledge of theoretical and applied statistics; and

Dr. Woodie Kessel who was especially helpful in making suggestions from the viewpoint of a community pediatrician and policy leader.

Finally, I must give thanks to those who were my greatest source of strength and inspiration:

My father, **Alcus Davis**, who always saw the best in me and is my number one champion;

My son, **Andrew T. Moss, III**, for sharing his mother's time. As I have many times looked into your eyes and said, "I hope you are proud of me some day;"

Mary Moss and **Emma Curry** for taking such wonderful care of my son while I was attending classes and working on my dissertation;

My friends and family, who loved me unconditionally even though I was many times preoccupied; and

My deepest gratitude to my husband**, Andrew**, who "stood in the gap" so I could accomplish my dream.

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Chapter 1: Introduction

The appropriate amount of weight to gain during pregnancy has been a topic of interest and debate for over a century in the United States (National Research Council, 2007). Gestational weight gain – which includes the fetus and placenta, increases in maternal fat stores, plasma volume, and uterine and breast tissue – has traditionally been poorly understood (Taffel, 1980). In the early 1900s, common medical practice was to restrict gestational weight gain to 15-20 lb (6.8-9.1 kg) in the belief that excessive gain might predispose women to the development of toxemia and other obstetrical problems (Abrams, 2000). In 1966, *Williams' Obstetrics*, a prestigious American textbook, stated "it is essential to curtail the increment in gain to 25 lb (12.5 kg) at most or preferably 15 lb (6.8 kg). The experienced obstetrician is convinced of the complications, both major and minor, caused by excessive weight gain in pregnancy" (Abrams, 2000). Williams et al. acknowledge that restriction in weight gain may be difficult, in many cases, requiring careful discipline and dietary control. They contend, however, that a gain in weight of 20 lbs (9.1 kg) "is a highly desirable objective (Abrams, 2000)."

This weight restriction policy was challenged in the late 1960s, when experts began to recognize that the relatively high rates of infant mortality, disability, and mental retardation were linked to low birth weight (National Center for Health Statistics (NCHS), 1986). In 1970, the National Academy of Sciences Committee on Maternal Nutrition followed with the *Maternal Nutrition and the Course of Pregnancy* report concluding the usual practice of restricting maternal weight gain was harmful and increased the formal recommendation to 24 lbs (20-25-pound range) (IOM, 2007; IOM, 2009).

Over the past several decades, a large body of literature has attempted to determine the ideal gestational weight gain necessary for maximizing the likelihood of positive pregnancy outcomes. Many of those findings were summarized in the 1990 Institute of Medicine (IOM) report, *Nutrition During Pregnancy: Weight Gain and Nutrient Supplements*, which offered weight gain recommendations specific to a woman's pre-pregnancy Body Mass Index (BMI, a measure of body fat based on weight and height).

The recommendations are known as the "IOM Recommended Weight Gain Guidelines" and are based on the amount of weight a woman should gain in order to meet the physiologic needs of pregnancy (e.g., the products of conception, expansion of plasma volume, red cell mass, and maternal fat stores). The calculation of a target weight gain based on an individual woman's pre-pregnancy height and weight, as opposed to a universal recommendation, reflects the finding that optimal outcomes are achieved within a range of weight gains.

In the more than two decades since the guidelines were issued, there have been dramatic changes in the average weight of U.S. women of childbearing age, in particular, a substantial increase in the proportion of overweight and obese women (CDC, 2010a). As such, the time had come for the IOM to reexamine the 1990 guidelines and to determine whether revisions were needed to meet the needs of American women today (IOM, 2009). In 2009, the Committee to *Reexamine IOM Pregnancy Weight Guidelines* undertook this challenge and issued new gestational weight gain recommendations. The 2009 guidelines (Table 1) differ from the 1990 guidelines in two ways. First, they are based on the World Health Organization (WHO) cutoff points for BMI categories rather

than the Metropolitan Life Insurance table categories which classified fewer women as overweight and more women as obese. Second, they now include a specific range of recommended weight gain for obese women.

The guidelines are formulated as a range of weight gain for each category of pre-pregnancy BMI. Recommendations include weight gains of (a) 28 to 40 lbs for women who are underweight (< 18.5 BMI); 25 to 35 lbs for women of normal weight (18.5-24.9 BMI); 15 to 25 lbs for women who are overweight (25 to 29.9 BMI); and 11 to 20 lbs for women who are obese (≥ 30.0 BMI). A divergence from the 1990 IOM report, the recommended weight gain ranges for short women and members of racial or ethnic minority groups are the same as those for the entire population. Additionally, adolescents are advised to use the adult BMI categories until more research is conducted to determine whether special weight gain range categories are needed (IOM, 2009).

Table 1: 2009 Recommendations for Total and Rate of Weight Gain during Pregnancy, by Pre-pregnancy BMI

Pre-Pregnancy BMI	BMI+(kg/m2)	Total Weight Gain (lbs)	Rates of Weight Gain* 2nd and 3rd Trimester (lbs/week)
Underweight	<18.5	28-40	1 (1-1.3)
Normal weight	18.5-24.9	25-35	1 (0.8-1)
Overweight	25.0-29.9	15-25	0.6 (0.5-0.7)
Obese (includes all classes)	≥30	11-20	0.5 (0.4-0.6)

Source: Institute of Medicine and National Research Council. Weight Gain During Pregnancy: Reexamining the Guidelines.
* Calculations assume a 0.5–2 kg (1.1–4.4 lbs) weight gain in the first trimester

It is noteworthy that in spite of the amended guidelines and clear benefits to an infant, only 30–40% of US women gain in accordance with the IOM recommendations (Abrams et al., 2000; National Research Council & IOM, 2007). Also of note, since the release of the 1990 guidelines, low (<16 pound) gestational weight gain has become more common (Abrams et al., 2000; IOM, 2009).

Extant evidence suggests that inadequate gestational weight gain is a risk factor for low birth weight, intrauterine growth restriction, preterm birth, and perinatal mortality (Langford et al., 2007; DeVader et al., 2007; Frederick et al., 2007). At the same time, excessive gestational weight gain, aside from contributing to postpartum weight retention and risks of future obesity, may also contribute to poor pregnancy outcomes. It is associated with increased risk of cesarean section delivery, hemorrhages, hypertensive syndromes in pregnancy, and fetal macrosomia (Langford et al., 2007; DeVader et al., 2007; Frederick et al., 2007; Kiel et al., 2007).

Although inadequate gestational weight gain has been linked to leading causes of infant mortality, such as preterm birth and fetal growth restriction, there is reason to believe that inadequate gestational weight gain may be associated with infant mortality independent of these factors. The potential mediating factors and biological mechanisms are still speculative, but an elevated risk of infant mortality may, indeed be part of a continuum emanating from stillbirth and perinatal mortality (Chen et al., 2009).

Stillbirth is a fetal death that occurs during pregnancy at 20 weeks or greater gestation. Approximately 25,000 stillbirths are reported every year representing roughly 60% of all perinatal mortality in the United States (ACOG, 2009). In two studies that were conducted when the formal gestational weight gain recommendation was 24 lbs (20-

25-pound range), Naeye (1979) and NCHS (1986) found that women with low pre-pregnancy BMI and low gestational weight gain tended to have elevated risks of fetal and perinatal mortality (a combination of stillbirth and neonatal mortality). Women with elevated pre-pregnancy BMI and excessive gestational weight gain had elevated risks of the same outcomes.

Perinatal mortality refers to the death of a fetus or death of an infant during the first week of life. Two U.S. studies have investigated the association between maternal weight gain and perinatal mortality, defining it as neonatal (i.e. infants aged less than 28 days) and fetal deaths (Kirchengast and Hartmann, 2003; Shapiro et al., 2000). Both studies used categorical measures of optimal and low weight gain and found a protective effect of optimal gestational weight on perinatal death. Women with low gestational weight gain had elevated risks of infant death.

Few studies have directly addressed the link between gestational weight gain and infant mortality (defined as death before the first year of life). There is also a lack of research into the causes of infant death associated with gestational weight gain. Moreover, many studies have not taken into account clinical and psychosocial factors during pregnancy that may modify the risk associated with gestational weight gain. Addressing these questions fills an important gap in the literature.

The present study was informed by two paradigms that offered useful conceptual frameworks for considering the association between gestational weight gain and infant mortality. The first—the "biomedical model" — focused primarily on the prenatal and neonatal periods, because they are the periods of fetal growth, development, and clinical care (Cwikel, 2006; IOM, 2009; Gillman, 2005). The second paradigm—the

"biopsychosocial model"— focused on the mother, her body, and her surrounding environment as essential components of the total system recognizing that psychosocial factors (e.g. thoughts, behaviors, family, stress) may operate to facilitate, sustain, or modify the course of illness and disease (Engel, 1977).

Five relationships between gestational weight gain and infant mortality were considered in this study: 1) the association between inadequate gestational weight gain and infant mortality that is independent of preterm birth and low birth weight; 2) whether or not the association between inadequate gestational weight gain and infant mortality is partially mediated by low birth weight or birth weight for gestational age; 3) the degree to which prenatal care influences gestational weight gain; 4) whether there is an association between maternal stress and inadequate gestational weight gain; and 5) the effect of various pre-pregnancy BMI categories and corresponding gestational weight gain on infant mortality.

To explore these relationships, data from Phase 5 of the Pregnancy Risk Assessment Monitoring System (PRAMS) and the 2005 Birth Cohort Linked Birth-Infant Death Data File (Cohort Linked File) were examined. A sample of 160,111 women who participated in PRAMS between 2004-2008 were used to analyze the association between gestational weight gain, adjusted for pre-pregnant BMI and infant death, as well as the influence of maternal stress on gestational weight gain. An analysis of 2,046,725 infants in the 2005 cohort linked birth-death file was conducted to examine the link between gestational weight gain and the risk of infant death, focusing on cause-specific mortality. Both samples were used to examine the association between prenatal care and inadequate gestational weight gain.

Descriptive, logistic regression, and Cox proportional hazards regression analyses were used to assess the odds of infant mortality associated with inadequate gestational weight gain compared to normal weight gain, as well as the extent to which low birth weight and preterm birth mediated these associations after controlling for biomedical and psychosocial factors. Implications for research, policy, and programs were also determined.

Chapter 2: Theoretical Framework

The conceptual frameworks guiding the generation of hypotheses and selection of variables included in this study are the Biomedical and Biopsychosocial Models. The key tenets of the models are described followed by examples of their applicability to the phenomenon of gestational weight gain and infant mortality. The role biological, demographic, and behavioral factors may play in mediating or moderating that relationship are also explained.

Biomedical Model

The Biomedical approach is based on a long tradition of physician-dominated medicine and assumes that lack of health is primarily due to disease (Cwikel, 2006). The model posits most diseases are caused by a biologic pathogen or imbalance in basic physiologic function and that diseases can be cured if imbalances are restored to their normal state (Engel, 1977). Disease is seen fundamentally as an alteration in body biochemistry in a predictable pattern. The task of the physician is to administer a series of diagnostic tests, identify the abnormalities associated with the disease, and employ methods for restoring individuals to a unitary standard (Jekel, 1998).

The Biomedical model can support analytic research aimed at identifying risks for specific health outcomes because inherent in the model are accepted scientific procedures for identifying deviations in physiologic functions. A biomedical explanation for the association between inadequate gestational weight gain and the risk of infant death is poor nutrition; fetal and infant growth are critically dependent on proper nutrients. Maternal nutrition plays an important role in the physiology of a fetus and the supply of nutrients can influence cell number and differentiation in the blastocyst (pre-

implantational embryo that consists of two cell types: the inner cell mass that becomes the fetus and outer cell mass that will form the placenta). Maternal nutritional restriction may lead to fewer cells in the inner cell mass. This, in turn, is associated with lower birth weight, which is related to elevated risk of infant mortality (Martin and Ozanne, 2006). The Biomedical model is best suited for research on the single source of any given disease. It calls attention to health risk factors (i.e. diabetes, hypertension) addressed at the individual level that contribute to poor birth outcomes and need to be controlled (Krieger, 1994).

Biopsychosocial Model

The Biopsychosocial model provides a broader framework within which to explore the multi-dimensional determinants of gestational weight gain. The approach recognizes the hierarchical structure of the natural biological system, but also takes into account the environmental, psychological, sociological, and other cultural factors that contribute to disease (Engel, 1980). An accumulating body of literature points to several hypotheses about how demographic factors are associated with gestational weight gain. One hypothesis is lack of knowledge about appropriate weight gain, which may be indicated by young age or low education. Chu et al. (2009) found that women with less than 12 years of education were more likely to gain less than 15 lbs compared to women with more than 12 years of education when analyzing 2004-2005 PRAMS data. In a finding that is not consistent with low education, researchers have reported that gestational weight gain is generally higher among adolescents and lower among women 35 years of age or older (IOM, 2009).

Another potential influence is access to quality, healthy foods, which could be a function of income level and number of children. Utilizing data from the 1980 National Natality Survey, Hickey (2000) and Taffel (1980) indicated that the risk of gaining < 16 lbs (7.3 kg) increased nearly 2-fold as annual household income fell (9% of women with incomes of $30,000 experienced low weight gain compared to 15.9% of women with household incomes < $9,000). However, in a study of 622 women who registered for prenatal care in a health care system serving a 10-county area of upstate New York, Olson and Strawderman (2003) reported that women with family incomes < 185% of the U.S. federal poverty line were 2.6 times more likely to have excessive weight gains than women with higher incomes. This contradictory finding may reflect reduced access to nutritious foods among mothers residing in low-income communities. Lack of supermarkets, fresh produce, and food affordability can lead to inadequate food supply, poor nutrition, overeating, and weight gain (Drewnowski, 2004).

In addition, it has long been known that primiparous women (first-time mothers) have smaller infants than multiparous women (had previous live births or stillbirths) and that they gain more weight during pregnancy. An analysis of 92,274 women participating in the Danish National Birth Cohort study between 1996-2002, Nohr et al. (2009) found the mean gestational weight gain was higher in primiparae women than in multiparae women (15.7 kg vs. 14.6 kg).

Moreover, marital status may offer protection against poor gestational weight gain through social support and resources. Husbands may feel a sense of solidarity with the pregnant woman and a responsibility for the well-being of the

pregnancy (Jones et al, 2010). Married women are more likely to have appropriate gestational weight gain than unmarried women. Using national data from 1992, Kleinman et al. (1991) and Ventura (1994) found unmarried mothers are more likely than married mothers to gain < 16 lbs (7.3 kg) during pregnancy (13% compared with 8%).

Finally, the mother's race and ethnicity may also need to be considered, because of the differences in body build, socioeconomic status, acculturation, access to care, and lifestyle choices (such as tobacco and alcohol use) that underlie well-known racial and ethnic differences in reproductive outcomes (Luke, 2005). In a review of birth records of 913,320 singleton births in New York City from 1995 to 2003, Stein and Savitz, found that Asian and Black women were more likely to gain 0 to 19.8 lbs (0- 9 kg) during pregnancy, whereas Hispanic and White women were more likely to gain 44 lbs (20kg) during pregnancy (information contributed to the 2009 IOM report). Studies of the influence of societal/institutional, environmental, and neighborhood determinants of gestational weigh gain among women of different racial and ethnic groups are lacking. More research on how gestational weight gain affects birth outcomes among women of different racial/ethnic groups is needed.

Psychosocial factors have been hypothesized to affect gestational weight gain through a direct impact on physiological weight control mechanisms (e.g., stress may affect metabolic efficiency or neuroendocrine mediation of abdominal fat accrual) or an indirect influence on weight regulation through lifestyle practices (e.g., nutritional habits, frequency of tobacco and alcohol use, etc) (Kyrou et al, 2006; Hickey, 2000; Bjorntorp,

2001; Lamounier-Zepter, 2006). In a study of 806 women in Alabama, Hickey and colleagues (1995) reported an increased risk of low weight gain in white women who had poor scores on psychosocial scales measuring trait anxiety, depression, mastery, and self-esteem. More recently Lu and Lu (2007) examined the link between maternal nutrition and infant mortality. Lifelong conditions of high stress, they argued, create physiological, psychological, and behavioral responses that place the mother at nutritional risk during pregnancy (Lu & Lu, 2007).

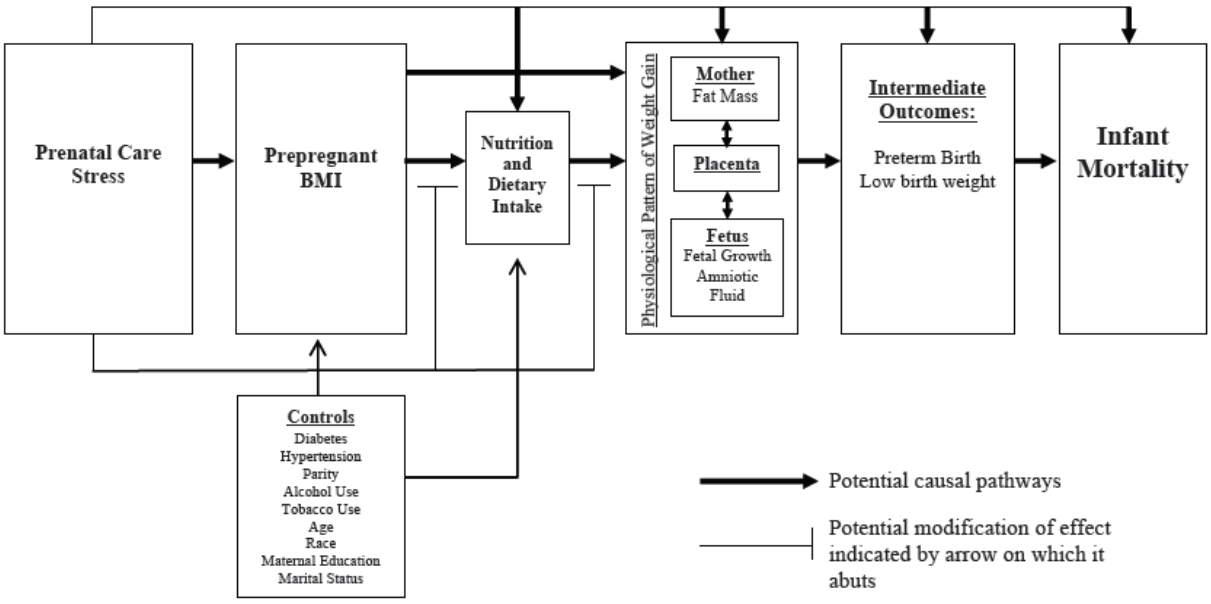
For example, in a study of 606 women who participated in the Pregnancy, Infection, and Nutrition prospective cohort study between 2000 and 2004, Laraia et al.(2006) found women who perceived more stress in their lives, or who had poorer scores on psychological state evaluations (trait anxiety, depression symptoms, chance locus of control, powerful others locus of control), were less likely to eat nutrient-dense foods compared to women who had higher scores on personal disposition indices, such as self-esteem and mastery. Moreover, stress precipitates binge eating, and women under acute stress increase "comfort food" intake (Lu & Lu, 2007). Foods high in fat and sugar concentrations reduce the negative effects of chronic stressors in the brain by stimulating the anterior, more pleasure-associated section and inhibiting the posterior, more defensive section (Epel et al., 2001). This shift in caloric intake, together with elevated glucocorticoids and insulin, reorganize energy stores in the body to a more central distribution (primarily as abdominal fat) and can predispose a woman to central obesity (Dallman et al., 2005). Chronic, uncontrollable stress may, therefore, be partly responsible for poor maternal nutrition.

In the face of persistent non-adherence to the IOM guidelines along with the wide variability in the amount of weight gained during pregnancy, more researchers have acknowledged that the determinants of the adequacy of gestational weight gain are multi-factorial in nature (Webb et al., 2009). The biopsychosocial approach can guide the development of testable hypotheses about correlates of improper gestational weight gain and poorer infant outcomes.

Chapter 3: Literature Review

This chapter, which includes five sections, reviews the existing literature on the association between gestational weight gain and infant mortality (see Figure 1). The first section highlights key demographic and health trends among women of childbearing age and the second describes the physiological pattern of weight gain. Section three summarizes the nutritional status of U.S. childbearing women and the use of pre-pregnancy BMI and gestational weight gain as indicators of maternal nutrition. Section four describes trends in infant mortality and other intermediate outcomes of poor maternal nutrition. Section five reviews other factors that may influence gestational weight gain and infant mortality. The final section presents the gaps in research and summarizes the research hypotheses that were investigated in this study.

Figure 1: Schematic Summary of the Association Between Gestational Weight Gain and Infant Mortality



Source: Adapted from IOM, 1990

Epidemiology and Trends among Women of Childbearing Age

Over the years since the release of the 1990 weight gain recommendations, significant shifts in the demographic and epidemiologic profile of the U.S. population have occurred (IOM, 2009). The educational levels of the population have continued to increase, with a greater proportion of women graduating from college than in 1990 (U.S. Department of Commerce, 1993). However, the United States now includes a higher proportion of childbearing-age women from diverse ethnic and racial subgroups, who are more socioeconomically disadvantaged (U.S. Department of Commerce, 1993). Between 1990 and 2007, there has been a steady increase in the proportion of infants born to non-white mothers, with the largest increase in births among Hispanics (NCHS, 2010a).

The prevalence of overweight and obesity has also increased among American women of childbearing age. According to the 2007-2008 National Health and Nutrition Examination Survey (NHANES), 62% of U.S. women 20 years of age and older are overweight and 35% are obese compared to 51% and 25 %, respectively, in 1988-1994 (NCHS, 2011). Thus, a greater proportion of women will begin pregnancy either overweight or obese. Although these trends are evident in all demographic subgroups, overweight is more common among less educated women and among black U.S. women (Kuczmarski et al., 1994); these groups are more likely to have poorer birth outcomes.

Additionally, more American women are entering pregnancy at an older age as well as bearing children unmarried. Although older women are more mature and knowledgeable, advanced maternal age (i.e. $\geq$ 35 years old) places women at higher risk

for a variety of chronic health conditions (e.g. diabetes and hypertension) and may lead to increased morbidity during post-pregnancy years (IOM, 2009). Childbearing by unmarried women has reached a record high. The birth rate for unmarried women has increased more than 15% from 43.7 per 1,000 in 2002 to 50.6 in 2009 (NCHS, 2010b). Today, fully one-third of births are to unmarried women. Such women are more likely than their married counterparts to be poorly educated, be in less favorable health, and have limited social and financial resources (Ventura, 2009; McLanahan, 1995).

In spite of the trends described above, the U.S. has experienced an impressive reduction in infant mortality over the past several decades. With the exception of 2002 and 2005, the infant mortality rate - the rate at which babies less than one year of age die - has steadily declined from 9.2 per 1,000 live births in 1990 to 6.6 per 1,000 live births in 2008 (MacDorman et al., 2008; Kochanek & Martin, 2006). Trends are similar for early, late, and post-neonatal mortality. Perinatal mortality has continued to decrease steadily since 1990 (Martin et al., 2008).

Despite decades of research and prevention efforts, low birth weight (LBW) remains a major public health challenge. Rates of low birth weight (<2,500g) and very low birth weight (VLBW, <1,500g) have increased since 1990, with the rate of low birth weight reported as 8% and the rate of very low birth weight as 1.5% in 2008 (the most recent year for which data are available) compared with 7% and 1.3%, respectively in 1990 (NCHS, 2010a).

Part of the explanation for the increase in babies born low birth weight is the increase in preterm births (delivery before 37 weeks gestation). In 2008, 12.3% of all births were delivered preterm. The preterm birth rate has increased 20% since 1990 and

6% since 2000 (NCHS, 2010a). The greatest increase has been among late preterm births (those occurring at 34-36 weeks gestation), which have climbed 20% since 1990. A 56% increase in the rates of cesarean deliveries [up to 32.3 from the most recent low of 20.7 in 1996 (Martin et al, 2010)] and induced births contributes to, but does not completely explain this trend in late preterm births (March of Dimes, 2011).

Finally, despite the wide clinical adoption of the IOM weight gain guidelines, evidence suggests women are not adhering to the recommendations. Excess gestational weight gain has increased across all population groups, particularly among minority and ethnic populations (Yeh and Shelton, 2005; Kim et al., 2007). Additionally, according to data from the 2009 Centers for Disease Control and Prevention (CDC) Pregnancy Nutrition Surveillance System (2010), approximately one of every five (21.2%) low-income pregnant women in the U.S. experienced less than ideal weight gain during pregnancy (CDC, 2010a). There were also significant racial-ethnic disparities in women who gained less than ideal weight, with about 22% of White and nearly 32% of Asian and Pacific Islander women gaining an inadequate amount of weight during pregnancy.

Physiological Pattern of Gestational Weight Gain

The pregnant woman undergoes biological changes in anticipation and in support of fetal growth. Many of the alterations in maternal physiology that must occur in order for a fetus and placenta to develop are directly related to changes in the components of gestational weight gain (IOM, 2009).

As pregnancy progresses, water, protein, minerals, and fat are deposited into the fetus, placenta, amniotic fluid, mammary gland, blood and adipose tissue. The products

of conception (placenta, fetus, amniotic fluid) comprise approximately 35% of a woman's total gestational weight gain (IOM, 2009).

Total body water (TBW) accretion is largely under hormonal control and is highly variable during pregnancy. TBW accretion averages about 7-8 liters in healthy pregnancies (Hytten and Chamberlain, 1991).

Perhaps the most striking maternal physiologic alteration occurring during pregnancy is the increase in blood volume. The magnitude of the increases varies according to the pre-pregnancy weight of a woman, the number of pregnancies she has had, the number of infants she has delivered, and whether there are multiple fetuses. Blood volume increases progressively by as much as 45-50% until 30-34 weeks of gestation to provide for the greater oxygen and nutritional transport needs of the maternal organs (DeCherney & Pernoll, 1996). Increases in maternal plasma volume account for a significant portion of the increase in total body water during pregnancy (IOM, 2009)

During normal pregnancy, approximately 1000g of weight gain is attributable to protein. Half of this is found in the fetus (42%) and the placenta (10%), with the rest distributed in the uterus (17%), breast tissue (8%), plasma, and hemoglobin (14%) (DeCherney & Pernoll, 1996; Hytten and Chamberlain, 1991).

Changes in carbohydrate and lipid metabolism also occur to ensure a continuous supply of nutrients to the growing fetus (Butte, 2000). In early pregnancy, glucose tolerance is normal and over the course of 40 weeks decreases 40-60% to increase the availability of energy (Catalano et al., 1991). Increased energy supports fetal growth, which in turn influences gestational weight gain.

In sum, besides the intra- and extravascular fluids, feto-placental unit, uterus, and mammary tissue, most of the weight gain that occurs over the course of a pregnancy lies in changes in maternal fat mass. The amount of fat gained is more strongly associated with total weight gain than any other component (Butte et al., 2000).

Maternal Nutrition and Gestational Weight Gain

Gestational weight gain is affected by the quantity and quality of maternal diet. Every cell, organ, and system inside a newborn baby originates mostly from its mother's food intake before or during pregnancy. Available data suggest that pregnant women in the U.S. consume more protein, fat and trans-fat, and carbohydrates than recommended, and a substantial proportion of pregnant women do not meet the recommended daily allowances (RDA) for iodine, calcium, magnesium, iron, zinc, vitamins A, B1, B2, B3, B6, B12, and vitamin C from food sources (Lu and Lu, 2007). Dietary intake of folate is inadequate for over 95% of women, and that of vitamin E is inadequate for 25% of pregnant women, which perhaps reflects low intake of fruits and vegetables. When multivitamins are accounted for, one in four women still do not consume adequate amounts of folate and vitamin E (Joint Center for Political and Economic Studies, 2007).

When women consume diets of sufficient caloric and micronutrient value (vitamins and minerals) they positively influence weight gain as well as ensure a continuous supply of nutrients to the growing fetus (Butte, 2000). Low gestational weight gain may, therefore, be associated with greater risks to the fetus and risks of low birth weight, preterm birth, and infant mortality.

Determination of the quality and quantity of the maternal diet is limited by the availability of valid measurement tools. The NHANES is the only national health survey with information on nutrition intake; however, because it is cross-sectional it cannot inform the role of pre-pregnancy or within pregnancy nutrition in birth outcomes. As a consequence, most studies of birth outcomes rely on pre-pregnancy Body Mass Index or maternal weight gain during pregnancy as a proxy for maternal nutrition (Newton, 2007).

Pre-pregnancy Body Mass Index (BMI) and Gestational Weight Gain

Body Mass Index (BMI) is defined as weight in kilograms divided by height in meters squared (kg/m2). It was developed because in the general population, it is correlated with body fat and provides a reliable indicator of whether a person is overweight or obese. Both pre-pregnancy BMI and pregnancy weight gains outside of the normal IOM ranges have been associated with increased risks for poor pregnancy outcomes (Kramer et al, 2000). Inadequate gestational weight gain among women who begin pregnancy underweight or obese is associated with increased risk for fetal death, preterm labor, preterm birth, low birth weight infants, and small-for-gestational-age (SGA) infants (Ehrenberg et al., 2003; Dietz et al., 2006; Villamor et al, 2004; Dietz et al, 2009b). Excessive gestational weight gain among women with an underweight or obese pre-pregnant BMI is associated with increased risk for gestational diabetes, cesarean delivery, preterm birth, large-for-gestational-age (LGA) infant, and postpartum weight retention (Tovar et al., 2009; Stotland et al., 2004; Dietz et al, 2006; Nohr et al., 2007; Dietz et al., 2009a; Oken et al., 2009).

Gestational weight gain is generally inversely proportional to maternal BMI. Chu et al. (2009) examined 2004-2005 PRAMS data to assess the amount of gestational

weight gain among 52,988 underweight, normal weight, overweight, and obese U.S. women. Overall, the investigators found that gestational weight gain decreased with increasing BMI. They also found that obese women gained less weight than normal or overweight women; yet about one-fourth still gained 35 lbs or more. A woman's weight at the start of pregnancy is known to have a strong bearing on how much weight is gained during pregnancy (Winikoff, 1981).

Maternal Nutrition and Infant Morbidity and Mortality

Maternal nutrition is a critical determinant of infant health, thus it is not hard to conceive that poor maternal nutrition can contribute, directly or indirectly, to infant mortality. There is strong evidence linking poor maternal nutrition to several leading causes of infant mortality, including fetal growth restriction, preterm birth, and birth defects (Lu & Lu, 2007).

Low pre-pregnancy BMI, commonly used as an indicator of poor maternal nutritional status before pregnancy, is associated with greater risk for fetal growth restriction, a condition in which a fetus is unable to achieve its genetically determined size (Kramer, 2003; Ross, 2010; Carmichael & Abrams, 1997; Rush, 2001). Kramer et al. (2000) estimated that low pre-pregnancy BMI and low gestational weight gain can account for up to 25% of cases of fetal growth restriction in developed countries.

Although the mechanism it is not clear, nutrition-related factors may mediate several of the major pathways leading to spontaneous preterm birth. Prolonged periods without food intake during pregnancy (i.e. fasting) have been associated with a greater risk for preterm birth. In an analysis of 2,065 women participating in the Pregnancy, Infection, and Nutrition Study from 1995 to 1998,

Women who ate fewer than 3 meals and 2 snacks per day had a 30% higher risk for delivering preterm when compared with pregnant women who met this level (Siega et al., 2000). In the same cohort, pregnant women who reported not eating for ≥13 hours per day had a 3-fold greater risk of delivering preterm at ≤34 weeks' gestation when compared with women who reported <13 hours without food per day. Evidence suggests that this association may be mediated via increased placental corticotropin-releasing hormone (CRH) gene expression and premature fetal hypothalamic-pituitary adrenal (HPA) activation (Hermann et al., 2001). This neuroendocrine pathway may stimulate placental-fetal signaling during late gestation and hasten delivery of an infant from an adverse environment (Hermann et al., 2001).

Birth defects account for approximately 20% of infant deaths (Martin et al., 2008). In a population-based case-control study within a cohort of 708,129 live births and fetal deaths occurring in California from 1989 to 1991, infants born to mothers who gained less than 22 lbs (<10 kg) during pregnancy were at elevated risk of neural tube defects compared to women who gained ≥10 kg (Shaw et al., 2001). Among this population, dieting to lose weight during the first trimester of pregnancy was also associated with an elevated risk (OR=2.1, CI: 1.1-4.1) of neural tube defects (Carmichael et al., 2003). The two most common neural tube defects are spina bifida and anencephaly. In spina bifida, the fetal spinal column does not close completely during the first month of pregnancy and nerve damage causes mild to severe disability. In anencephaly, much of the brain does not develop and infants are either stillborn or die shortly after birth (ACOG, 2004).

The effectiveness of macro- or micronutrient supplementation for preventing fetal growth restriction, preterm birth, and birth defects has been demonstrated with folic acid supplementation before and during pregnancy to prevent neural tube defects, fish oil for prevention of recurrent preterm birth, and balanced protein-energy supplementation for prevention of fetal growth restriction (Lu & Lu, 2007). Given the fact that nutritional supplementation during pregnancy may reduce the risk of some birth defects and adverse birth outcomes, the notion that inadequate nutrition during pregnancy could have an influence on the life prospects of an infant is not difficult to bear in the mind.

The "Dutch Hunger Winter" offers clues to understanding the contribution of maternal nutrition to infant survival. Occurring in mid-September of 1944, the exiled Dutch government in London called for a national railway strike to hamper German troop's movement of food and the population was reduced to 500 calories a day. The effect on mortality was immediate for all ages, but there were forty thousand fetuses in utero during the siege (Hart, 1993). Some of the effects of the malnutrition during pregnancy were immediately apparent in higher rates of stillbirths, birth defects, and infant mortality and others are still being discovered (Paul, 2010). Maternal malnutrition in the last trimester of pregnancy has been found to diminish infant viability and predispose survivors to later episodes of morbidity, with fatal consequences (Hart, 1993). Over a series of studies, David Barker and others have demonstrated poor maternal nutrition predisposes individuals to coronary heart disease and Type II diabetes later in life (Osmond & Barker 2000; Phillips, 2006; Godfrey & Barker, 2000).

While the research clearly documents the effects of intrauterine deprivation on subsequent adult health, the studies also have provided fundamental insights for the growing field of the developmental origins of health and disease (Schulz, 2010). The emerging science hypothesizes the fetus is influenced by what the pregnant women consumes and the maternal diet can modify the fetus' epigenome in ways that affect its future health and well-being (Paul, 2010).

The Barker Hypothesis is also known as Fetal Programming Hypothesis. The word "programming" illustrates the idea that during critical periods in fetal development, there are changes in the body function and structure as a result of environmental stimuli (Byrne & Phillips, 2000). These changes relate to the concept of developmental plasticity, which is the ability of genes to express different physiological or morphological states in response to adverse environmental conditions during development (Barker, 2004). Developmental plasticity enables the production of phenotypes that are better matched to their environment than would be otherwise possible.

For example, a fetus' main adaptation to a lack of nutrients is to slow its rate of cell division; particularly in tissues undergoing critical periods, or those not essential for survival such as the heart and the liver (Barker, 1997). The decrease in cell numbers is sometimes referred to as functional reduction and is one of the mechanisms by which undernutrition may permanently change or program the body (Lucas, 1991). Some programming events may have immediate effects (i.e. an organ is altered at a critical

stage and an infant subsequently fails to thrive); other programming effects may be deferred (Desai & Hales, 1997).

Maternal undernutrition can change the programming and development of the human kidney. According to Widdowson and McCance (1975), malnourishment can result in decreased number of structural and functional units in the kidney (e.g. nephrons). In addition to that, there is an associated increase in the flow of filtered fluid through the kidney (e.g. glomerular filtration rate) and hydrostatic pressure (e.g. systolic force of the heart). Consequently, the infant is at elevated risk of developing glomerular sclerosis (e.g. or nephrotic syndrome) and progressive kidney failure (Lackland, 2005).

Another example regarding the kidney is the influence of the intrauterine events on the development of hypertension (Zandi-Nejad et al., 2006). The decreased number of nephrons can lead to elevated retention of sodium and water making the infant more prone to elevated blood pressure (Bagby, 2007).

Nutritional programming has been demonstrated convincingly in a range of mammals, such as rats, mice, sheep, pigs and primates (Desai & Hales, 1997). Numerous animal experiments have shown undernutrition in utero leads to persisting changes in blood pressure, cholesterol metabolism, insulin response to glucose, and a range of organs and tissues, including the pancreas, liver, and blood vessels (Barker, 1997).

Given the evidence for fetal programming in general and the evidence for nutritional programming in mammals, additional endpoints such as mortality among infants exposed to undernutrition during gestation might also be possible. Examining

this association is not only a matter of great importance, it also provides a more nuanced understanding of how maternal nutrition influences the health of infants.

Additional Predictor Variables

Prenatal Care

There is international consensus that prenatal care should begin as early as possible and include regular health care visits. In the United States, 96% of women who have a live birth receive prenatal care and on average, pregnant women are seen for 12 or 13 prenatal visits (Ventura et al, 1998). The frequency of prenatal visits offers the health care provider the opportunity to identify the medical conditions that may place a woman and her fetus at risk of adverse outcomes and implement a treatment strategy. The frequency of these visits also offers an opportunity for a woman and her provider to set a weight gain goal early in pregnancy and to monitor progress towards that goal regularly. In addition to being made aware of their weight gain as pregnancy progresses, the American College of Obstetricians and Gynecologists has recommended women be provided with advice about both diet and physical activity (ACOG, 2002). This may require referral to a dietitian and other appropriately qualified individuals, such as those who specialize in helping women increase physical activity (IOM, 2009).

To date, only a limited number of investigators have tested clinical interventions that help women gain within the IOM guidelines. In a systematic review of 10 trials, Kramer and Kakuma (2003) found that advice to increase energy and protein intake was successful in achieving the goals of increased energy and protein intake, but not in increasing gestational weight gain. Balanced energy and protein supplementation were

associated with modest increases (21 g/week) in gestational weight gain. High-protein supplements were not. In contrast, two trials reviewed in Kramer and Kakuma among women who were obese or had high gestational weight gain showed that energy and protein restriction was associated with a significant reduction in weekly weight gain. The weighted mean difference was 255 g per week.

Although the IOM recommendations have been in existence for over two decades, between 35-60% of pregnant women report receiving no advice from their providers about appropriate pregnancy weight gain (Brawarsky et al., 2005; Olson & Strawderman, 2003). Only two studies to date have evaluated the type of gestational weight gain advice being given and how it compares to the IOM recommendations. In a survey of 2,237 predominantly white, middle-class women, Cogswell et al. (1999) found, of the 1,643 women who recalled weight gain advice, 14% were advised to gain less than the recommended levels, 22% were advised to gain more than the recommended levels, and the advice provided correlated strongly with actual weight gains (both associations had an AOR of 3.6). Some 27% reported receiving no advice about gestational weight gain placing them at risk for both too high (AOR 2.0) and too low (AOR 1.8) gains. Black women were also more likely to report receiving advice to gain less than the recommended amount for their pre-pregnant BMI value.

In a recent longitudinal cohort study of pregnant women in the San Francisco Bay area, Stotland et al. (2005) found that 79% of the nearly 1,200 women reported a target gestational weight gain (i.e. how much weight women think thought should gain during pregnancy) that fell within the IOM guidelines. While, 33% of the women received no advice from health professionals regarding gestational weight gain, almost half (49%)

received advice within the guidelines. Taken as a whole, the findings suggest that the amount of weight gained during pregnancy may be influenced by healthcare providers. As such, prenatal care was included as potential factor that influences gestational weight gain.

Maternal Stress

Although, stress is increasingly becoming recognized as an important risk factor for two of the leading causes of infant mortality (preterm birth and low birth weight), evidence for the influence of stress on gestational weight gain is limited (Cooper et al. 1996). Stress may be simply defined as any challenge that threatens or is perceived to threaten homeostasis (e.g., the stability of the internal milieu of the organism) (Black & Garbutt, 2002). Stress can occur psychologically such as in a perceived inability to cope emotionally with a challenging event or physiologically as in the body's hormonal response to a biological threat or challenge.

Only a few studies have examined the relationship between psychosocial stress and gestational weight gain, with a majority having focused on determinants of inadequate weight gain. In investigations using the Perceived Stress Scale (Cohen et al., 1983), a widely used 10-item self report questionnaire that measures persons' evaluation of the stressfulness of the situations in the past month of their lives, some have found significant associations between self-reported stress and low maternal weight gain (Brawarsky, 2005; Orr, 1996); other studies during pregnancy have not (Hickey et al., 1995). Generally, there does not appear to be a robust association between appraisals of stress, sufficiency of coping resources, and

adequacy of gestational weight gain. However, when evaluating the observed risk ratio differences between women who gained inadequate or excessive weight relative to women who gained adequate weight, women who gained inadequate weight tended to perceive more stress than women who gained excessive weight (IOM, 2009).

Picone et al. (1982) examined the influence of psychological stress as a factor in gestational weight gain and pregnancy outcomes in a controlled prospective study of a group of 60 women utilizing an urban prenatal clinic. Psychological stress was assessed using a social readjustment rating scale from the Holmes-Rahe life events questionnaire. The investigators found a correlation between higher stress scores and lower gestational weight gain, independent of nutrient or caloric intake suggesting that stress may impact the utilization of calories and nutrients from the foods consumed to support pregnancy, rather than affecting food intake.

There is a dearth of research evaluating the influence of stress on gestational weight. Thus, stress was included in this study as an additional predictor variable. An examination of the current literature related to psychosocial determinants of pregnancy outcomes suggests two theoretical pathways that may explain the observation.

Maternal psychosocial stress may function to affect gestational weight gain through activation of the maternal Hypothalamic-Pituitary Adrenal (HPA) axis ("fight or flight" response). HPA activation is the biological production of cortisol, norepinephrine, and several other adrenalines in response to a threat or stressful

situation. When the threat or challenge recedes, the stress system ceases and the body returns to its normal state. During periods of repeated stress, however, the body is subjected to exaggerated production (Sapolsky, 1995). Hyperactivity of the HPA axis has been hypothesized to play a role in the development of abdominal obesity and insulin resistance (Bjorntorp, 2001). Women with high levels of stress may, therefore, be at greater risk for excessive gestational weight gain.

Alternatively, and perhaps concurrently with HPA hyperactivity, poor psychosocial status may interfere with the achievement of the positive energy balance required for gains in fetal and maternal fat tissue. Positive energy balance is when the amount of calories ingested is greater than the amount of calories expended during metabolism which in turn increases body weight. Stress can cause changes in sleep patterns, physical activity, tobacco use, and other health behaviors which can influence calorie intake and metabolism (Hickey, 2000).

Mediators

Fetal Growth

It is widely recognized that an infant's size at delivery is a major determinant of its potential for survival (Taffel, 1980). Smaller size at birth is associated with elevated risks of fetal and infant mortality, cerebral palsy, birth asphyxia, and persistent deficits in neurocognitive performance (Pryor et al., 1995). Because an infant's size is a function of both duration of gestation and rate of fetal growth, clinicians often use Small for Gestational Age (SGA) and Large for Gestational Age (LGA) to classify fetal growth instead of birth weight. SGA and LGA are indicators that compare an infant's weight to

the distribution of other infants born in the same week of gestation. The most common definition of the indicators, refer to birth weights below the 10th percentile and above the 90th percentile for gestational age, respectively (IOM, 2009).

The two tails of the birth-weight-by-gestational-age distribution are referred to as Intrauterine Growth Restriction (IUGR) and macrosomia (IOM, 2009). IUGR is generally applied to infants with lower weights and patterns of fetal growth that deviate from the expected norm; and macrosomia is defined as birth weight > 90% for gestational age or > 4,000 g (8.8 lbs.).

Observational studies have consistently linked inadequate gestational weight gain with increased risk for SGA in underweight and normal weight women and excessive gestational weight gain with LGA among overweight and obese women. The Agency for Healthcare Research and Quality (AHRQ) evidence-based review of outcomes related to gestational weight gain identified 15 studies of SGA that demonstrated relative risks of SGA with low gestational weight gain on the order of 2-3 (Viswanathan et al., 2008). Thirteen studies examined the relationship of gestational weight gain to risk of low birth weight (LBW, defined as < 2,500 g). As noted in the 1990 IOM report and by others, the risk of LBW diminishes as gestational weight gain increases, particularly as total gain exceeds 25-30 lbs (IOM, 2009).

At the other end of the birth weight spectrum, 12 studies considered infant macrosomia. Relative risks were 2-3 for macrosomia in the highest compared to the lowest gestational weight gain category. Infants born LGA are at elevated risk of cesarean delivery, shoulder dystocia, other forms of birth injury, and poor breastfeeding.

Among the most important long-term outcomes is obesity and its sequelae, chiefly cardio-metabolic consequences (IOM, 2009).

Aside from pre-pregnancy BMI, the only other factor that appears to impact the association between gestational weight gain and fetal growth is time during pregnancy that weight gain occurs. There is modest support for a stronger effect of gestational weight gain that occurs during the first or second trimester than during the third trimester (Viswanathan et al., 2008).

Finally, according to the IOM, the question of whether the association between gestational weight gain and fetal growth is causal cannot be answered with certainty based on the available research. Observational data provide indications of a strong association between lower gestational weight gain and increased risk of SGA, especially in underweight and normal weight women, and between higher gestational weight gain and increased risk of LGA, particularly among overweight and obese women (IOM, 2009).There are several possible explanations for these associations: 1) gestational weight gain is causally related to fetal growth, 2) both gestational weight gain and fetal growth are independently affected by maternal diet and/or physical activity, or 3) both gestational weight gain and fetal growth have shared genetic or other intrinsic biological determinants (IOM, 2009). The available randomized trials are either from less-relevant populations and time periods; involved only a particular form of supplement (e.g., protein); or are too small to provide strong evidence of causality (IOM, 2009). Given the demonstrable and substantial associations of poor fetal growth with both inadequate gestational weight gain and infant mortality, birth weight, preterm birth, and weight for gestational age were included in this study as potential mediators to determine if fetal

growth is a mechanism that underlies the relationship between inadequate gestational weight gain and infant mortality.

Preterm Birth

Preterm delivery (before 37 weeks completed gestation) is a major contributor to infant morbidity and mortality in the United States (Dietz et al., 2006). Morbidity risks associated with preterm birth include acute respiratory, central nervous system, and gastrointestinal disorders; long-term deficits in neurobehavioral development; and adverse cardiometabolic outcomes (IOM, 2009). Regardless of whether it is caused by natural processes or induced by clinical intervention, the 12.3% frequency of preterm births in the United States make prematurity a critical endpoint to consider in relation to gestational weight gain (IOM, 2009). There is strong evidence of an increased risk of preterm birth among women in both the inadequate and excessive gestational weight gain categories. In a review of 12 published studies, the Agency for Healthcare Research and Quality found relative risks of preterm birth of 1.5-2.5 for both higher and lower gestational weight gain compared to the middle range, and greater consistency for the influence of lower pregnancy weight gain on preterm delivery among underweight women (Viswanathan et al., 2008). Effect modification by pre-pregnancy BMI was examined in five of these studies. The authors of these studies consistently reported a stronger effect of a lower rate of gestational weight gain on preterm delivery among underweight women. As pre-pregnancy BMI increased, the magnitude of increased risk associated with a lower rate of gestational weight gain diminished.

Control Variables

Other factors may influence gestational weight gain and infant mortality. The following identifies maternal age, maternal race, maternal education, marital status, tobacco use, alcohol consumption, diabetes, hypertension, and parity as important determinants of gestational weight gain and infant mortality.

Maternal Age

A large body of literature exists describing the impact of maternal age on pregnancy outcomes. Young women are generally healthy and have lower risks of poor outcomes although adolescents who conceive soon after menarche may still be growing and competing for nutrients with their developing fetus (Scholl et al, 1994). Older maternal age has been associated with elevated risks of preterm delivery, low birth weight, SGA births, and neonatal mortality (Cleary-Goldman et al., 2005; Chen et al., 2007). Women who become pregnant at an older age may also be entering pregnancy with chronic conditions (e.g. hypertension, diabetes, etc.) leading to increased risks of pregnancy complications. (Cleary-Goldman et al., 2005). Younger women apparently also have higher gestational weight gain. In a retrospective review of data from the CDC 2000 natality file, Howie and colleagues (2003) reported an increased likelihood of excessive gestational weight gain among adolescents $\leq$ 19 years compared to women 19 years and older. Other authors have also corroborated that adolescents have higher gestational weight gain compared to mothers older than adolescence (Hediger et al., 1990; Scholl et al., 1990; Stevens-Simon et al., 1993a); and insufficient weight gain is higher among women 30 years and older (Siega-Riz and Hobel, 1997).

Maternal Race

There are longstanding disparities in birth outcomes between women of different racial and ethnic populations in the United States. African American women, for example have rates of infant mortality at least two times those for white women, and the gap has been increasing over time (Kochanek et al, 2011). Arline Geronimus (1992) has proposed a "weathering hypothesis" to help explain this pattern. The weathering hypothesis posits that the health of African American women begins to deteriorate in early adulthood as a physical consequence of racism, stress, and cumulative socioeconomic disadvantage. Racial and ethnic differentials in infant mortality are larger at older maternal ages than at younger ages as a result.

There are very few studies that have examined racial and ethnic differences in gestational weight gain. In a study of 3,870 women delivering at a university hospital, Caulfield et al. (1996) found only 28.2% and 32.5% of black and white women, respectively, gained within the IOM recommended ranges. Studies have also found racial and ethnic differences in weight gain outside of the IOM ranges. Chu et al. (2009) assessed gestational weight gain among 52,988 women participating in the 2004-2005 Pregnancy Risk Assessment Monitoring System and found black women were more likely than white women to gain <15 lbs, but less likely than white women to gain >34 lbs. Further, several studies have found Asian women have lower gestational weight gain as well as lower pre-pregnancy weight, on average (Abrams et al., 1989). The 2009 Pregnancy Nutrition Surveillance found nearly 27% of Asian and Pacific Islander women achieved less than ideal weight gain according to the IOM recommendations.

The limited data on the influence of maternal race on weight gain is suggestive of inadequate gestational weight gain among some racial and ethnic groups. However, the paucity of data on a national level and the lack of observational studies based on pre-pregnancy BMI preclude drawing any significant conclusions (IOM, 2009).

Maternal Education

Maternal education is widely held to be a key determinant of fertility and reproductive health. Education may improve a woman's knowledge of healthy pregnancy behaviors; for example, education may increase a woman's knowledge about appropriate weight gain and how to achieve it. Two studies of educational status suggest that lower education is associated with increased risk of insufficient gestational weight gain. In a study of 19,017 Black and White women participating in the Special Supplemental Nutrition Program for Women, Infants and Children (WIC) program in Alabama, Hickey et al. (1999), found the adjusted odds ratio for inadequate gestational weight gain decreased 5-6% with each additional year of maternal education. In an analysis of 4,944 women participating in the Colorado Pregnancy Risk Assessment Monitoring System, Wells et al. (2006) found <12 years education was associated with an increased risk of inadequate gestational weight gain (AOR 1.64) compared to >12 years education. However, the same study also found having $\geq$12 years of education was associated with excessive weight gain. Although this finding is inconsistent with greater education resulting in greater knowledge, having completed 12 years of schooling or more is not a good indicator of higher levels of education. More research on the association between maternal education and gestation weight gain is needed.

Marital Status

In 2009, 41% of infants in the U.S. were born to an unmarried mother. Nearly 73% of all black infants, 65% of American Indian infants, 53% of Hispanic infants, 29% of White infants, and 17% of Asian and Pacific Islander infants were born to single mothers (Hamilton et al, 2009). Infants born to unmarried mothers are at greater risk for negative birth outcomes than those born to married mothers. The reason for this is not fully understood, but has commonly been attributed to single mothers' relative lack of support and resources (Raatikainen et al, 2005). Marital status appears to buffer the impact of stress on birth outcomes by increasing social support and resources (Bennett, 1992). However, not all relationships outside of marriage are broken and without resources. Several studies have found that infants born to unmarried mothers in cohabitating relationships are at lower risk for infant death than those born to single mothers, Infants of cohabitating mothers, however, are still at higher risk of infant mortality than infants born to married mothers (Raatikainen et al, 2005).

Several studies have examined the relationship between marital status and gestational weight gain. In a cohort of 622 healthy adult women, Olson and Strawderman (2003) found 38% of married women gained above the IOM guidelines compared to 42% of women who were separated or divorced, and 48% of single women. The investigators also found 21% of married women gained below the guidelines, compared to 23% of single women and 29% of separated or divorced women. Married women were more likely to have appropriate gestational weight gain than single or separated or divorced women.

Tobacco Use

Smoking is a modifiable health behavior with well-established harmful effects on fetal growth. Smoking during pregnancy is associated with low birth weight, preterm birth, and intrauterine growth restriction (Laraia et al., 2007). A recent study estimated that, nationally, 11% of women smoke during pregnancy (Martin et al., 2005). A few studies have found that smoking may be associated with low pregnancy weight gain although the mechanisms that affect gestational weight gain are not completely clear (National Research Council, 2007; Wells et al., 2006; Olson and Strawderman, 2003). Kleinman (1990) used a logistic regression model to analyze 1980 National Natality Survey data on smoking for married mothers with live singleton births with low weight gain (<6.8 kg) as the dependent variable. Smokers had a 46% greater risk of low weight gain than did nonsmokers. Hellerstedt and colleagues (1997) studied smoking and weight change in a retrospective analysis of 1,343 obese and normal-weight pregnant women. Slightly over 36% of normal-weight women and 41.7% of obese women who smoked were observed to have prenatal weight gain below the IOM guidelines, compared to 23.2% and 36.0%, respectively, of normal-weight and obese non-smokers. There is limited evidence that smoking may be inversely associated with gestational weight gain (IOM, 2009). More research is needed to determine the association between smoking and maternal weight gain.

Alcohol Consumption

Although, little information is available about the effects of alcohol consumption on gestational weight gain, infants may be at risk of nutritional deficits due to maternal malnutrition. Chronic alcoholics typically have inadequate nutrient intake.

In a prospective study of alcohol use during pregnancy, those with positive scores on the Michigan Alcoholic Screening Test had lower intakes of protein from meat and vegetable sources, dairy foods, cereal and breads, calcium, B Vitamins, and Vitamin D. Heavy alcohol intake may interfere with nutrient absorption and lead to impaired nutrient metabolism by the liver (IOM. 1996).

Studies examining associations between gestational weight gain and alcohol use show inconclusive results. In an analysis of the 2000–2002 Colorado Pregnancy Risk Assessment Monitoring System, Wells et al. (2006) found no significant association between drinking and gestational weight gain outside the1990 IOM guidelines. In a study of determinants of gestational weight gain in poor black adolescent mothers, Stevens-Simon and McAnarney (1992) found alcohol use was more frequent among mothers who experienced rapid weight gain. In 2008, about 7.2% of U.S. women used alcohol during pregnancy (CDC, 2008). Alcohol is associated with preterm birth, miscarriage, growth retardation, and fetal alcohol syndrome, making it the leading preventable cause of birth defects and developmental disabilities in the United States (Chuang et al, 2010).

Diabetes

Diabetes is a common clinical problem that has an important impact on maternal nutrition and infant health. Diabetes can preexist before pregnancy (Type II) and be worsened by pregnancy, or its onset can occur during pregnancy (gestational diabetes) as a result of hormonally-induced insulin resistance (Korenbrot et al, 2002). Pre-gestational diabetes can cause fetal death and congenital anomalies, especially if poorly controlled (Gabbe and Graves, 2003). Gestational diabetes can increase the risk of fetal macrosomia, birth trauma, newborn hypoglycemia, and hyperbilirubinemia (Gabbe and Graves, 2003).

In a longitudinal cohort of 1,100 pregnant women who delivered singleton, full-term infants, Brawarsky and colleagues (2005) sought to quantify the effect of medical factors known to be related to pregnancy outcomes on the risks of inadequate and excessive gestational weight gain. Women with chronic or gestational diabetes had increased odds of inadequate gestational weight gain (AOR 2.70, CI: 1.18-2.19) compared to women with no diabetes.

Hypertension

High blood pressure is the most common medical problem encountered during pregnancy, complicating 5-15% of pregnancies (Magee et al, 2008). Hypertensive disorders during pregnancy include chronic hypertension, pregnancy-induced hypertension, preeclampsia, and eclampsia. Although the relationship between hypertensive disorders and pregnant women who are overweight or obese is fairly well established, the association between these disorders and gestational weight gain is less clear (Bodnar et al., 2007). For example, preeclampsia is noted for a decrease in the normal (50-60%) expansion in maternal plasma volume which may also affect weight gain early in pregnancy through placental dysfunction. In addition, increased vascular permeability and decreased plasma pressure, caused by preeclampsia, can lead to increased edema and excessive weight gain in late gestation. Preeclampsia can affect weight gain in both directions (IOM, 2009). Decreases in plasma volume or increased accumulation of body fluids caused by edema make it difficult to use total weight as a measure of gestational weight gain when exploring the influence of hypertensive disorders.

Parity

Parity is a commonly used clinical term referring to the number of times a woman has given birth to a fetus with a gestational age of 24 or more weeks (CDC, 2010a). Nulliparity refers to no births, primiparity only one birth, and multiparity denotes more than one birth. In an analysis of 1980 National Natality Survey data, Kleinman (1990) reported that multiparous women tend to gain less weight than primiparous women. Harris and colleagues (1997) confirmed this finding using a combination of cross-sectional and longitudinal analyses of 523 women in the United Kingdom who had been weighed regularly during pregnancy.

Conclusions and Gaps in Research

The research study sought to update previous research by exploring the relative importance of inadequate gestational weight gain as a cause of infant mortality. The research study also examined biomedical and psychosocial contexts during pregnancy and the extent to which these factors influence gestational weight gain. The study focused mainly on the association between inadequate gestational weight gain and infant mortality. Because overweight and obesity are a major public health concern, findings on excessive weight gain were also considered.

Since the release of the IOM weight gain recommendations, low (< 16 pound) gestational weight gain has become more common (IOM, 2009; Abrams, 2000). There is currently, however, very limited literature assessing the link between gestational weight gain and infant mortality. In the 1990 IOM 1990 report, only one National Center for Health Statistics (NCHS) study on infant mortality was examined and it used 1980 vital

health statistics data (Abrams, 2000; IOM, 1990; NCHS, 1986). There has been only one additional study since then. As part of the 1988 National Maternal and Infant Health Survey (NMIHS), Chen et al. (2009) examined maternal pre-pregnancy BMI and gestational weight gain in 4,265 infant deaths and 7,293 controls. Among women with inadequate gestational weight gain, the relative risks for infant death were 3.3 among underweight women, 2.6 among normal weight women, 1.4 among overweight women, and 1.04 among obese women, showing a diminishing effect of low gestational weight gain with increasing pre-pregnancy BMI. Among women with excessive gestational weigh gain, the relative risks for infant mortality for underweight, normal weight, overweight, and obese women were 0.8, 1.1, 1.2, and 1.6, respectively (IOM, 2009). There is a lack of research linking gestational weight gain to infant death (Chen et al, 2009). The importance of this adverse birth outcome warrants not only further research, but that findings in other studies be confirmed.

Additionally, the research study follows Hickey's suggestion to use more comprehensive conceptual frameworks in the design of research on gestational weight gain (Hickey, 2000; Olson & Strawderman, 2003). Few studies have explicitly included behavioral and psychosocial factors along with biomedical and sociodemographic characteristics in examining gestational weight gain (Olson & Strawderman, 2003; Dipetro et al, 2009). The bulk of research on gestational weight gain has focused on biological characteristics such as pre-gravid BMI, parity, height, race, age, and age at menarche (Hickey, 2000; Walter & Minseong, 2002). Contextual indicators (i.e. psychosocial and behavioral) as predictors of weight gain during pregnancy remain an important candidate for scientific inquiry (Webb et al, 2009).

Last, the Committee to *Reexamine IOM Pregnancy Weight Guidelines*; Food and Nutrition Board; and Board on Children, Youth, and Families has issued a national call for more sophisticated analyses to address the gaps within available literature (IOM, 2009). More studies, they have recommended, should be conducted in large and diverse populations to better understand the determinants and consequences of gestational weight gain. The research study addresses some of the limitations of earlier work. Namely, previous studies used relatively old data before infant mortality had declined and most large data sources lack all the variables needed for proper interpretation (e.g. pre-pregnancy height and weight, etc.). This analysis fills these gaps in research by using data from both a recent national data file and U.S. surveillance system to assess the association between the degree to which women are meeting weight gain recommendations and the risk of infant death.

Research Hypotheses

To better understand the implications of these findings, the association between gestational weight gain and infant mortality among U.S. infants was examined through the following hypotheses:

1. *Hypothesis 1:* Women with inadequate gestational weight gain will be at elevated risk of infant mortality.
2. *Hypothesis 1a:* There will be an association between inadequate gestational weight gain and infant mortality due to causes that are potentially nutritionally linked, such as disorders related to short gestation.

3. *Hypothesis 2*: The association between inadequate gestational weight gain and mortality will be partially mediated by an infant's gestational age or birth weight.
4. *Hypothesis 3:* Women who receive adequate prenatal care will be less likely to have inadequate gestational weight gain.
5. *Hypothesis 4:* Women who report high levels of stress during pregnancy will be more likely to have inadequate gestational weight gain.
6. *Hypothesis 5:* The effect of gestational weight gain will depend upon pre-pregnancy BMI.

Chapter 4: Methods

Dataset

The research study analyzed data from Phase 5 of the Pregnancy Risk Assessment Monitoring System (PRAMS) and the 2005 Birth Cohort Linked Birth - Infant Death Data File.

PRAMS is an ongoing population-based surveillance program of the CDC and state health departments designed to collect state-specific information on maternal experiences before conception, during pregnancy, and immediately following delivery. The available data represent approximately 75% of all live births in the United States during each phase of the questionnaire (CDC, 2010b). The original PRAMS questionnaire was developed in 1987. As surveys are revised, new questionnaires reflecting new topics of interest are implemented. PRAMS uses a mixed-mode data collection methodology. Each month, a stratified, systematic sample of 100-300 mothers who have given birth during the previous 2-6 months (median 3.7 months) is selected from participating states' certificate of live birth file (CDC, 2010b). Mothers receive self-administered questionnaires on topics such as reproductive history, lifestyle, barriers to and content of prenatal care, economic status, and neonatal health. If there is no response to three mailings, mothers are contacted by phone and interviewed using standardized web-based Computer Assisted Telephone Interviewing (CATI) software (CDC, 2005). The data collection cycle from the mailing of the pre-letter to the close of telephone follow-up lasts approximately 60 to 95 days (CDC, 2010b). All states have adopted the use of some type of participation incentive such as certified birth certificates, participation in raffles, postage stamps, bibs, cash, and magnetic picture frames.

The PRAMS questionnaire, available in English and Spanish, consists of 56 core questions that appear on all state surveys. Mothers' self-reported responses are linked to extracted birth certificate data items and weighted to allow statistical inferences. Currently, 37 states and New York City voluntarily administer PRAMS [six other states and the Yankton Sioux Tribe previously conducted surveillance (CDC, 2010b)]. Most states oversample low birth weight births and stratify by mother's race or ethnicity. Annual sample sizes range from 1,000 to 3,400 and are divided among three to six strata. The annual sample is typically large enough for estimating statewide risk factor proportions within 3.5% at 95% confidence and estimated proportions within strata are 5% at 95% confidence (CDC, 2010b).

Questionnaires for Phase 5 were administered from January 2004 through July 2009 to 200,008 women 12 to 54 years of age. Respondents were selected from the 35 states whom participated as well as New York City. Response rates (the number of women who completed a questionnaire divided by the number of women sampled) ranged from 65% to 89% and the overall response rate was 73% (CDC, 2010b).

The Birth Cohort Linked Birth - Infant Death Data File (cohort linked file) contains information from birth and death certificates for all infants less than 1 year of age who were born in the United States in 2005. The linkage of the various variables in the birth certificate allows detailed analyses of infant mortality patterns (DHHS, 2011). The dataset consists of three data files. The first, which is referred to as "Numerator" file, provides linked records of deaths of infants born in the United States in 2005 (residents and nonresidents). The second file provides data on all live births in the United States in 2005 and is referred to as the "Denominator-Plus" file. Variables include year of birth,

state and county of birth, characteristics of the infant (age, sex, race, birth weight, gestation), characteristics of the mother (origin, race, age, education, marital status, state of birth), characteristics of the father (origin, race, age, education), pregnancy items (prenatal care, live births), and medical data. Additional variables include infant death identification number, exact age at death, day of birth and death, month of birth and death, underlying cause of death, autopsy, and place of accident. The third file, the "Unlinked" file, consists of infant death records that could not be linked to their corresponding birth records (NCHS, 2002). For the 2005 cohort linked file, 1.3% of all infant death records could not be linked to their corresponding birth certificates.

As a result of the phased transition to the 2003 U.S. Standard Certificate of Live Birth, the 2005 cohort linked file includes data for states that use the 2003 revision of the U.S. Standard Certificate of Live Birth (revised) as well as data for states that use the 1989 U.S. Standard Certificate of Live Birth (unrevised) (IOM, 2009). This study file includes data for seventeen states (California, Connecticut, Florida, Idaho, Kansas, Michigan, Montana, Nebraska, New Hampshire, New Jersey, New York, Oklahoma, South Carolina, South Dakota, Utah, Washington, and Wyoming), which implemented the 2003 revision of the U.S. Standard Certificate of Death by January 1, 2005 and for the District of Columbia which revised during 2005 (DHHS, 2006). Data from all other states are based on the 1989 revision.

Advantages of PRAMS and the Birth Cohort Linked Birth - Infant Death Data File

There are several advantages to using the two datasets in this study. PRAMS provides population-based data both about pregnancy and the first few months following delivery not available from other sources (CDC, 2010b). Additionally, women who

experienced stillbirths, fetal deaths and induced abortions are excluded, thus the PRAMS dataset only includes pregnancies resulting in live-born infants. Mothers whose infants died after delivery are also included. Their participation in the surveillance project permits the elucidation of maternal behaviors of women who have experienced infant mortality and the exploration of any unique health conditions these babies may have experienced.

The Birth Cohort Linked Birth/ Infant Death Data File comprises the entire population of births in 2005. The linkage of birth and infant death certificates also allows exploration of the inter-relationships between infant death and risk factors present at birth (CDC, 2009).

Other Sources of Data

The only other large U.S. data source on pre-pregnancy BMI and gestational weight gain is the Pregnancy Nutrition Surveillance System (PNSS). The surveillance system collects data on low-income pregnant women participating in federally funded public health programs (predominantly the Special Supplemental Nutrition Program for Women, Infants, and Children) from twenty-six states, five tribal governments, and one U.S. territory. Information is collected at prenatal and postpartum clinic visits and is aggregated at the contributor or state level. Although the dataset permits exploration of whether women are meeting IOM weight gain recommendations, it is only representative of the population served by the public health program submitting the surveillance data. It is not representative of more diverse populations and may not be readily extrapolated to all pregnant women.

Sample

The study examined women from the PRAMS Phase 5 data set and women from the 2005 Birth Cohort Linked Birth - Infant Death Data File.

PRAMS Phase 5 Data Set

The first analytic data set consisted of 160,011 mothers who responded to the PRAMS Phase 5 questionnaire. The sample was used for descriptive analyses and to examine the association between maternal stress during pregnancy and outcomes related to gestational weight gain and infant mortality. Its advantage is that it contains pre-pregnancy BMI as well as other psychosocial and behavioral factors.

Birth Cohort Linked Birth - Infant Death Data File

The second data set consisted of all infants born in the United States in 2005. The population of 2,046,725 infants was used for descriptive analyses as well as to assess the odds of infant mortality associated with inadequate and excessive gestational weight gain compared to normal weight gain; this included quantifying the risk of neonatal death, post-neonatal death, and cause-specific infant death to explore biologically plausible mechanisms.

Measures

This section defines the variables used in this study and the way they were operationalized in the research hypotheses (Figure 2, page 55).

Independent Variable

Gestational weight gain was used as the main independent variable. Gestational weight gain was calculated as the difference between maternal weight at delivery and

pre-pregnancy weight. For the sample of PRAMS mothers, pre-pregnancy height and weight was abstracted from questionnaire responses to calculate pre-pregnancy BMI and then categorized according to the IOM definitions as underweight (< 18.5 BMI), normal-weight (18.5-24.9 BMI), overweight (25-29.9 BMI), and obese (≥ 30 BMI). The adequacy of gestational weight gain was also classified according to the IOM guidelines as inadequate, normal, or excessive. The recommended weight gain varied by pre-pregnancy BMI such that "underweight" women were expected to gain 28–40 lbs., normal weight women 25–35 lbs., overweight women 15–25 lbs., and obese women 11–20 lbs. In both samples, normal recommended weight gain and BMI served as reference categories as they have been associated with minimum mortality for infants in other populations (IOM, 2009).

In the PRAMS sample, a measure using three categories based on the IOM guidelines (inadequate, normal, and excessive) was created; normal was omitted. Alternate sets of categories based upon pre-pregnant weight and gestational weight gain were also created. Categories were created for underweight women with inadequate weight gain; normal weight women with inadequate weight gain; overweight women with inadequate weight gain; obese women with inadequate weight gain; underweight women with excessive weight gain; normal weight women with excessive weight gain; overweight women with excessive weight gain; and obese women with excessive weight gain. Normal weight women and women of normal weight gain have the lowest risk of adverse outcomes, thus served as the reference group in the analysis. These classifications permitted testing the interaction between pre-pregnancy weight and gestational weight gain.

For analysis of the cohort linked file, the stated number of total lbs of weight gained during pregnancy was used to classify maternal weight gain. The lower limit of the 2009 IOM recommended range was used to define inadequate weight gain and gestational weight gain was classified into three outcome categories: inadequate ($\leq$24 lbs.), normal (between 25 and 40 lbs), or excessive ($\geq$ 41 lbs).

Dependent Variable

The risk of infant mortality was used as the dependent variable. For the cohort linked file, infant mortality was classified as deaths that occurred within 121 days (4 months) of birth. To explore cause-specific infant mortality, International Classification of Diseases, 10th revision (ICD-10) information was abstracted from the death certificate to categorize the causes of infant death into broad etiologically-related categories. Endocrine, nutritional and metabolic diseases (E00-E88; n=71); Diseases of the genitourinary system (N00-N95; n=52); Disorders related to length of gestation and fetal malnutrition (P05-P08; n=1,501); Respiratory distress syndrome or other respiratory conditions (P20-P28; n=858), Birth defects (Q00-Q99; n=2076); and Sudden infant death Syndrome (SIDS: ICD code R95; n=787) were evaluated as potentially nutritionally linked causes; and rare, implausible, and external causes such as unintentional injuries were classified in a seventh non-related "Other" category. The categories are based on previous research on maternal obesity and infant death and other existing literature pertinent to pre-pregnancy BMI (Chen et al, 2009; Cnattinguis et al., 1998). A pediatrician on the dissertation committee also reviewed the categories for biological plausibility.

The PRAMS dataset neither includes information about cause of death nor allows computation of age of death. For analyses in this sample, mortality was drawn from whether the respondent reported whether or not her infant was currently alive. The variable was measured dichotomously according to whether the mother answered yes (=0) or no (=1).

Additional Predictor Variables

Prenatal Care: Adequacy of prenatal care was assessed using the Kotelchuck Adequacy of Prenatal Care Index. The adequacy of prenatal care was classified into three categories based on month when prenatal care began and gestational age at time of delivery (Kotelchuk, 1994): inadequate prenatal care if the mother attended less than 50% of expected visits; intermediate prenatal care if the mother attended less than 50-79% of expected visits; and adequate or adequate plus prenatal care if the respondent attended more than 80% of expected visits. This variable was be explored both for the sample of birth cohort mothers as well as for the sample of PRAMS mothers.

Stress: Stress was measured through the use of a thirteen item list of events that are considered stressful to a pregnant mother. The PRAMS questionnaire asks the woman if she experienced any of the following events during the twelve months before she delivered her baby and provides dichotomous information (yes/no): family member hospitalization, separation/divorce, residential move, homelessness, unemployment, increased arguing with husband/partner, husband/partner lost job, husband/partner did not want pregnancy, financial hardship, involved in a physical fight, husband/partner incarcerated, loved one had substance abuse problem, and death of a loved one. The 13 stressful events were adapted from the Modified Life Events Inventory developed by

Newton and colleagues (1979). When summed, higher scores reflect greater distress and lower confidence in personal coping resources. Previous research has linked stressful life events to the risk of delivery of premature and low birth weight infants (Newton et al, 1979; Newton & Hunt, 1984). The stress variable was analyzed as a binary variable with the top 25% of the distribution as indicating high stress.

Mediator Variables

Birth weight was included as a potential mediator both in the sample of birth cohort mothers as well as the sample of PRAMS mothers. A categorical variable of low birth weight (less than 2,500 g at the time of delivery) compared with normal birth weight was included. Very low birth weight (less than 1500 grams, or 3 lbs 4 ozs) and low birth weight (between 1500 and less than 2500g) compared with normal birth weight were also explored.

Gestational Age: Weeks of gestation were based on the interval between the last menstrual period and the infant date of birth and treated as a dummy variable indicating if the infant was born after 36 weeks of gestation at the time of delivery or less.

Birth Weight for Gestational Age: Infant size at delivery was classified into three groups: Small for Gestational Age (SGA), Appropriate for Gestational Age (AGA), and Large for Gestational Age (LGA). An infant was considered SGA if its birth weight was below the 10th percentile for gestational age; AGA if its birth weight was equal to or greater than the 10^{th} percentile and less than or equal to the 90 percentile for gestational age; and LGA if its weight is greater than the 90^{th} percentile for gestational age.

Control Variables

Several covariates were assessed as known potential confounders in both the sample of birth cohort mothers and sample of PRAMS mothers. The covariates included:

Maternal Age: Maternal age was based on the mother's information regarding age at the time of birth. Advanced maternal age, associated with infant mortality, was treated as a dummy variable indicating if the mother was at least age 35 at time of delivery or younger than 35.

Maternal Race, in both samples, was drawn from the Hispanic origin and racial background description reported by the respondent. Categories of race and ethnicity included White, Black or African American, Hispanic, Asian, American Indian or Alaska Native, and Native Hawaiian or other.

Maternal Education: This information was drawn from the highest level of education that the respondent completed. Maternal education was classified into four groups: less than high school (< 12 years of school), high school graduate (12 years of school), some college (13–15 years of school), and college graduate ($\geq$ 16 years of school).

Marital Status: Maternal relationship was defined on the basis of maternal reporting about current marital status. A dummy variable was created indicating if the mother was married or living with a steady partner vs. single, separated, or divorced.

Tobacco use: Cigarette smoking was defined on the basis of reporting whether the mother smoked cigarettes during the last three months of pregnancy. The number of cigarettes smoked daily during that time period was categorized as none, one to five cigarettes per day, and six or more cigarettes per day.

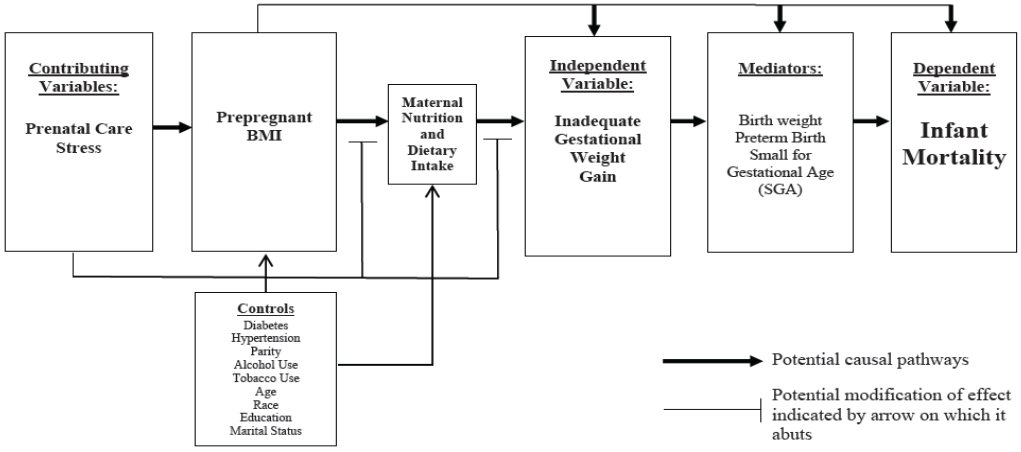
Alcohol use: Alcohol use was measured as the number of drinks consumed per week during the last three months of pregnancy. Alcohol consumption was categorized as none, one to three drinks a week; four to six drinks a week; and seven or more drinks a week.

Diabetes: Previously diagnosed and gestational diabetes was assessed based on reporting of high blood sugar either before or during pregnancy. A dummy variable was created indicating the presence or absence of diabetes.

Hypertension: High blood pressure, including pregnancy-induced hypertension, preeclampsia, and chronic hypertension was assessed based on the response to questions about maternal morbidity during pregnancy. A dummy variable was created indicating the presence or absence of hypertension.

Parity: Reproductive history in both samples was assessed based on previous pregnancy outcomes. Women were defined as either nulliparous (never given birth to an infant), primiparous (their first live birth with no previous stillbirths), or multiparous (two or more previous live births).

Figure 1: Conceptual Model



Source: Adapted from IOM, 1990

Plan of Analysis

A secondary data analysis was conducted using existing quantitative survey data. Descriptive statistics was used to summarize data for each sample and for all BMI groups. Univariate and multivariate analyses were performed to examine the relationship between gestational weight gain, maternal pre-pregnancy BMI, stress, and infant mortality. Ninety-five percent confidence intervals (CI) were computed to evaluate the precision of each odds ratio and a P value of < 0.05 was considered statistically significant. Multivariate analyses controlled for potential confounders of the associations stated above, including the maternal characteristics of age, race or ethnicity, education, marital status, cigarette smoking, alcohol use, diabetes, hypertension, and parity.

For the purpose of this study, only women with a singleton, live birth were selected as the weight gain guidelines vary for women with multiple fetuses. Furthermore, only women with available and plausible information for gestational weight change, birth weight, substance use, and medical and demographic characteristics were included. Statistical analyses in both datasets were conducted using SAS Software version 9.2 (SAS Institute, Cary, NC). Appropriate sample weights were used in all analyses. Because PRAMS uses a complex sampling technique, the survey procedure in SAS was used to provide risk estimates based on sampling weights for each individual in the sample.

The following details the analytical approach for testing each hypothesis:

Hypothesis 1: Women with inadequate gestational weight gain will be at elevated risk of infant mortality. Hypothesis 1a: There will be an association between inadequate

gestational weight gain and infant mortality due to causes that are potentially nutritionally linked, such as disorders related to short gestation and fetal malnutrition.

To test Hypotheses 1 and 1a, the dependent variable of infant mortality was regressed on the independent variable of gestational weight gain. Maternal weight gain was divided into three categories (inadequate, normal, and excessive), with normal weight gain serving as the reference category.

For the PRAMS sample, logistic regression analysis was used to evaluate the outcome of infant mortality because it allowed for the analysis of dichotomous and categorical variables. Each model contained all the control variables in the study.

In the cohort linked file, Cox proportional hazards regression was used to compute the hazard of infant death by day after birth up to 121 days. Infants who survive were censored after 4 months. Censoring infants in the cohort linked file created a relatively comparable sample to the infants of the mothers participating in PRAMS who on average, give birth 121 days months before completing the survey. It also allowed the distributions of deaths in the two samples to be compared. To investigate biological plausibility, the distribution of deaths were investigated for nutrition -specific causes of death using the six etiologically-related categories. For this investigation, Cox proportional hazards regression on the likelihood of infant death in each of the categories of gestational weight gain was used. The analysis of death by day was also used to classify deaths as either occurring in the neonatal or post-neonatal period given early mortality is more likely linked inadequate gestational weight gain. Frequency and chi-square analyses were used.

Hypothesis 2: The association between inadequate gestational weight gain and mortality will be partially mediated by an infant's gestational age or birth weight.

Hypothesis 2 tested for a mediating effect. Low birth weight, preterm birth, and weight for gestational age were added to the regression for Hypothesis 1 and evidence for mediation was a decline in the coefficient for weight gain, preterm birth, or fetal growth after the addition of the maternal and fetal health dummy variables. Mediation analysis was also conducted using the definition of a mediator provided by Baron & Kenny (1986). Low birth weight, preterm birth, or SGA was considered a mediator if (1) inadequate gestational weight gain significantly predicted infant mortality, (2) inadequate gestational weight gain significantly predicted LBW, preterm birth or SGA, and (3) LBW, preterm birth or SGA significantly predicted infant mortality controlling for inadequate gestational weight gain. If the effect of inadequate gestational weight gain on infant mortality decreased to zero with the inclusion of LBW, preterm birth or SGA, perfect mediation was determined to have occurred. If the effect of inadequate gestational weight gain on infant mortality decreased by a nontrivial amount, but not to zero, partial mediation was deemed to have occurred.

To provide a more direct test of whether the mediator carries the influence of inadequate gestational weight gain to infant mortality, the Sobel test was employed. The regression coefficients and standard errors for the association between the inadequate gestational weight gain and the mediator variables, as well as the association between the mediator variables and infant mortality were entered into an online tool that evaluates the significance of the mediators. If the Sobel test (as evaluated by the significance of the mediators) was significant ($p < 0.05$), the variable was determined to have mediated the

association between inadequate gestational weight gain and infant mortality. All control variables were entered into each regression model.

Hypothesis 3: Women who receive adequate prenatal care will be less likely to have inadequate gestational weight gain.

To test Hypothesis 3, the dependent variable of gestational weight gain was regressed on prenatal care using logistic regression. Gestational weight gain was divided into three categories: inadequate, normal, and excessive. Prenatal care was divided into three categories: inadequate, intermediate, adequate/adequate plus. Odds ratios were used to quantify the strength of the association between inadequate gestational weight gain and receiving inadequate prenatal care compared to receiving adequate prenatal care. The model contained all the control variables in the study.

Hypothesis 4: Women who report high levels of stress during pregnancy will be more likely to have inadequate gestational weight gain.

To test Hypotheses 4, the dependent variable of gestational weight gain was regressed on stress using logistic regression. Gestational weight gain was divided into three categories: inadequate, normal, and excessive. The stress variable was analyzed as a continuous and dichotomous variable. Odds ratios were used to quantify the strength of the association between inadequate gestational weight gain and a high number of stressful life events compared to lower numbers. The model contained all the control variables in the study.

Hypothesis 5: The effect of gestational weight gain will depend upon pre-pregnancy BMI. .

To test Hypothesis 5, the cross classifications of gestational weight gain with pre-pregnant BMI were used to analyze their effects on infant mortality. Statistical interactions were included in the confounder adjusted multivariable regression models to assess potential moderating effects of pre-pregnancy weight on the relationship between gestational weight gain and infant mortality.

Weights

In the PRAMS Phase 5 file, data are weighted annually for each state to adjust for sampling, non-responsive, and non-coverage fractions. For each respondent, the initial sampling weight is the reciprocal of the sampling fraction applied to the stratum. Sampling fractions in PRAMS range from 1 in 1 (for very low birth weight strata in small states) to approximately 1 in 211 (for normal birth weight, non-minority strata in populous states). Corresponding sampling weights, thus, range from 1 to 211.

Nonresponse adjustment factors attempt to compensate for the tendency of women having certain characteristics (such as being unmarried or of lower education) to respond at lower rates than women without those characteristics. Where multivariate analysis shows that these characteristics affect the propensity to respond in a particular stratum, the adjustment factor is the ratio of the sample size in that category to the number of respondents in the category. If analysis shows that no characteristic distinguishes respondents from non-respondents, the adjustment factor is the ratio of the sample size in that stratum to the number of respondents in the stratum. In the first case, each category so identified has an adjustment factor; in the second, there is a single factor

for the whole stratum. The magnitude of the adjustment for nonresponse depends on the response rate for a category. If 80% (or 4/5) of the women in a category respond, the non-response weight is 1.2 (or 5/4). Categories with lower response rates have higher non-response weights.

The frame non-coverage weights are derived by comparing frame files for a year of births to the calendar year birth tape that states provided to CDC. The effect of the non-coverage weights is to bring totals estimated from sample data in line with known totals from the birth tape. In mail/telephone surveillance, the magnitude of non-coverage is small (typically from 1% to 5%), so the adjustment factor for non-coverage is not much greater than 1.

Multiplying together the sampling, non-response, and non-coverage components of the weight yields the analysis weight. The weight can be interpreted as the number of women like herself in the population that each respondent represents.

The 2005 Birth Cohort Linked Birth - Infant Death Data File adds a weight to the linked numerator file to correct for biases in percent of records linked by major characteristics (e.g. birth weight-specific infant mortality rates). The number of infant deaths in the cohort linked file are weighted to equal the sum of the linked plus unlinked infant deaths by age at death and state

Human Subjects Considerations

The research study is based on secondary data analysis. The Birth Cohort Linked Birth - Infant Death Data File and PRAMS dataset do not contain identifiable or private information. Both datasets were approved by the CDC Institutional Review Board and

respondents provided informed consent. The proposed project was also determined exempt from oversight from the University of Maryland, College Park Institutional Review Board (see appendix A).

Chapter 5: Results

The purpose of this study was to examine the association between inadequate and excessive gestational weight gain and the risk of infant mortality and the extent to which low birth weight and preterm birth may mediate this association after controlling for a number of biomedical and socio-demographic factors. This study also sought to determine if there is a possible protective effect associated with the amount of prenatal care a mother receives as well as the influence of maternal stress on gestational weight gain. This chapter presents the findings from the analyses of the Pregnancy Risk Assessment Monitoring System (PRAMS) and the Birth Cohort Linked Birth-Infant Death Data File (Cohort Linked File). First, descriptive statistics for the mothers, infants, and variables investigated in the two analytic samples are presented. Next, results of the logistic regression and proportional hazards analyses for each of the five research hypotheses are presented. Finally, odds ratios and their corresponding significance levels are presented estimating the likelihood of women with inadequate gestational weight gain experiencing infant mortality, cause-specific infant mortality, higher levels of stress, or inadequate prenatal care compared to women with normal weight gain.

Model Assumptions

Logistic regression involves the assumption that the relationship between the logit of the probability of the outcome is linearly related to the set of covariates. There is no assumption about the covariates being linearly related to each other.

In the PRAMS sample, to determine whether a possible nonlinear relationship exists between maternal age or stress and the logit of the probability of death or

inadequate gestational weight gain, data were transformed by squaring the variables and including them in the model. A -2 log-likelihood difference between the two maternal age models was significant at the 0.05 level, but neither the age squared nor continuous age variable was significant and using the continuous age variable would have created an additional 2,797 cases with missing information. Exploratory analyses also indicated that neither the continuous stress nor the stress squared measure was significant. Therefore, it was reasonable to treat maternal age and maternal stress as dichotomous variables in all models.

The key assumption in the Cox Proportional Hazard model (cohort linked file) is that the survival curves for two strata have hazard functions that are proportional over time (i.e. constant relative hazard). All model assumptions for Cox proportional hazard regressions were tested prior to fitting. Proportionality was initially assessed by using the lifetest procedure to graph survival function versus the survival time as well as log(-log(survival)) versus log of survival for all covariates. Graphs with parallel curves were determined to have satisfied the proportional hazard assumption. Time interaction terms were created for all variables that suggested a violation of the assumption and placed inside the procedure. A time interaction term of "0" was used for the referent group (value=0); and the test group (value=1) took on the value of time, which therefore adjusted the models for the lack of proportionality by estimating the time function for the test group (value=1). The weight gain beyond the recommended range interaction term had a p-Value of significance (of <0.0001). It was not retained for model analysis because the results were unstable and there were a small number of deaths associated with weight gain beyond the recommended range. The small for gestational age

interaction term was also significant. It was not included in the model because the deviation was small.

Pregnancy Risk Assessment Monitoring System (PRAMS) Analysis

Among respondents to the PRAMS questionnaire, 160,011 mothers with singleton births (only one infant delivered) were eligible for the study. Mothers in the sample had a mean gestational weight gain of 30.7 lbs. Gestational weight gain values were used to evaluate whether mothers adhered to IOM recommendations. As presented in Table 2, nearly 25% experienced inadequate weight gain, 34.2% gained the recommended amount of weight, and 40.8% of mothers gained more than recommended. The majority of the study sample was White (56.5%), followed by 16.7% Black, 12.7% Hispanic, 8.4% Asian or Pacific Islander, 4% American Indian/Alaska Native, and 1.6% who indicated a race other than the five groups shown ("Other" category). The majority of the sample also had a high school education or above, representing 83.6% of the mothers; however, 16.4% of the sample had less than a high school diploma. Almost 85% of the sample was 34 years old or younger and 62% was married. Seventy-six percent of mothers attended 80% or more of their prenatal care visits and 31.6% reported three or more stressful life events during the twelve months before delivering their baby. Mothers who had not previously given birth to a fetus, whether or not the infant was born alive or stillborn, composed 44.2% of the sample.

The PRAMS dataset neither includes information about cause of death nor allows computation of age of death. For analyses in this sample, mortality was determined by whether the respondent reported whether or not their infant was currently alive. With

regards to birth outcomes, 1.7% of infants died. Of the infants whose mothers gained an inadequate amount of weight during pregnancy, 3.9 % died, compared with 1.9 % of those whose mothers gained a normal or more than recommended amount of weight. Almost 27% and 22% of the infants in the sample were born low birth weight and preterm, respectively. Of the infants born low birth weight, moderately low birth weight, or very low birth weight, 5.5%, 1.4%, and 19.7% died, respectively compared with 0.27% of those born normal birth weight. Among infants born SGA, 2.3% died compared with 1.6% of those born average for gestational age. Table 2 shows the descriptive characteristics of mothers and infants included in the analysis.

Table 2. Descriptive Statistics of Mothers and Infants, PRAMS Phase 5

Variable	%
Mortality	
Surviving	98.32
Died	1.68
Pre-Pregnant BMI	
Underweight (<18.5)	5.73
Normal Weight (18.5-24.9)	51.76
Overweight (25.0-29.9)	23.03
Obese (30+)	19.48
Gestational Weight Gain	
Inadequate	24.97
Normal	34.26
Excessive	40.77
Birth weight, grams	
Normal (> 2500g)	73.25
Low (≤2500g)	26.75
Moderately Low (1500-2499g)	20.70
Very Low (<1500g)	6.05
Birth weight for Gestational Age	
SGA	17.03
AGA	73.94
LGA	9.03
Gestational Age	
Term Birth (>36 weeks)	78.24
Preterm Birth	21.76
Kotelchuck Prenatal Care Utilization Index	
Inadequate (<50% of prenatal visits)	11.52
Intermediate (50-79% of prenatal visits)	12.86
Adequate (>80% of prenatal visits)	75.62

Stressful Events during Year Before Delivery	
<3	68.38
≥3	31.62
Maternal Age, years	
≤34	84.75
≥35	15.25
Maternal Education, y	
Less than High School (<12)	16.39
Completed High School (=12)	30.76
Some College (13-15)	24.39
Completed College (≥16)	28.46
Maternal Race/Ethnicity	
White	56.52
African American	16.71
Hispanic	12.71
Asian or Pacific Islander	8.42
American Indian/Alaska Native	4.01
Other	1.63
Marital Status	
Married	62.25
Other	37.75
Diabetes during Pregnancy	
Yes	4.06
No	95.94
Hypertension during Pregnancy	
Yes	7.97
No	92.03
Number of Previous Live Births	
0	44.19
1	30.67
2+	25.33
Number Cigarettes per Day during Last 3 Months of Pregnancy	
None	84.94
1-5 cigarettes	7.81
6+ cigarettes	7.25
Number of Alcoholic Drinks per Week During Last 3 Months Pregnancy	
None	93.51
1-3 drinks	6.10
4-6 drinks	0.21
7+ drinks	0.18
Mean Maternal Weight Gain	30.71 lbs
Mean BMI	25.52 kg/m2
Mean age of infant when questionnaire completed	121.01 days
Mean number of Stressors	1.89 life events
Sample Size	160,111

A total of 30,099 women were excluded from the study as a result of missing or implausible information on pre-pregnant BMI (N= 11,172), weight gain during

pregnancy (N=11,463), birth weight (N=377), gestational age (N= 1,295), birth weight for age (N=1,021), parity (N=950), maternal age (N=10), maternal race/ethnicity (N=1,441), maternal education attainment (N=2,724), marital status (N=104), diabetes (N= 1,515), hypertension (N=1, 585), stress reported during pregnancy (N=2,223), and number of prenatal care visits (N=6,513) (15.82% of the eligible sample). Two-sample *t* test analyses comparing women included in the sample with those excluded showed many statistical differences resulting from the large sample size, but only a few differences of practical significance (Table 3). Excluded women were more likely to have had a previous live birth. Included women were more likely to be married and to have >12 years of education.

Table 3 *t*-tests for Included and Excluded Mothers, PRAMS Phase 5

Variable	T	Mean Difference	Standard Deviation	Diff (1-2) Std Dev	p Value
Previous Live Births	-20.42	-0.10	5.44	-0.019	<.0001
Marital Status	31.20	0.09	3.25	0.029	<.0001
Maternal Education	72.20	0.50	7.24	0.069	<.0001
Gestational Age	15.65	0.03	1.89	0.015	<.0001
Maternal Age	4.33	0.01	2.36	0.004	<.0001
Prenatal Care	42.81	0.20	4.62	0.044	<.0001

Hypothesis 1 - Women with inadequate gestational weight gain will be at elevated risk of infant mortality

Table 4 shows the results from a series of nested logistic regression models predicting infant mortality. In all models, inadequate gestational weight gain was significantly associated with infant mortality. Model 1 displays the odds ratios for infant death associated with the two weight gain categories—inadequate and excessive. The reference group for the two categories included infants whose mothers had a total pregnancy weight gain within the normal range. Inadequate maternal weight gain was

associated with increased odds of infant mortality (OR [odds ratio] = 2.58, $p<0.0001$, 95% CI [confidence interval]: 2.09, 3.71), whereas weight gain beyond the recommended amount was not.

In Model 2, inadequate gestational weight gain remained significant after controlling for maternal and infant characteristics. The regression coefficient decreased 13.4% after adding controls to the model, but the significance level remained constant. Weight gain beyond the recommended range also reached significance (OR = 0.64, $P<0.01$, 95% CI: 0.50, 0.83). The addition of the age variable substantiated the previous research on infant mortality. Mothers who were 35 years or older had an increased chance of infant death when compared to mothers 34 years or younger (OR = 1.48, $P<0.05$, 95% CI: 1.12, 1.95). Mothers who smoked 1-5 cigarettes on an average day during the last three months of pregnancy also had an elevated chance of infant death when compared to non-smokers (OR = 1.47, $P<0.05$, 95% CI: 1.08, 2.01).

Gestational age was added to Model 3 because the period of gestation for preterm birth is shorter than that for full-term birth, resulting in a lower average weight gain. As would be expected, total weight gain during pregnancy was related to the length of the gestational period and the risk of infant mortality was reduced. Infants born to women with inadequate gestational weight gain had odds of infant death that were 84.5% higher than the odds for the reference group of infants. Mothers that gained more than the recommended weight were 26% less likely to experience infant death than those with weight gain within the normal range.

Model 3 also shows an association between gestational age and infant mortality. Babies born preterm had odds of infant death that were 9.86 times the odds for infants

born after 36 weeks gestation (*P*<0.0001, 95% CI: 8.21, 11.83). The association between maternal age over 34 and infant mortality also persisted (OR = 1.42, *P*<0.01, 95% CI: 1.07, 1.87).

Additionally, there was a declining risk of mortality with increasing maternal education. For instance in Model 2, mothers with some college were 29% less likely to experience infant death than those with less than a high school education, but for those with a college degree, the odds were 59% lower. The results were significant at the *P*<0.05 and *P*<0.0001 level, respectively. Consistent with previous research (NCHS, 2011), Black mothers had an elevated chance of infant death when compared to White mothers (OR = 1.61, *P*<0.0001, 95% CI: 1.28, 2.01). Mothers with at least one child had as much as a 26% reduced chance of infant death when compared to women with no previous live births (*P*<0.05, 95% CI: 0.64, 0.96).

Table 4 Association between Inadequate Gestational Weight Gain and Infant Mortality

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Gestational Weight Gain						
Inadequate	2.58***	2.09,3.17	2.28 ***	1.83, 2.81	1.85 ***	1.49, 2.30
Normal (Ref)	-	-	-	-	-	-
Excessive	0.69	0.54,0.88	0.64**	0.50, 0.83	0.74*	0.57, 0.96
Maternal and Infant Characteristics						
>34 years old			1.48*	1.12,1.95	1.42*	1.07,1.87
Prematurity(<36 weeks)					9.86 ***	8.21,11.83
< 50% of prenatal visits	-	-	-	-	-	-
50-79% of prenatal visits			0.78	0.52,1.17	0.97	0.64,1.46
>80% of prenatal visits			0.99	0.74,1.35	0.92	0.67,1.24
Married			0.87	0.70,1.08	0.91	0.73,1.12
Single or Divorced	-	-	-	-	-	-
Gestational Diabetes			0.87	0.49,1.55	0.79	0.44,1.43
Hypertension			1.23	0.84,1.79	0.73	0.49,1.08
Zero previous live births	-	-	-	-	-	-
One previous live birth			0.74*	0.60,0.90	0.78*	0.64,0.96
2+ previous live births			0.96*	0.76,1.21	0.99*	0.79,1.25
Zero drinks per week	-	-	-	-	-	-
1-3 drinks per week			0.80	0.56,1.16	0.85	0.58,1.23

4-6 drinks per week			1.04	0.30,3.66	1.07	0.30,3.76
7+ drinks per week			1.12	0.39,3.17	1.31	0.47,3.68
Zero cigarettes per day	-	-	-	-	-	-
1-5 cigarettes per day			1.47*	1.08,2.01	1.33	0.97,1.82
6+ cigarettes per day			1.32	0.95.1.82	1.19	0.85,1.66
Race/Ethnicity						
White	-	-	-	-	-	-
Hispanic			0.79	0.55,1.11	0.80	0.57,1.14
African American			1.87***	1.49,2.36	1.60***	1.28,2.01
Asian or Pacific Islander			1.22	0.81,1.84	1.22	0.81,1.84
American Indian			1.42	0.79,2.55	1.33	0.73,2.43
Other			1.04	0.48,2.26	1.12	0.51,2.47
Maternal Education						
Less than High School (<12y)	-	-	-	-	-	-
High School (=12y)			0.78*	0.60,0.99	0.80	0.62,1.03
Some College (13-15y)			0.71*	0.53,0.95	0.76	0.57,1.02
College Graduate (>16y)			0.41***	0.30,0.56	0.43***	0.31,0.60
-2 Log Likelihood	451282.26		440609.23		402451.84	

*p < .05, ** p < .01, *** p < .0001

Hypothesis 2 - The association between inadequate gestational weight gain and mortality will be partially mediated by an infant's gestational age or birth weight

Table 5 presents the relationship of gestational weight gain and the mediators of low birth weight, preterm birth, and small for gestational age to infant mortality. In Model 1, preterm birth and birth weight were added to the model with maternal and infant characteristics found in table 3. The fit of the model improved (Chi square = 18.18, df = 1, p<0.0001). The coefficient for inadequate weight gain declined 42%, from 0.82 to 0.47 (not shown), but remained significant and positive. After controlling for low birth weight and gestational age, infants of women with inadequate gestational weight gain were 61% more likely to die than infants of women achieving the recommended range (AOR = 1.61, P<0.0001, 95% CI: 1.29, 1.99). Thus, low birth weight was a partial mediator for infant mortality. Newborns weighing less than 2,500 g had odds of infant death that were 5.93 times the infants of normal birth weight (P<0.0001, 95% CI: 4.69,

7.50). Babies born preterm had odds of infant death that were 241% higher than those born after 36 weeks gestation. The association between advanced maternal age and infant mortality as well as Black race and infant mortality persisted in both cases, babies had odds of infant death that were 35% higher than younger mothers and white women, respectively. In contrast, mothers with chronic hypertension, preeclampsia, and pregnancy-induced hypertension had a reduced chance of infant death when compared to mothers with normal blood pressure (OR = 0.59, *P*<0.01, 95% CI: 0.40, 0.89).

In Model 2, the mediators of very low birth weight (less than 1500 grams, or 3 pounds 4 ounces) and moderately low birth weight (between 1500 and less than 2500g) compared with normal birth weight were explored. The effect of inadequate weight gain remained significant (AOR = (1.38, *P*<0.01, 95% CI: 1.09, 1.74) after low birth weight was introduced. Newborns weighing between 1500 and 2499g had odds of infant death that were 3.07 times the infants of normal birth weight. Infants weighing l500g had odds of infant death that were 207% higher than those born weighing >2500g. Premature babies had an increased chance of infant death when compared to full term babies (OR = 1.87, *P*<0.0001, 95% CI: 1.29, 2.70). Hypertensive mothers had a reduced chance of infant death when compared to mothers with normal blood pressure (OR = 0.46, *P*<0.001, 95% CI: 0.30, 0.70).

In Model 3, SGA was also a significant predictor of infant mortality after controlling for maternal and infant characteristics. Infants born to women with inadequate gestational weight gain had odds of infant death that were 2.22 times the infants born to women with normal weight gain (*P*<0.0001, 95% CI: 1.79, 2.76). Conversely, mothers that gained more than the recommended weight were 34% less likely to experience infant

death than those with weight gain within the normal range (OR = 0.66, *P*<0.01, 95% CI: 0.52, 0.85). Newborns were born small for gestational age had odds of infant death that were 1.66 times the infants born appropriate for gestational age. Mothers that were 35 years or older had an increased chance of infant death when compared to mothers 34 years or younger (OR = 1.46, *P*<0.01, 95% CI: 1.11, 1.99). Black mothers had an increased chance of infant death when compared to White mothers (OR = 1.88, *P*<0.0001, 95% CI: 1.50, 2.36). Mothers who smoked 1-5 cigarettes on an average day during the last three months of pregnancy also had an elevated chance of infant death when compared to non-smokers (OR = 1.41, *P*<0.05, 95% CI: 1.03, 1.93). Mothers with at least one child had as much as a 34% reduced chance of infant death when compared to women with no previous live births (*P*<0.01, 95% CI: 0.62, 0.93).

Consistent with previous research, mortality was strongly linked to maternal education, with increased years of school predicting lower levels of infant mortality across all models. In sum, low birth weight, preterm birth, and small for gestational age partially mediate the association between inadequate gestational weight gain and infant mortality

Table 5. Inadequate Gestational Weight Gain and Infant Mortality Mediated by Birth Weight

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Gestational Weight Gain						
Inadequate	1.61***	1.29,1.99	1.38 ***	1.09, 1.74	2.22***	1.79,2.76
Normal (Ref)	-	-	-	-	-	-
Excessive	0.80	0.62,1.04	0.83	0.63, 1.82	0.66*	0.52,0.85
Maternal and Infant Characteristics						
Prematurity (<36 weeks)	3.41***	2.73,4.25	1.87**	1.29, 2.70	-	-
>2500g (Ref)	-	-	-	-	-	-
<2500g (LBW)	5.93***	4.69,7.50	-	-	-	-
1500-2499g (MLBW)	-	-	3.07***	2.17,4.35	-	-
<1500g (VLBW)	-	-	44.68***	29.87, 66.83	-	-
SGA	-	-	-	-	1.66***	1.36,2.02

LGA	-	-	-	-	0.94	0.61,1.45
>34 years old	1.35*	1.02,1.79	1.28	0.95, 1.73	1.46**	1.11,1.99
< 50% of prenatal visits	-	-	-	-	-	-
50-79% of prenatal visits	1.0	0.66,1.51	0.96	0.63, 1.48	0.77	0.52,1.16
>80% of prenatal visits	0.89	0.66,1.21	0.82	0.59, 1.13	0.99	0.74,1.34
Married	0.94	0.76,1.17	0.96	0.77, 1.21	0.88	0.71,1.10
Single or Divorced	-	-	-	-	-	-
Gestational Diabetes	0.86	0.45,1.55	0.97	0.53, 1.79	0.88	0.49,1.58
Hypertension	0.59**	0.41,0.89	0.46**	0.30, 0.70	1.19	0.81,1.74
Zero previous live births	-	-	-	-	-	-
One previous live birth	0.86	0.70,1.06	0.92	0.74, 1.15	0.76**	0.62,0.93
2+ previous live births	1.12	0.89,1.41	1.26	0.99, 1.60	0.99	0.79,1.25
Zero drinks per week	-	-	-	-	-	-
1-3 drinks per week	0.85	0.59,1.24	0.84	0.57, 1.24	0.80	0.55,1.16
4-6 drinks per week	1.03	0.28,3.77	1.07	0.29, 3.95	1.05	0.30,3.68
7+ drinks per week	1.13	0.40.3.20	1.12	0.39, 3.21	1.13	0.40,3.20
Zero cigarettes per day	-	-	-	-	-	-
1-5 cigarettes per day	1.20	0.87,1.65	1.28	0.91, 1.81	1.41*	1.03,1.93
6+ cigarettes per day	1.04	0.75,1.46	1.14	0.80, 1.62	1.24	0.90,1.70
Race/Ethnicity						
White	-	-	-	-	-	-
Hispanic	0.77	0.54,1.09	0.75	0.52, 1.08	0.79	0.56, 1.12
African American	1.35*	1.07,1.67	1.20	0.95, 1.52	1.88**	1.50,2.36
Asian or Pacific Islander	1.12	0.74,1.70	1.24	0.80, 1.91	1.216	0.81,1.83
American Indian	1.42	0.77,2.61	1.43	0.76, 2.71	1.452	0.90,2.61
Other	1.00	0.45,2.21	0.981	0.43, 2.25	0.997	0.46,2.17
Maternal Education						
Less than High School (<12y)	-	-	-	-	-	-
High School (=12y)	0.80	0.62,1.03	0.73*	0.56, 0.96	0.78*	0.61, 0.99
Some College (13-15y)	0.77	0.57,1.03	0.70*	0.51, 0.95	0.72*	0.54, 0.96
College Graduate (>16y)	0.45***	0.33,0.62	0.42**	0.30, 0.59	0.41***	0.30, 0.57
-2 Log Likelihood	388731.69		363107.74		439383.18	

*p < .05, ** p < .01, *** p < .0001

Hypothesis 3 - Women who receive adequate prenatal care will be less likely to have inadequate gestational weight gain.

Table 6 shows the results from two logistic regression models predicting inadequate gestational weight gain. Attending more than 80% of prenatal care visits (adequate prenatal care) was protective against inadequate gestational weight gain by itself (Model 1) and remained significant after controlling for gestational age and

maternal characteristics. The regression coefficient decreased by 20% after adding controls. Model 2 shows how an increase in the utilization of prenatal care reduces the likelihood of a woman gaining an inadequate amount of weight during pregnancy. Women who attended 80% or more of expected visits were 38% less likely to experience inadequate gestational weight gain (OR = 0.62, $P<0.0001$, 95% CI: 0.59, 0.66) when compared to women with inadequate prenatal care. Women who attended 50-79% of expected visits had odds of inadequate gestational weight gain that were 0.70 times that of the women attending <50% of expected visits ($P<0.0001$, 95% CI: 0.65, 0.75). In addition, mothers with chronic hypertension, preeclampsia, or pregnancy-induced hypertension had a reduced likelihood of inadequate gestational weight gain when compared to mothers with normal blood pressure. Increasing years of education were also protective against inadequate gestational weight gain.

In contrast, infants born preterm (2.03), mothers who delivered at age 35 or older (1.11), mothers with gestational diabetes (1.33), mothers with one or more children (1.30), and mothers who smoked six or more cigarettes a day during the last three months of pregnancy (1.29) had increased likelihoods of inadequate gestational weight gain when compared to the referent group. Black mothers, Hispanic mothers, Asian or Pacific Islander mothers, and women who indicated "Other" as a race category were 32%, 17%, 56%, and 25% more likely, respectively to experience inadequate gestational weight gain when compared to White women. The results were all significant at the $p<0.0001$ level.

Table 6 Prenatal Care and Inadequate Gestational Weight Gain

	Model 1		Model 2	
	OR	95% CI	OR	95% CI
Maternal and Infant Characteristics				
Inadequate prenatal care (< 50% of visits)	-	-	-	-

Intermediate prenatal care (50-79% of visits)	0.61***	0.57, 0.66	0.70***	0.65,0.75
Adequate prenatal care (>80% of visits)	0.55***	0.52, 0.58	0.62***	0.59,0.66
Advanced Maternal Age (>34 years old)	-	-	1.11**	1.05,1.17
Prematurity (<36 weeks)	-	-	2.03***	1.93,2.14
Married	-	-	1.00	0.95,1.05
Single or Divorced	-	-	-	-
Gestational Diabetes	-	-	1.33***	1.21,1.47
Hypertension	-	-	0.71***	0.62,0.78
Zero previous live births	-	-	-	-
One previous live birth	-	-	1.30***	1.25,1.37
2+ previous live births	-	-	1.41***	1.34,1.49
Zero drinks per week	-	-	-	-
1-3 drinks per week	-	-	0.98	0.91,1.06
4-6 drinks per week	-	-	1.24	0.83,1.87
7+ drinks per week	-	-	1.172	0.71,1.95
Zero cigarettes per day	-	-	-	-
1-5 cigarettes per day	-	-	0.99	0.92,1.07
6+ cigarettes per day	-	-	1.29***	1.19,1.40
White	-	-	-	-
Hispanic	-	-	1.17***	1.10,1.25
African American	-	-	1.32***	1.25,1.39
Asian or Pacific Islander	-	-	1.56***	1.45,1.69
American Indian	-	-	1.01	0.88,1.16
Other	-	-	1.25*	1.03,1.52
Less than High School (<12y)	-	-	-	-
High School (=12y)	-	-	0.86***	0.81,0.92
Some College (13-15y)	-	-	0.76***	0.72,0.82
College Graduate (>16y)	-	-	0.72***	0.68,0.78
-2 Log Likelihood	7218264.8		7079794.5	

*p < .05, ** p < .01, *** p < .0001

Hypothesis 4 - Women who report high levels of stress during pregnancy will be more likely to have inadequate gestational weight gain.

Table 7 shows an independent association between maternal stress and inadequate gestational weight gain. Initially, the continuous measure of stressful events during pregnancy as well as a quadratic term of stress were modeled (not shown). Neither the continuous stress nor the stress squared measure was statistically significant; thus maternal stress was grouped into two outcome categories based on its distribution. A value of three or more stressful life events represented the cut point at 75% of the

distribution and was categorized as high stress. A value of two or fewer stressful life events was categorized as low stress.

Model 1 shows high maternal stress as a significant predictor of inadequate gestational weight gain ($p < .0001$). This significance disappeared after adding gestational age and maternal characteristics to the model and the odds ratio decreased from 1.12 to 0.959 (Model 2). Correlations between model variables were examined. Stress was negatively correlated with marriage (-0.32) and high levels of education (-0.25). Consequently, controlling for these two variables may account for some of the variation initially explained by stress. Thus, hypothesis four was not supported in that women who experience a greater number of stressful life events during pregnancy do not have an increased risk of inadequate gestational weight gain. The results indicate that, once sociodemographic and health behaviors as well as weeks of gestation of the infant are considered, the odds of inadequate gestational weight gain are no longer higher in women with high stress compared to those with low stress.

Model 2 also shows an association between several maternal and infant characteristics and inadequate gestational weight gain. Mothers who were 35 years or older had an elevated chance of inadequate gestational weight gain when compared to mothers 34 years or younger (OR = 1.11, $P<0.0001$, 95% CI: 1.05, 1.17). Mothers who gave birth early had odds of inadequate gestational weight gain that were 2.03 times the odds for mothers who gave birth after 36 weeks gestation ($P<0.0001$, 95% CI: 1.93, 2.14). Women who attended 80% or more or 50-79% of expected prenatal visits were 38% and 30%, respectively less likely to experience inadequate gestational weight gain ($P<0.0001$) when compared to women with inadequate prenatal care. Mothers with

gestational diabetes and Mothers with hypertension were 33% more likely and 29% less likely, respectively to experience inadequate gestational weight gain compared to mothers with no medical problems. Mothers with at least one child had as much as a 41% elevated chance of inadequate gestational weight gain when compared to women with no previous live births (P<0.0001, 95% CI: 1.34, 1.49). Mothers who smoked 1-5 cigarettes on an average day during the last three months of pregnancy had an elevated chance of inadequate gestational weight gain when compared to non-smokers (OR = 1.29, P<0.01, 95% CI: 1.19, 1.40). Asian mothers followed by Black, Other Race, and Hispanic mothers had an increased chance of inadequate gestational weight gain when compared to White mothers (P<0.01). There was a declining risk of inadequate gestational weight gain with increasing maternal education (P<0.01).

Table 7. Stressful Events During 12 Months Before Delivery and Inadequate Gestational Weight Gain

	Model 1		Model 2	
	OR	95% CI	OR	95% CI
Maternal and Infant Characteristics				
1-2 Stresses during pregnancy (Ref)	-	-	-	-
3-13 Stresses during pregnancy	1.12***	1.08,1.17	0.96	0.96,1.05
Advanced Maternal Age (>34 years old)	-	-	1.11**	1.05,1.17
Prematurity(<36 weeks)	-	-	2.03***	1.93,2.14
Inadequate prenatal care (< 50% of visits)	-	-	-	-
Intermediate prenatal care (50-79% of visits)	-	-	0.70***	0.65,0.75
Adequate prenatal care (>80% of visits)	-	-	0.62***	0.59,0.66
Married	-	-	1.00	0.95,1.05
Single or Divorced	-	-	-	-
Gestational Diabetes	-	-	1.33***	1.21,1.47
Hypertension	-	-	0.71***	0.62,0.78
Zero previous live births	-	-	-	-
One previous live birth	-	-	1.30***	1.25,1.37
2+ previous live births	-	-	1.41***	1.34,1.49
Zero drinks per week	-	-	-	-
1-3 drinks per week	-	-	0.98	0.91,1.06
4-6 drinks per week	-	-	1.24	0.83,1.87
7+ drinks per week	-	-	1.172	0.71,1.95

Zero cigarettes per day	-	-	-	-
1-5 cigarettes per day	-	-	0.99	0.92,1.07
6+ cigarettes per day	-	-	1.29***	1.19,1.40
White	-	-	-	-
Hispanic	-	-	1.17***	1.10,1.25
African American	-	-	1.32***	1.25,1.39
Asian or Pacific Islander	-	-	1.56***	1.45,1.69
American Indian	-	-	1.01	0.88,1.16
Other	-	-	1.25*	1.03,1.52
Less than High School (<12y)	-	-	-	-
High School (=12y)	-	-	0.86***	0.81,0.92
Some College (13-15y)	-	-	0.76***	0.72,0.82
College Graduate (>16y)	-	-	0.72***	0.68,0.78
-2 Log Likelihood	7218264.8		7079794.5	

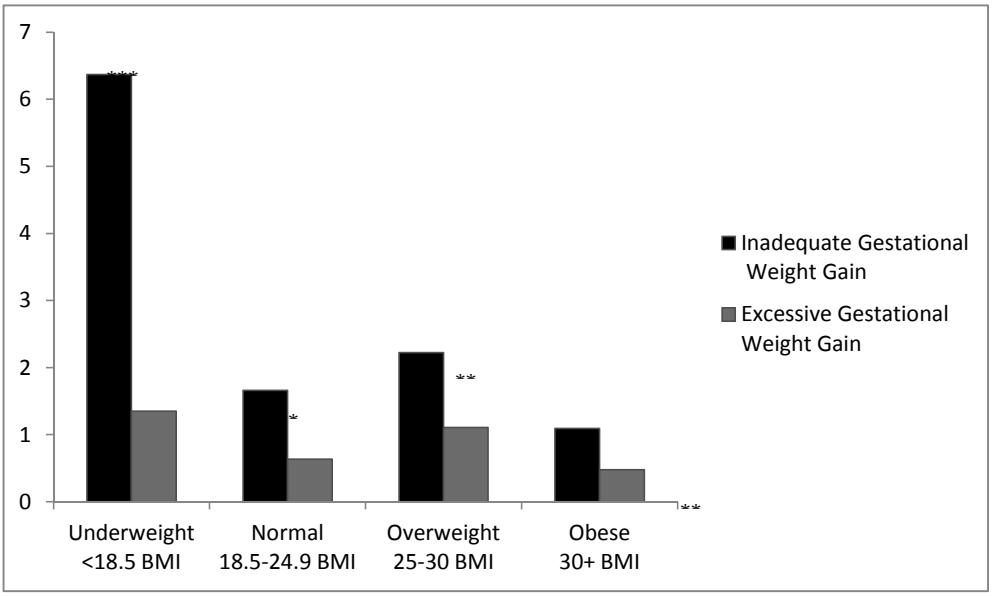
*p < .05, ** p < .01, *** p < .0001

Hypothesis 5 - The effect of gestational weight gain will depend upon pre-pregnancy BMI.

The interaction between inadequate gestational weight gain and pre-pregnancy BMI and their effects on infant mortality were explored (Figure 3). The significant p-Value of <0.0001 for inadequate gestational weight gain and underweight prepregnancy BMI as well as <0.05 for weight gain beyond the recommended range and obese prepregnancy BMI suggests pre-pregnancy BMI is a moderator for the association between weight gain and infant death (not shown). Women with inadequate gestational weight gain had a higher risk of infant death across all weight gain categories; however, the influence of weight gain on the risk of infant mortality depended on the mother's pre-pregnancy BMI. For underweight women, inadequate gestational weight gain was associated with increased risk of infant death (OR=6.37). The association was less pronounced, but present, in normal weight women (OR=1.66). In overweight women, inadequate gestational weight gain also was associated with greater infant mortality (OR=2.22). In obese women, inadequate gestational weight gain did not reach

significance (OR = 1.09, *P*<0.71, 95% CI: 0.69, 1.74), but weight gain above the recommended range was associated with a 52% decreased likelihood of infant death compared to weight gain within the normal range (OR = 0.48, *P*<0.01 CI: 0.30, 0.76). The results indicated a generally declining risk of infant mortality with increasing BMI, but beginning pregnancy underweight conferred a substantial increased risk.

Figure 3 Odds Ratios for Infant Mortality by Pre-pregnant BMI

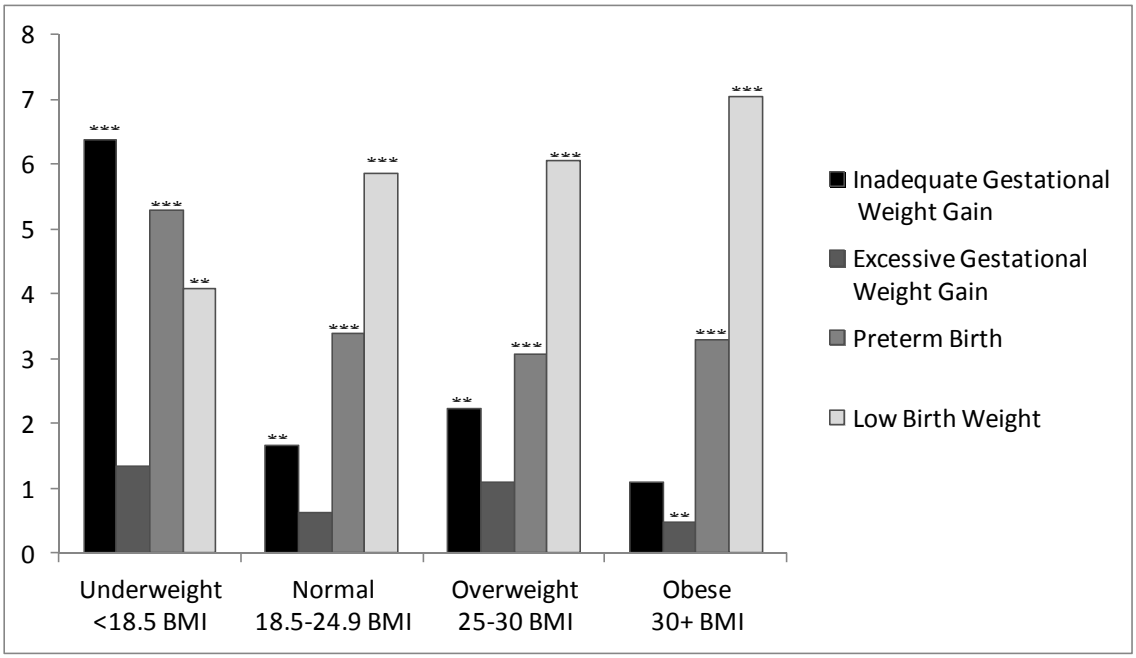


***Note.* Includes controls for gestational age and maternal characteristics. Mothers with normal pre-pregnancy BMI served as reference group.**
***** p < .001; ** p < .01; * p< .05**

Compared with women in the reference group, underweight women also had elevated risks of infant mortality associated with preterm delivery (OR = 5.30, *p*<0.0001, 95% CI: 1.85, 15.12) and low birth weight (OR = 4.08, *p*<0.01, 95% CI: 1.30, 12.84) (Figure 4). Across the normal, overweight and obese strata, the effect of preterm birth and low birth weight on infant mortality was not significantly different. Newborns who were born preterm had odds of infant death that were three times those of infants born

full term (*P*<0.0001). Newborns weighing less than 2,500g had odds of infant death on the order of five to seven times those of infants of normal birth weight (*P*<0.0001). The associations did not change after adjustments for maternal race-ethnicity, education, parity, marital status (not shown), or after exclusions for diabetes, hypertension, smoking, and drinking. The results are shown on the same graph as gestational weight gain to demonstrate the substantial influence of inadequate weight gain on infant mortality for underweight women, compared with the risk from preterm birth and low birth weight.

Figure 4 Odds Ratios for Infant Mortality and Adverse Birth Outcomes by Pre-pregnant BMI



Note. **Includes controls for gestational age and maternal characteristics. Mothers with normal pre-pregnancy BMI served as reference group.**
***** P < .001; ** p < .01; * p< .05**

Birth Cohort Linked Birth-Infant Death Data File (Cohort Linked File) Analysis

Among infants in the cohort linked file, a total of 2,046,725 had complete information on the variables in the model. Mothers in the sample had a mean age of 27.4 years and the age at delivery ranged from 12 to 50 years. The mean gestational weight gain was 30.39 lbs. Nearly 32% of mothers experienced inadequate weight gain, 50.2% gained the recommended amount of weight, and 18.12% gained more than recommended. The majority of the study sample was white (62.2%), followed by 16% Black, 15.9 % Hispanic, 4.7% Asian or Pacific Islander, and 1.4% American Indian. The majority of the sample also had a high school education (30.08%), followed by 28.86% with a college degree, and 22% who attended some college; however, 18.81% of the sample had less than a high school diploma. Slightly over 86% of the sample was 34 years old or younger and 63.5% was married. Seventy-five percent of mothers attended 80% or more of their prenatal care visits and 66.6% had previously given birth to a fetus, whether or not the infant was born alive or stillborn.

The Linked Cohort File includes information from the death certificate, such as age at death and underlying and multiple cause of death, of each infant under 1 year of age who dies in the United States. The risk of infant death was quantified by day after birth up to 121 days to allow comparisons to the PRAMS dataset. A total of 9,268 infants were included in the subsample. Of the infants whose mothers gained an inadequate amount of weight during pregnancy, 0.90 % died, compared with 0.25% of those whose mothers gained a normal or excessive amount of weight. Of the infants born low birth weight, moderately low birth weight, or very low birth weight, 4.8%, 1.3%, and 22% died, respectively compared with 0.16% of those born normal birth weight. Among

infants born SGA, 1.1% died compared with .038% of those of born appropriate and large for gestational age. Table 8 shows the descriptive characteristics of mothers and infants included in the analysis.

Table 8. Descriptive Statistics of Mothers and Infants, Cohort Linked File, 2005

Variable	%
Mortality	
Surviving	99.46
Died ≤ 365 days	0.54
Died ≤ 121 days	0.46
Died < 28 days	0.32
Gestational Weight Gain	
Inadequate	31.64
Normal	50.24
Excessive	18.12
Birth weight, grams	
Normal (> 2500g)	93.63
Low (≤2500g)	6.37
Moderately Low (1500-2499g)	5.30
Very Low (<1500g)	1.07
Birth weight for Gestational Age	
SGA	10.62
AGA	77.23
LGA	12.15
Gestational Age	
Term Birth (>36 weeks)	89.09
Preterm Birth	10.91
<32 weeks	2.00
32-36 weeks	8.90
Kotelchuck Prenatal Care Utilization Index	
Inadequate (<50% of prenatal visits)	10.93
Intermediate (50-79% of prenatal visits)	13.77
Adequate (>80% of prenatal visits)	75.30
Maternal Age, y	
≤34	86.10
≥35	13.90
Maternal Education, y	
Less than High School (<12)	18.81
Completed High School (=12)	30.08
Some College (13-15)	22.21
Completed College (≥16)	28.86
Maternal Race/Ethnicity	
White	62.19
African American	15.95
Hispanic	15.86
Asian or Pacific Islander	4.61

American Indian/Alaska Native	1.38
Marital Status	
Married	63.51
Other	36.49
Diabetes during Pregnancy	
Yes	3.58
No	96.42
Hypertension during Pregnancy	
Yes	3.95
No	96.05
Number of Previous Live Births	
0	33.41
1	29.06
2+	37.53
Causes of Death for infants who died ≤ 121 days (n=9,268)	
Endocrine, Nutritional, and Metabolic Diseases	0.77
Diseases of the Genitourinary System	0.56
Disorders related to Gestation and Fetal Malnutrition	16.19
Respiratory Distress Syndrome or other conditions	9.25
Birth defects	22.39
Sudden Infant Death Syndrome (SIDS)	8.51
Other implausible causes	42.33
Mean Maternal Weight Gain	30.39 lbs
Mean Maternal Age	27.41 years
Sample Size	2,046,725

A total of 1,959,148 infants were excluded from the study as a result of missing or implausible information on weight gain during pregnancy (N=708,602), birth weight (N=519), gestational age (N= 28,582), birth weight for age (N=66,591), parity (N=22,210), maternal education attainment (N=40,418), diabetes (N= 10,788), hypertension (N=10,788), and number of prenatal care visits (N=1,318,940). A comparison of women included and excluded from the sample by two-sample *t* test analyses showed the women were similar with respect to age, marital status, previous birth, and delivering a low birth weight infant (Table 9). Excluded women were more likely to have inadequate or excessive weight gain and to be of Hispanic race. Included women were more likely to be White and have >12 years of education.

Table 9. *t*-tests for Included and Excluded Mothers in 2005 Cohort Linked File

Variable	T	Mean Difference	Standard Deviation	Diff (1-2) Std Dev	p Value
Inadequate Weight Gain	-22.32	-0.01	0.467	-0.02	<.0001
Adequate Weight Gain	105.47	0.06	0.500	0.12	<.0001
Excessive Weight Gain	105.47	-0.05	0.399	-0.13	<.0001
Hispanic Race	-406.22	-0.17	0.422	-0.40	<.0001
White Race	286.06	0.14	0.492	0.28	<.0001
Less than High School	-1332.9	-0.55	0.414	-1.33	<.0001
High School	497.38	0.20	0.392	0.51	<.0001
Some College	443.50	0.15	0.346	0.43	<.0001
College	535.92	0.20	0.379	0.53	<.0001

Hypothesis 1 - Women with inadequate gestational weight gain will be at elevated risk of infant mortality

Table 10 shows the results from a series of nested proportional hazards regression models. Model 1 displays the odds ratios for infant death associated with inadequate and excessive gestational weight gain. The reference group for the two categories included infants whose mothers had a total pregnancy weight gain within the normal range. Inadequate maternal weight gain was associated with increased odds of infant death (OR =3.39, p<0.0001, 95% CI: 3.24, 3.55), whereas weight gain beyond the recommended range was associated with a decreased risk of infant death (OR =0.80, p<0.0001, 95% CI: 0.74, 0.87). Infants born to women with inadequate gestational weight gain had odds of infant death that were 239% higher than the odds for the reference group of infants. Gaining more than the recommended weight was associated with a 19.6% reduction in the chance of infant mortality compared with weight gain within the normal range.

In Model 2, inadequate and excessive gestational weight gain remained significant after controlling for maternal and infant characteristics. The regression coefficients decreased 6.9% and 28.7%, respectively after adding controls to the model, but the significance level of <.0001 remained constant. Mothers who were 35 years or

older had an increased chance of infant death when compared to mothers 34 years or younger (OR = 1.15, *P*<0.0001, 95% CI: 1.08, 1.23). The association between Black race and infant mortality persisted. Babies of Black mothers had odds of infant death that were 67.5% higher babies of white mothers. In contrast, Native American, Asian Pacific Islander, and Hispanic mothers, women with at least one child, and women with increasing years of education had a reduced chance of infant death when compared to the referent group. Adjustments for mothers who smoked and drank during pregnancy in addition to the current covariates were also explored. A substantial proportion of data was missing on these two variables. Their inclusion did not markedly change the risk estimates of inadequate gestational weight gain and infant mortality (not shown) and were dropped from the final models so as not to create additional cases with missing information.

Gestational age was added to Model 3. Infants born to women with inadequate gestational weight gain had odds of infant death that were 2.47 times that of infants born to women with normal weight gain (*P*<0.0001, 95% CI: 2.36, 2.59). Mothers who gained more than the recommended weight were 15% less likely to experience infant death than those with weight gain within the normal range (OR = 0.85, *P*<0.0001, 95% CI: 0.78, 0.92).

Model 3 also shows an association between gestational age and infant mortality. Babies born preterm had odds of infant death that were 13.48 times the odds for babies born after 36 weeks gestation (*P*<0.0001, 95% CI: 12.90, 14.09). Consistent with previous research, Black mothers had an elevated chance of infant death when compared

to White mothers (OR = 1.33, *P*<0.0001, 95% CI: 1.27, 1.40). The declining risk of mortality with increasing maternal education also remained.

An exploratory analysis of the influence of three categories of gestational age (<33 weeks, 33-36 weeks, >36 weeks) was also performed. The sample size for a gestational age of less than 33 weeks was 41,025 and between 33 and 36 weeks was 182,269. The odds ratio for deaths to infants born to women with inadequate gestational weight gain attenuated to 1.89 (P<0.0001, 95% CI: 1.80, 1.98), but statistical significance remained (not shown).

Table 10. Association between Inadequate Gestational Weight Gain and Infant Mortality, 2005 Cohort Linked File

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Gestational Weight Gain						
Inadequate	3.39***	3.24,3.55	3.11 ***	2.97, 3.26	2.47 ***	2.39, 2.57
Normal (Ref)	-	-	-	-	-	-
Excessive	0.80***	0.74,0.87	0.74***	0.68, 0.80	0.85***	0.78, 0.92
Maternal and Infant Characteristics						
>34 years old			1.15***	1.08,1.22	1.05	0.98,1.11
Prematurity(<36 weeks)			-	-	13.5 ***	12.9,14.1
< 50% of prenatal visits	-	-	-	-	-	-
50-79% of prenatal visits			0.68 ***	0.62,0.74	1.08	0.99,1.76
>80% of prenatal visits			1.06 ***	0.99,1.13	0.99	0.93,1.05
Married			0.72 ***	0.69,0.76	0.82 ***	0.78,0.86
Single or Divorced	-	-	-	-	-	-
Gestational Diabetes			0.92	0.83,1.03	0.84 **	0.75,0.93
Hypertension			1.08	0.98,1.2	0.68** *	0.61,0.75
Zero previous live births	-	-	-	-	-	-
One previous live birth			0.83* **	0.78,0.87	0.86* **	0.82,0.91
2+ previous live births			0.92* *	0.87,0.96	0.91* **	0.86,0.95
Race/Ethnicity						
White	-	-	-	-	-	-
Hispanic			0.69 ***	0.65,0.74	0.71***	0.66,0.76
African American			1.68***	1.59,1.76	1.33***	1.27,1.40
Asian or Pacific Islander			0.65 ***	0.57,0.74	0.63***	0.55,0.72
American Indian			0.74**	0.61,0.89	0.72**	0.59,0.87
Maternal Education						
Less than High School (<12y)	-	-	-	-	-	-
High School (=12y)			0.92* *	0.87,0.97	0.99	0.94,1.04
Some College (13-15y)			0.71* **	0.67,0.77	0.81***	0.76,0.86
College Graduate (>16y)			0.56***	0.52,0.61	0.67***	0.62,0.72
-2 Log Likelihood	268092.96		265849.74		252174.1	

*p < .05, ** p < .01, *** p < .0001

Hypothesis 1a - There will be an association between inadequate gestational weight gain and infant mortality due to causes that are potentially nutritionally linked, such as disorders related to short gestation.

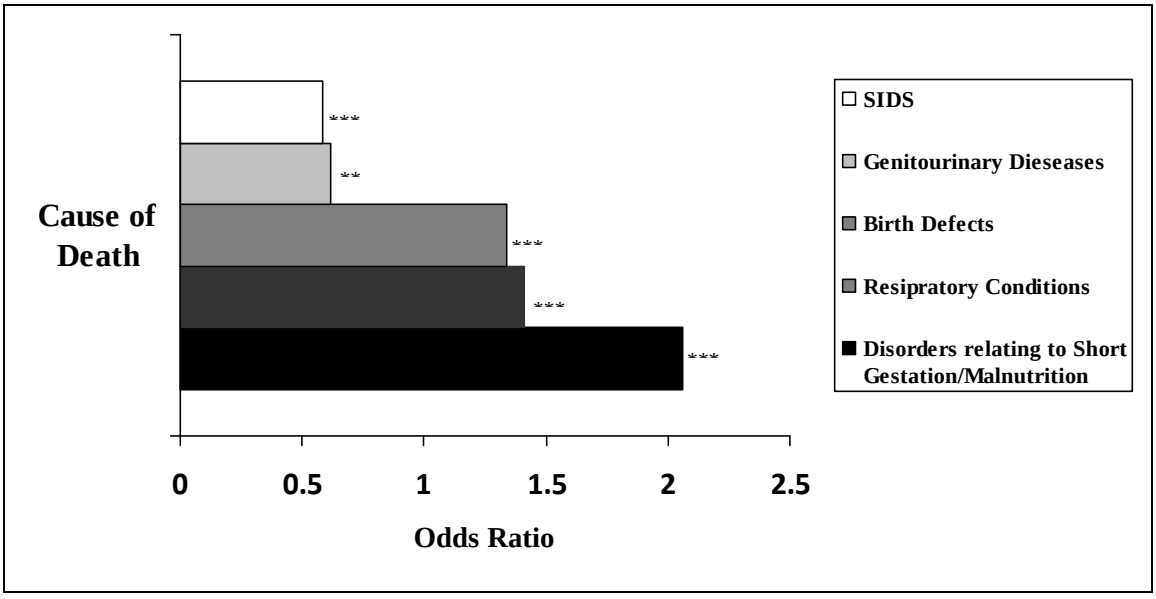
The association between inadequate gestational weigh gain and cause-specific infant death were analyzed using 9,268 infants to search for plausible mechanisms. The International Classification of Diseases, 10th revision (ICD-10) was used to group the causes of infant deaths (based on the death certificate) into six broad, etiologically related categories. Endocrine, nutritional and metabolic diseases (E00-E88; 0.77%); Diseases of the genitourinary system (N00-N95; 0.56%); Disorders related to length of gestation and fetal malnutrition (P05-P08; 16.19%); Respiratory distress syndrome or other respiratory conditions (P20-P28; 9.25%), Birth defects (Q00-Q99; 22.36%); and Sudden Infant Death Syndrome (SIDS: ICD code R95; 8.51%) were evaluated as potentially nutritionally linked causes. The odds ratios for different causes of infant death were calculated in separate proportional hazards regression models with infants who died from implausible and rare causes (n=3,923; 42.33%) among the mothers with inadequate gestational weight gain serving as the referent (Figure 4).

Among causes of death, infants of mothers of inadequate gestational weight gain had odds of infant death from disorders related to length of gestation and fetal malnutrition that were 2.06 times the infant deaths from rare or implausible causes (P<0.0001, 95% CI: 1.92, 2.12). Inadequate gestational weight gain was also associated with deaths from respiratory conditions (OR = 1.42, P<0.0001, 95% CI: 1.30, 1.54) and birth defects (OR = 1.34, P<0.0001, 95% CI: 1.25, 1.44). Mothers with inadequate gestational weight gain had approximately 40% lower risks for infant deaths from

diseases of the genitourinary system and SIDS. Deaths from endocrine, nutritional and metabolic diseases did not reach significance (OR = 0.86, *P*<0.33, 95% CI: 1.63, 1.72).

Frequency and chi-square analysis of causes of death during the neonatal and post-neonatal periods were also conducted because deaths during the first month of life are typically associated with conditions surrounding the prenatal period and post-neonatal deaths are more likely to be associated with conditions that arise after delivery. Nearly 72% of infants who died, did so within the first 28 days of life. Among causes of neonatal death, 25% of infants died of birth defects, followed by 22% due to disorders related to length of gestation and fetal malnutrition and 12% due to respiratory distress syndrome or other respiratory conditions. Among post-neonatal deaths, sudden infant death syndrome (26%) and birth defects (17%) were most prevalent (not shown).

Figure 5. Odds Ratios for Infant Cause of Death in Women with Inadequate Gestational Weight Gain



Note. **Includes controls for gestational age and maternal characteristics. Infants who died from implausible and rare causes among the mothers with inadequate gestational weight gain served as reference group.**
***** P < .001; ** p < .01; * p< .05**

Hypothesis 2 - The association between inadequate gestational weight gain and mortality will be partially mediated by having an infant who is born preterm or low birth weight

Table 11 presents the relationship of inadequate gestational weight gain and the mediators of low birth weight, preterm birth, and small for gestational age to infant mortality. In Model 1, preterm birth and birth weight were added to the model with maternal and infant characteristics found in Table 10. The coefficient for inadequate weight gain declined 27%, from 0.9039 to 0.6574 (not shown), but remained significant and positive. After controlling for low birth weight and gestational age, infants of women with inadequate gestational weight gain were 93% more likely to die than infants of women achieving the recommended range, showing the importance of these two mediators (AOR = 1.93, *P*<0.0001, 95% CI: 1.84, 2.02). Thus, low birth weight was a partial mediator for infant mortality. Newborns weighing less than 2,500 g had odds of infant death that were 10.92 times those of the infants of normal birth weight (*P*<0.0001, 95% CI: 10.33, 11.55). Babies born preterm had odds of infant death that were 294% higher than those born after 36 weeks gestation. The association between Black race and infant mortality persisted. Babies of Black mothers had odds of infant death that were 14% higher than babies of White mothers. Surprisingly, mothers with hypertension had a reduced chance of infant death when compared to mothers with normal blood pressure (OR = 0.49, *P*<0.0001, 95% CI: 0.44, 0.54).

In Model 2, very low birth weight (less than 1500 grams, or 3 pounds 4 ounces) and moderately low birth weight (between 1500 and less than 2500g) compared with normal birth weight were examined as mediators. The effect of inadequate weight gain remained significant (OR = (1.46, *P*<0.0001, 95% CI: 1.39, 1.53) after low birth weight

was introduced. Newborns weighing between 1500 and 2499g had odds of infant death that were 5.06 times the infants of normal birth weight. Infants weighing less than l500g had odds of infant death that were 74.7 times the infants born weighing >2500g. Premature babies had an increased chance of infant death when compared to full term babies (OR = 2.04, *P*<0.0001, 95% CI: 1.90, 2.19). Hypertensive mothers had a reduced chance of infant death when compared to mothers with normal blood pressure (OR = 0.41, *P*<0.0001, 95% CI: 0.37, 0.45).

In Model 3, SGA was also a significant predictor of infant mortality after controlling for maternal and infant characteristics. Infants born to women with inadequate gestational weight gain had odds of infant death that were 2.97 times the infants born to women with normal weight gain (*P*<0.0001, 95% CI: 2.83, 3.11). Conversely, mothers that gained more than the recommended weight were 22% less likely to experience infant death than those with weight gain within the normal range (OR = 0.78, *P*<0.0001, 95% CI: 0.72, 0.84). Newborns born small for gestational age had odds of infant death that were 2.50 times that of infants born of size appropriate for gestational age. Mothers 35 years or older had an increased chance of infant death when compared to mothers 34 years or younger (OR = 1.15, *P*<0.0001, 95% CI: 1.08, 1.22). Black mothers had an increased chance of infant death when compared to White mothers (OR = 1.76, *P*<0.0001, 95% CI: 1.67, 1.85). Married mothers had a reduced chance of infant death when compared to single mothers (OR = 0.75, *P*<0.0001, 95% CI: 0.71, 0.79). Mothers with at least one child had as much as a 14% reduced chance of infant death when compared to women with no previous live births (*P*<0.0001, 95% CI: 0.82, 0.91).

Consistent with previous research (IOM, 2009), mortality was strongly linked to maternal education, with increased years of school predicting lower levels of infant mortality across all models. In sum, low birth weight, preterm birth, and small for gestational age partially mediated the association between inadequate gestational weight gain and infant mortality

Table 11. Inadequate Gestational Weight Gain and Infant Mortality Mediated by Birth Weight 2005 Cohort Linked File

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Gestational Weight Gain						
Inadequate	1.93***	1.84,2.02	1.46***	1.40, 1.54	2.97***	2.83,3.11
Normal (Ref)	-	-	-	-	-	-
Excessive	0.95	0.93,1.09	1.00	0.93, 1.09	0.78***	0.72,0.84
Maternal and Infant Characteristics						
Prematurity (<36 weeks)	3.94***	3.73,4.17	2.04***	1.90, 2.19	-	-
>2500g (Ref)	-	-	-	-	-	-
<2500g (LBW)	10.9***	10.3,11.5	-	-	-	-
1500-2499g (MLBW)	-	-	5.06***	4.69,5.46	-	-
<1500g (VLBW)	-	-	74.73***	69.17, 80.74	-	-
SGA	-	-	-	-	2.50***	2.39,2.63
LGA	-	-	-	-	0.94	0.87,1.00
>34 years old	0.99	0.93,1.09	0.95	0.88, 1.01	1.45***	1.08,1.22
< 50% of prenatal visits	-	-	-	-	-	-
50-79% of prenatal visits	0.99	0.91,1.07	0.93***	0.86, 1.02	0.66***	0.61,0.72
>80% of prenatal visits	0.94*	0.88,0.99	0.86***	0.81, 0.91	1.09**	1.03,1.16
Married	0.89***	0.85,0.94	0.91***	0.86, 0.95	0.75***	0.71,0.79
Single or Divorced	-	-	-	-	-	-
Gestational Diabetes	0.95	0.85,1.06	1.04	0.93, 1.16	0.96	0.86,1.07
Hypertension	0.49***	0.44,0.54	0.41***	0.37, 0.45	0.97	0.90,1.10
Zero previous live births	-	-	-	-	-	-
One previous live birth	0.99	0.94,1.04	1.07*	1.01, 1.13	0.87***	0.82,0.91
2+ previous live births	1.05	0.99,1.10	1.14***	1.09, 1.20	0.97	0.93,1.02
Race/Ethnicity						
White	-	-	-	-	-	-
Hispanic	0.79***	0.74,0.84	0.77***	0.72, 0.82	0.7***	0.68, 0.78
African American	1.14***	1.09,1.20	0.97	0.92, 1.02	1.8***	1.67,1.85
Asian or Pacific Islander	1.12***	0.52,0.68	0.65***	0.57, 0.75	0.7***	0.57,0.75
American Indian	0.85	0.70,1.02	1.07	0.89, 1.29	0.78**	0.64,0.94
Maternal Education						
Less than High School (<12y)	-	-	-	-	-	-
High School (=12y)	0.99	0.95,1.05	0.95	0.90, 1.00	0.94*	0.89, 0.99

Some College (13-15y)	0.84***	0.79,0.90	0.68***	0.63, 0.73	0.75***	0.71, 0.80
College Graduate (>16y)	0.72***	0.67,0.77	0.79***	0.74, 0.84	0.60***	0.56, 0.65
-2 Log Likelihood	243958.02		234867.10		264539.30	

*p < .05, ** p < .01, *** p < .0001

Hypothesis 3 - Women who receive adequate prenatal care will be less likely to have inadequate gestational weight gain.

Table 12 shows the results from two logistic regression models predicting inadequate gestational weight gain. Attending more than 80% of prenatal care visits (adequate prenatal care) was protective against inadequate gestational weight gain by itself (Model 1) and remained significant after controlling for gestational age and maternal characteristics. The regression coefficient decreased by 30% after adding controls. Model 2 shows how an increase in the utilization of prenatal care reduces the likelihood of a woman gaining an inadequate amount of weight during pregnancy. Women who attended 80% or more of expected visits were 33% less likely to experience inadequate gestational weight gain (OR = 0.67, *P*<0.0001, 95% CI: 0.66, 0.67) when compared to women with inadequate prenatal care. Women who attended 50-79% of expected visits were 24% less likely to have inadequate gestational weight gain than women attending <50% of expected visits (*P*<0.0001, 95% CI: 0.75, 0.77). In addition, mothers with hypertension during pregnancy had a reduced likelihood of inadequate gestational weight gain when compared to mothers with normal blood pressure. Increasing years of education and preterm birth were also protective against inadequate gestational weight gain.

In contrast, infants born preterm (OR=1.69), mothers who delivered at age 35 or older (OR=1.14), mothers with gestational diabetes (OR=1.82), mothers with one or more children (OR=1.40), and married mothers (OR=1.10) had increased likelihoods of

inadequate gestational weight gain when compared to the referent group. Black, Hispanic, Asian or Pacific Islander, and American Indian mothers were 45%, 34%, 19%, and 32% more likely, respectively, to experience inadequate gestational weight gain when compared to White women. The results were all significant at the <0.0001 level.

Table 12 Prenatal Care and Inadequate Gestational Weight Gain, 2005 Cohort Linked File

	Model 1		Model 2	
	OR	95% CI	OR	95% CI
Maternal and Infant Characteristics				
Inadequate prenatal care (< 50% of visits)	-	-	-	-
Intermediate prenatal care (50-79% of visits)	0.65***	0.64, 0.66	0.76***	0.75,0.77
Adequate prenatal care (>80% of visits)	0.57***	0.56, 0.57	0.67***	0.66,0.67
Advanced Maternal Age (>34 years old)	-	-	1.14***	1.30,1.15
Prematurity(<36 weeks)	-	-	1.69***	1.67,1.70
Married	-	-	1.10***	1.09,1.11
Single or Divorced	-	-	-	-
Diabetes	-	-	1.82***	1.79,1.84
Hypertension	-	-	0.82***	0.81,0.84
Zero previous live births	-	-	-	-
One previous live birth	-	-	1.40***	1.39,1.41
2+ previous live births	-	-	1.59***	1.57,1.60
White	-	-	-	-
Hispanic	-	-	1.34***	1.33,1.35
African American	-	-	1.45***	1.44,1.47
Asian or Pacific Islander	-	-	1.19***	1.17,1.21
American Indian	-	-	1.32***	1.29,1.35
Less than High School (<12y)	-	-	-	-
High School (=12y)	-	-	0.87***	0.86,0.88
Some College (13-15y)	-	-	0.79***	0.79,0.80
College Graduate (>16y)	-	-	0.62***	0.61,0.63
-2 Log Likelihood	2540214.3		2472794.5	

*p < .05, ** p < .01, *** p < .0001

The following table provides a summary of the five research hypotheses in the study.

Table 13. Summary of Results

Research Hypothesis	Results
1) Women with inadequate gestational weight gain will be at elevated risk of infant mortality.	Supported. The rates of infant mortality for women with inadequate gestational weight gain were significant in all models. Specifically, the odds ratios for infant mortality for women with inadequate gestational weight gain were higher than that of women with normal weight gain.
1a) There will be an association between inadequate gestational weight gain and infant mortality due to causes that are potentially nutritionally linked, such as disorders related to short gestation.	Supported. Infants of mothers with inadequate gestational weight gain had odds of infant death from nutrition-related causes that were higher than the infant deaths from rare or implausible causes.
2) The association between inadequate gestational weight gain and mortality will be partially mediated by having an infant who is born preterm or low birth weight.	Supported. Low birth weight and preterm birth partially mediated the effect of inadequate gestational weight gain on infant mortality. The odds ratio for infant mortality declined after the addition of low birth weight and preterm birth
3) Women who receive adequate prenatal care will be less likely to have inadequate gestational weight gain.	Supported. Women who attended the majority of their prenatal visits had a lower risk of inadequate gestational weight gain than women who attended less than half of their prenatal visits. There was also dose-response with the higher proportion of prenatal visits attended lowering the risk.
4) Women who report high levels of stress during pregnancy will be more likely to have inadequate gestational weight gain.	Not Supported. Women who reported higher levels of stress did not have an elevated risk of inadequate gestational weight gain.
5) The effect of gestational weight gain will depend upon pre-pregnancy BMI.	Supported. The interaction between gestational weight gain and pre-pregnancy BMI was statistically significant. The results showed that the effect of gestational weight gain differed across BMI groups.

Chapter 6: Discussion

The current study utilized the Biomedical and Biopsychosocial models to examine how gestational weight gain influences pregnancy outcomes as well as the health and well-being of infants. Overall, the study data support the conclusion that inadequate pregnancy weight gain is associated with increased odds of infant death. The research study documents the effects of intrauterine deprivation on subsequent infant health and provides support for the growing field of the developmental origins of health and disease. Following is a point-by-point discussion of the key findings and implications.

Inadequate gestational weight gain and infant mortality

The results strongly support hypothesis one that inadequate gestational weight gain is associated with elevated risks of infant mortality. Consistent with the Biomedical model, all models predicting infant mortality from inadequate gestational weight gain showed a statistically significant relationship. The significance remained even after controlling for confounding by medical, behavioral, and interpersonal factors suggesting that inadequate gestational weight gain may indeed cause an imbalance in basic physiologic function. The magnitude of the association is consistent with the results of other studies that have linked inadequate gestational weight gain with infant mortality (Chen et al., 2009; IOM, 2009). The study also confirms earlier research that has found that only 30–40% of American women actually gain within the IOM recommended ranges (IOM, 2009; Abrams et al., 2000).

Inadequate gestational weight gain and cause-specific infant mortality

The results support Hypothesis 1a. Infants of mothers with inadequate gestational weight gain had higher risks of infant deaths from disorders related to length of gestation

and fetal malnutrition; respiratory conditions; and birth defects, controlling for maternal and infant characteristics. Previous studies have demonstrated the effects of adverse birth outcomes on infant mortality—namely, low birth weight, preterm birth, and IUGR. However, to the author's knowledge, this is the first study to examine the causes of infant death associated with inadequate gestational weight gain. The results need to be confirmed in additional studies.

The study also illuminated that neonatal mortality due to short gestation and low birth weight continues to be a public health issue. Similar to the national statistic of 25%, prematurity and its complications caused about 22% of neonatal deaths (Matthews, 2005). The causes of preterm birth are not thoroughly understood. In some cases, a pregnant woman may have medical problems, pregnancy complications, or poor health behaviors that increase her risk of delivering prematurely. However, more often preterm labor develops in pregnancies that have been problem-free. Although infant deaths due to prematurity are still too common, the outlook for premature babies is improving. Surfactant and other treatments are saving more premature babies after birth; and treatment before birth can sometimes prevent or lessen the complications of prematurity (March of Dimes, 2010).

Inadequate gestational weight gain and the mediators of low birth weight, preterm birth, and small for gestational age

Hypothesis 2 was partially supported in that the association between inadequate gestational weight gain and the odds of infant death declined after the inclusion of birth weight. However, although birth weight explained some of this effect and was itself strongly associated with infant death, inadequate maternal weight gain was a significant

predictor of infant death even after adjusting for gestational age and low birth weight. This supports the proposed premise that the model in which increased caloric intake increases maternal weight and maternal weight, in turn, increases fetal weight, is likely to be more complex. As demonstrated, the effects of gestational weight gain may have long-term effects on the infant without any alterations of fetal growth or length of gestation. Large prospective studies that provide data on the direct associations of gestational weight gain with various health outcomes in the offspring are needed.

Prenatal care and inadequate gestational weight gain

In hypothesis 3, the receipt of adequate prenatal care services as protective against inadequate gestational weight gain was supported. Results suggest that for mothers who attend more than 80% of prenatal care visits, there is a 33% reduced risk of gaining less than the recommended amount of weight during pregnancy compared to women with inadequate prenatal care. The Kotelchuck Index was used in both the PRAMS and Cohort Linked File to measure adequacy of prenatal care utilization. The index uses the time when prenatal care was initiated and the number of prenatal visits from when prenatal care began until delivery to classify the adequacy of received services. The underlying assumption is that the earlier prenatal care begins, the better. The number of prenatal visits is compared to the expected number of visits for the period between when care began and the delivery date. The expected number of visits is based on the American College of Obstetricians and Gynecologists (2007) prenatal care standards for uncomplicated pregnancies. The index defines adequate prenatal care as a score of 80% or greater, or the sum of the Adequate and Adequate Plus categories.

Mothers who attended 50-79% of expected visits were 24% less likely to gain less than the recommended amount of weight. This finding has meaning for health care providers and public health researchers. It confirms that delayed or infrequent prenatal care is better than none; however the evidence is clear that mothers who begin prenatal care after the first trimester are at a higher risk for poor pregnancy outcomes (IOM, 1990).

Further research is needed to better understand why there is not much difference in the odds of inadequate gestational weight gain among women who completed 50-79% of recommended prenatal visits and women who attended 80% of visits. The similarity could perhaps be related to the timing of weight gain during pregnancy. Pregnant women typically gain 4.0-8.8 lbs during the first trimester (IOM, 2009). According to the new IOM recommendations, women should gain 0.5-1.0 lbs per week in the second and third trimesters of pregnancy depending on pre-pregnant BMI. It is possible that corrective counseling could have been provided when beginning prenatal care which allowed women to achieve the appropriate amount of weight prior to delivery. Further, the Kotelchuck Index also depends on the accuracy of the patient or health care provider's recall of the timing of the first visit and the number of subsequent visits, thus there potentially could be limitations in the measurement of adequacy of prenatal care. A higher proportion of women who attended 80% or more of prenatal visits may have also done so because they experienced complications (adequate plus or intensive utilization is defined as prenatal care begun by the fourth month and 110% or more of expected visits). This could offset the positive effect of a greater proportion of visits. Finally, it is also

important to note that the study had a large number of cases of missing data on prenatal care.

Stressful life events and inadequate gestational weight gain

Hypothesis 4 was not supported. The study failed to find an association between high maternal stress and inadequate gestational weight gain after controlling for maternal and infant characteristics. There is a lack of consistent evidence in support of a relationship between stress and gestational weight gain. The impact of stress on gestational weight gain may be underestimated as a result of limitations in assessment measures (IOM, 2009). The area of research is complicated by cross-cultural and sub-cultural differences in the perception and meaning of individual psychosocial characteristics or states, and thus by the related issue of culturally appropriate measurement tools that are suitable for use in the clinical setting (Hickey, 2000). For example, likely explanations for the lack of association between maternal stress and low prenatal weight gain among women of different racial and socioeconomic groups may involve different perceptions of what constitutes psychosocial stress; variation in biological and behavioral responses to specific stressors; variation in the availability of stress mediators; or the existence of entirely separate mechanisms for low prenatal weight gain. Examples of the latter would include differences in the nutrition-related content of prenatal care provided to minority women (Chassan-Taber et al., 2008).

The lack of association of could also perhaps be related to the emerging concept of Reproductive Social Capital. Reproductive Social Capital is defined as those features of social organization (e.g., networks, norms, and social trust) that facilitate coordination and cooperation to promote reproductive health within a community (Jones et al., 2010).

With respect to pregnancy, it describes the degree of social connectedness of the pregnant woman to her community and is characterized not only by how many neighbors a pregnant woman can turn to for help and support, but also by how a community treats a pregnant woman (Jones et al., 2010). The relationship between lower adverse birth outcome rates and communities with high levels of social cohesion, civic participation, and social trust remains largely unexplained. One possible explanation is that reproductive social capital does at the neighborhood level what social support does at the interpersonal level—buffers the impact of stress on birth outcomes. Lack of child care or transportation to a prenatal care appointment can be stressful; but the ability to count on one's neighbors for child care or a ride to the health care provider's office buffers the impact of that stress (Lu & Lu, 2007).

Perceived stress has been associated with adverse birth outcomes, such as low birth weight and preterm birth, when high levels are found in pregnant women (Hogue, Hoffman and Hatch, 2001). Acute stressors, typically the types measured in the stressful life events scale in PRAMS, have also been linked to adverse birth outcomes (Hogue, Hoffman and Hatch, 2001). The evidence for the role of stress as a determinant of gestational weight gain is mixed and inconclusive (IOM, 2009). More studies that describe the relationship between modifiable psychosocial risk factors and adequacy of total weight are needed.

Effects of pre-pregnancy BMI and gestational weight gain on the risk of infant death

The results strongly support the hypothesis that the effect of gestational weight gain on infant death depends upon pre-pregnancy BMI. Among women with inadequate gestational weight gain, there was a generally declining risk of infant death with

increasing pre-pregnancy BMI. The results confirm the IOM findings and suggest that having access to stored fat may protect against mortality when weight gain is less than optimal. Higher risks of infant death among underweight women with inadequate gestational weight gain was expected as similar results have been found in infant birth weight (Chen, 2009). What was not anticipated, however, was overweight (but not obese) women with inadequate weight gain would also have higher risks of infant death than women of normal weight gain.

A physiologic difference in how overweight women mobilize their fat stores to enhance fetal development is suspected as a cause, but any direct evidence is lacking. Insulin sensitivity combined with other mechanisms may also be responsible for deleterious outcomes in infants. Weight gain in pregnancy is partly a gain in adiposity, which is accompanied by a state of relative insulin resistance, among other metabolic alterations (King, 2006). In overweight and obese pregnant women, insulin resistance is more severe than in normal weight women and substantially raises the risk of gestational diabetes. Increased fetal production of anabolic hormones and growth factors, in combination with the increased levels of glucose, lipids, and amino acids that are typical of diabetes can increase the risk for neonatal complications (Catalano et al., 2003). The extent to which this metabolic dysfunction has relevance to infant mortality is unclear, but support of this hypothesis can be found in animal experiments. For example, Samuelsson et al. (2008) reported that maternal obesity in rats resulted in cardiovascular and metabolic dysfunction in their offspring which was not present in the offspring of lean dams (IOM, 2009).

Weight gain beyond the recommended range among obese women also presented an unexpected statistically significant association with infant survival. Infants of obese mothers with high gestational weight gain had a reduced risk of mortality. Further exploration is necessary to determine why weight gain beyond the recommended range had a protective effect as previous research has found obese pre-pregnancy BMI is one of the strongest modifiable risk factors for poor birth outcomes (i.e. birth defects, still birth, LGA, etc.) (Siega-Riz & King, 2009). The findings could perhaps be related to obese women being able to provide a continuous supply of nutrients to their fetus and differences in biologic and metabolic processes. In addition, the fact that pre-pregnancy BMI was ascertained by recalled height and weight which is subject to misreporting. Investigators frequently point out data showing women tend to underreport their weight and overreport their height, and that the underreporting of weight becomes exaggerated as BMI increases (Bodnar et al., 2010). This presents an opportunity to improve the reporting and collection of BMI data, to allow for a more accurate assessment of how BMI affects infant mortality rates. Investigators designing research studies should consider measuring women's weight and height before pregnancy and then again at the first prenatal visit.

The study found an interaction between maternal BMI and weight gain on the risk of infant death that needs to be confirmed in other studies. With overweight and obese women becoming the fastest growing segment of the U.S. population, discussions for optimal weight gain should now include the risk of infant mortality for overweight women (but not obese) in addition to preeclampsia, cesarean section, and large- and small-for gestational age infants.

Risk factors for gestational weight gain and infant death

A number of sociodemographic, behavioral, and medical factors both during and before pregnancy were considered as potential risk factors for maternal weight gain and infant mortality. Sociodemographic factors included level of education, marital status, maternal age, and maternal race. Cigarette smoking and alcohol consumption were explored as behavioral factors. Medical factors included previous live births, diagnosis of diabetes, and mothers with chronic hypertension, preeclampsia, or pregnancy-induced hypertension. The large sample sizes in the two datasets permitted an informative assessment of risk factors in the study.

Adverse birth outcomes have been strongly associated with socioeconomic status (SES) (Abu-Saad, 2010). SES is a complex construct that has been used to define social status and usually includes measures of income, occupation, or educational attainment. Educational level has been the strongest and most consistent SES predictor of health. A low educational level limits access to jobs and other social resources, and thus increases the risk of poverty. Kramer et al. (2000) used the conceptual model of causal pathways to explain the effects of social disparities on health. Society-level determinants (e.g., income levels) are considered antecedent to, or "upstream" from, individual-level exposures and behaviors (Kramer et al., 2000). The results for infant mortality associated with education show decreasing statistically significant rates for mothers with a high school education, some college, or a college degree. For mothers who did not graduate from high school, there appears to be increased odds of infant mortality.

Studies of maternal dietary intake have also confirmed the importance of SES. In a study of the diet quality of pregnant Kenyan women, Kamau-Mbuthia and Elmadfa

(2007) reported that SES (e.g., education and employment) were important predictors of nutrient intake and diet quality. Among rural Indian women, intake of dairy products was strongly associated with SES and was also associated with birth size (Abu-Saad, 2010).

Consistent with the biopsychosocial model, marital status appears to offer protection against infant mortality through social support and resources. Almost 64% of the mothers were married. Marriage was statistically significantly associated with decreased risk of infant death across all regression models in the Cohort Linked File. Several studies have found married women are more likely to gain within the IOM recommended weight gain range than single or separated/divorced women (Olsen and Strawderman, 2003). The data in this study supports the theory that partners can have a positive influence on maternal health behaviors during pregnancy (Teitler, 2001). More research is needed to better understand the impact increasing the role of partners can have on pregnancy outcomes and the health of families.

Increased maternal age is also associated with higher risks for adverse pregnancy outcomes, including stillbirth, low birth weight, preterm birth, and small-for-gestational age (IOM, 2009). In addition to poor outcomes, pregnancy in older women is associated with increased risk for comorbidities and pregnancy complications such as hypertension, diabetes, placenta previa, and placental abruption (Joseph et al., 2005). Higher rates of infant mortality were found among mothers 35 years of age and over. Maternal age is an important indicator of gestational weight gain. Researchers have reported that gestational weight gain is generally higher among adolescents and lower among women > 35 years of age (IOM, 2009).

The results supported previous research that has shown disparities in infant mortality according to maternal racial or ethnic group. Infants born to Black women were at especially high mortality risk. Models developed to explain this disparity have integrated explanations such as the "weathering" hypothesis and the life course perspective to elucidate the effects of racism, discrimination, and the stress accompanying those experiences that are unique to the lives of African-American women (Hogue, Hoffman and Hatch, 2001; Geronimus, 1992; Lu & Halfon, 2003).

Smoking during pregnancy, use of alcohol, and the number of times a woman has given birth have been well-established as risk factors for adverse birth outcomes. In most cases there has been little research about how gestational weight gain may interface with these risk factors to either elevate or reduce risks of adverse birth outcomes. The few extant studies of smoking, maternal energy intake, and SGA seemed to suggest a lack of association, but no other aspect of the diet was evaluated. Other studies have suggested that women who are pregnant for the first time (primiparous women) have smaller infants than women who have given birth to more than one child and that they gain more weight during pregnancy (Kleinman, 1990). This means that primiparous women must gain more weight during pregnancy to have an equally low risk of an SGA birth. The trade-off between lowering the risk of having an SGA infant and increasing the risk of excessive weight gain appears to occur at a different gestational weight gain value for primiparous and multiparous women (IOM, 2009). This is a novel finding that warrants additional study.

Summary

This study contributes to the body of research addressing gestational weight gain and prepregnancy BMI. It fills an important gap in the literature by examining how maternal weight gain affects infant viability; underscores the influence of prenatal care on birth outcomes; provides further understanding of the influence of psychological factors on gestational weight gain; and presents opportunities for further research. The findings of the study also suggest that maternal nutrition is vital to infant health.

Thus, researchers need to begin focusing on maternal nutritional status throughout the periconceptional, pregnancy, and lactation periods as a continuum that affects maternal, fetal, and infant health (Abu-Saad & Fraser, 2010). This approach has implications for when and how maternal dietary intake is assessed, when interventions are begun, and how study results are interpreted.

Biologic Plausibility

The existence of plausible biological mechanisms is one criterion for establishing causal relationships between gestational weight gain and infant health outcomes based on observational data. The following discusses the causes of death examined in this study as potential mechanisms linking gestational weight gain to infant mortality.

As mentioned in chapter three, early developmental programming could potentially influence gestational weight gain. Developmental, or in utero, programming refers to physiological, metabolic, or behavioral adaptations resulting from exposure or lack thereof to hormones, nutrients, stress, and other agents at critical periods during embryonic or fetal development (IOM, 2009). There is evidence that developmental

programming influences patterns of fetal growth. This could explain why infants with inadequate gestational weight gain were at highest risks of deaths to due to disorders related to length of gestation and fetal malnutrition. Birth weight is affected by the balance of macronutrients in the maternal diet (Moore et al, 2004). Imbalances of protein and carbohydrate intake during pregnancy have been associated with reduced birth weight, altered metabolism, and increased blood pressure (DeBoo & Harding, 2006). By adapting to a limited supply of nutrients, the human fetus trades off the development of non-essential organs, in favor of more essential organs such as the brain. These developmental adaptations can permanently change an organ's function and lead to a number of diseases developed throughout life (Lu & Lu, 2007).

In addition, low gestational weight gain and low pre-pregnancy body mass index (BMI) have been linked to greater risk for preterm birth. A number of nutrient deficiencies have been implicated in the pathogenesis of preterm birth, but a causal relationship has not been firmly established (Lu & Lu, 2007). Research studies have linked nutritional factors to accelerated maturation of the fetal hypothalamic-pituitary-adrenal axis and and/or increased oxidative stress, suggesting that a direct causal relationship is a biologic plausibility. However, important questions regarding the timing, threshold, content, and interactions in these pathways still remain to be answered (IOM, 2009).

Inasmuch as inadequate gestational weight gain has been linked to preterm birth, it is plausible that gestational weight gain may also be linked to respiratory distress syndrome or other respiratory conditions, given that prematurity is a risk factor for suboptimal lung function and resulting neonatal respiratory morbidity (Dombkowski et

al., 2008). For instance, in a case-control study of 262 African American 4- to 9-year-old children receiving care at a hospital based clinic, Oliveti et al. (1996) used gestational weight gain and child medical records to examine pre- and perinatal risk factors for asthma. Multivariate logistic regression analyses showed that the odds of asthma were 3.42 times higher for children of women who gained less than 20 total pounds during pregnancy compared to children of women who gained more.

Another way that gestational weight gain could lead to the propensity for respiratory conditions in infants is through alteration of the developing fetal immune system. For example, Willwerth et al. (2006) found that both inadequate and excessive gestational weight gain were associated with increased cord blood mononuclear cell proliferative responses to stimulation (OR = 2.3 and 2.6, respectively), compared to adequate gestational weigh gain. In that study, maternal smoking was the major determinant of the response (IOM, 2009).

Some types of developmental programming may be mediated through epigenetic events— chemical modifications to the DNA and histone proteins that influence gene expression and manifest as phenotypic differences (IOM, 2009). Epigenetic events begin early after fertilization, hence the reason why nutritional deficiencies during organogenesis can cause birth defects in susceptible individuals. Organogenesis occurs early in pregnancy (e.g., the heart begins to beat at 22 days post-conception) and nutritional deficiencies in early pregnancy can be harmful to the developing fetus. For example, it is generally accepted that inadequate intake of folic acid, before and during early pregnancy, is associated with an increased risk of spina bifida, anencephaly, and other neural tube defects (Lu & Lu, 2007). The mechanism underlying the association

between folate deficiency and brain and central nervous system defects has not been established, but has been hypothesized to involve disruption of nucleic acid synthesis and various methylation reactions (Lu & Lu, 2007). Nutrient deficiencies other than folate, in particular B vitamins, vitamin K, magnesium, copper, and zinc have also been linked to other birth defects (Keen et al, 2003). Nutritional excesses, such as vitamin A, have also been to birth defects.

It is also critical to recognize that gestational weight gain, or any nutritional factor that alters the in utero environment, may influence infants without any alterations of fetal growth or length of gestation. A relationship between gestational weight gain and sudden infant death syndrome (SIDS) has not been established. However, maternal malnutrition is a risk factor for low birth weight, which in turn is a risk factor for SIDS (Sullivan et al., 2001). Micronutrient deficiencies during pregnancy, such as magnesium deficiency, have been linked to sudden infant death syndrome (Durlach, 2004). Because SIDS has been attributed to numerous mechanisms (i.e. cardiovascular, respiratory and infectious diseases), evidence is far from conclusive. This study found no positive link between inadequate gestational weight gain and SIDS.

The biologic plausibility of these mechanisms have been well established with animal studies; however the impossibility of obtaining experimental data from randomized controlled trials in humans impedes efforts to determine how much of any observed association is causal. The animal models have demonstrated that altering the supply of nutrients, hormones, and oxygen to the growing fetus can produce effects beyond birth and much of the research has focused on outcomes such as fat distribution,

insulin sensitivity, glucose intolerance, and blood pressure. All of these outcomes are related to the leading causes of morbidity in the United States and ultimately, mortality.

Strengths and Limitations of Analyses

One of the major strengths of the proposed analyses is the use of two high quality population-based data sets from the CDC. The Birth Cohort Linked Birth - Infant Death Data File is a nationally representative dataset and has a sample size large enough to ensure sufficient power for relatively rare outcomes such as post neo-natal death. PRAMS utilizes a standardized data collection methodology and allows for the calculation of pre-pregnancy BMI and the evaluation of weight gain adequacy at delivery which is an improvement over previous studies that have analyzed total gestational weight gain, older datasets, or geographically restricted samples.

However, several limitations of the data must be noted. First, the study relied solely on self-reported prepregnancy BMI and final pregnancy weight and thus, gestational weight gain data could have been subject to misclassification error. Self-reported data on behavioral and medical factors may have also been prone to information bias. Women may not accurately recall events prior to or during the early part of their pregnancies; be hesitant to report behaviors perceived to be unhealthy; or recall their pregnancy differently based on whether their newborn survived. While self-reported height and weight could have been under- or over-reported, some studies have shown self-reported weight to be highly correlated and within three pounds of the actual measured weight (Jeffrey, 1996). Nonetheless, greater underreporting of weight has been documented at higher BMI levels, with differences in agreement by race (IOM, 2009).

Thus, errors in body mass index could have diminished the effect of body mass index on infant mortality, particularly for heavier women.

Second, although efforts were made to control for several known confounders, dietary habits and physical activity behaviors could not be addressed. These two factors could have biased results, as diet composition and regular physical activity can potentially influence total gestational weight gain. In addition, prepregnant BMI and weight gain during pregnancy served as a proxy for maternal nutrition. Given the role of nutrition during pregnancy nutrition in birth outcomes, information on nutrition intake would have ideally been included.

Third, evidence has shown that the rate of gestational weight gain during the course of pregnancy may be as or more important to adverse pregnancy outcomes than the total amount of gestational weight gain (Langford et al., 2008). The information provided in the data set did not lend itself to assessing the rate of gain during pregnancy or the risk of infant mortality among women with inadequate weight gain by trimester.

Fourth, the causes of infant death were derived from death certificates which could potentially contain errors. The classification by broad causes of death may have also decreased the precision of estimation.

The methodological limitations noted are not unique to the present study, but rather reflect the limitations of existing data sources. There are currently not, however, other large datasets that include more detailed data on pregnant women's and their infant's experiences, behaviors, health status, psychosocial factors, and birth outcomes than the two examined. The nationwide adoption of the revised U.S. Certificate of Live Birth may yield more useful information for maternal weight gain research in the very

near future. Until then, these datasets will continue to be the definitive source of information on U.S. births and infant mortality for federal agencies and researchers.

Public Health Program Implications

The results of this study have meaningful public health and clinical implications. In light of the fact that most U.S. women do not gain weight within the IOM-recommended ranges and that more prenatal visits are associated with a lower likelihood of inadequate weight gain, the data provide a strong rationale to develop effective interventions that facilitate providing child bearing women with BMI-specific gestational weight gain information.

To stem the tide of inadequate gestational weight gain, women should not only gain within the ranges recommended in the new 2009 guidelines, but also not be underweight when they conceive. However, the diet revolution and idealized images of thin American women could make it difficult for women to meet the guidelines for gestational weight gain. For example, one diet trend is the increase in consumption of foods with low nutrient density. This has special implications for pregnancy, which requires modest increases in energy but greater increases in vitamin and mineral intake. Also, national data indicate that a high proportion of women of childbearing age fail to meet current guidelines for physical activity. Services directed toward improvements in both of these behaviors could contribute toward helping women enter pregnancy at a healthy weight. They could also contribute toward helping women meet the proposed guidelines for gestational weight gain.

This reinforces the importance of preconceptional counseling which in addition to providing advice to women about discontinuing unhealthy behaviors such as tobacco use and alcohol consumption, should also include counseling about improving the quality of their diets and increasing physical activity. Integrating nutrition counseling into pre- and interconceptional care can be an important approach to achieving optimal pregnancy outcomes for both mother and infant.

For women who have already conceived, a number of interventions should be implemented while caring for the patient. Health care providers should provide counseling tailored to women's needs including recording prepregnancy height and weight, setting a weight gain goal together early in pregnancy, charting women's weight gain throughout pregnancy, and sharing results so women are aware of their progress . In addition, women should be provided with individualized advice about both diet and physical activity (ACOG, 2002). When deemed necessary, such advice should come from qualified professionals including dietitians and physical activity specialists. These providers could continue to provide assistance through the postpartum period to help women return to their prepregnancy weight within the first year and better their chance of returning to a normal BMI value at the time of a subsequent conception. Particular attention should be given to maternal age. Several studies report lower mean gestational weight gain among older women (>35 years old), compared to women <34 year and younger.

The findings confirm that the seeds for low weight gain can be sown before pregnancy and follow women through gestation. As such, underweight women should be targeted in the development of programs because of the potential to modify health

outcomes. Normal weight women had lower risks of infant mortality in the study despite having inadequate gestational weight gain and even when compared to overweight women. This suggests there are important but unclear protective factors derived from conceiving at the appropriate weight.

In addition, special attention should be given to low-income and minority women, who are more likely to be at risk of consuming diets of lower nutritional value, and performing less physical activity (IOM, 2009). The low health literacy levels that characterize this group also represent a major barrier for understanding and acting upon health recommendations (IOM, 2004). The use of culturally appropriate channels and approaches to convey this information at both the individual and population level is essential (Glanz et al., 2002). This will not only enhance attempts to promote positive maternal and infant outcomes secondary to gestational weight gain among women of diverse ethnicities and socioeconomic backgrounds, it is also sensitive to family- and community level factors.

Last, in order for women and their healthcare providers to know and understand the new guidelines, they need to first know they exist. Government agencies, organizations that provide health care to pregnant women, private voluntary organizations, and medical societies that have adopted the guidelines could play a particularly important role in this education. Approaches to consider include social marketing campaigns, including questions about gestational weight gain in medical board exams or self assessment modules, and providing tools to health care providers that communicate gestational weight gain recommendations at an individual level (Haughton and George, 2008). In separate studies, Cogswell et al. (1999) and Stotland et al. (2005)

reported that a high proportion of women were either given no advice on how much weight to gain during pregnancy or were advised to gain outside of the recommended range for their prepregnant BMI value. Greater efforts are needed to educate women and health care providers about the IOM guidelines.

Public Health Policy Implications

Although coordination and cooperation between public health workers and clinical health care providers are vital to promoting adequate gestational weight gain, they must be coupled with policies and regulations enacted by the government and private sector if we are to move closer to meeting the public's health needs. The IOM was established as the health arm of the National Academy of Sciences and since 1970 has provided evidence-based standards and recommendations that have improved the quality of life of millions (IOM, 2001). The 2009 IOM guidelines appear to influence what women believe to be appropriate weight gain during pregnancy (IOM, 2009). Policies should focus on consumer education and strategies to assist practitioners and public health programs with adopting the recommended weight gain guidelines.

Another example of how policy can influence gestational weight gain is the Special Supplemental Food Program for Women, Infants, and Children (WIC). The WIC program helps maintain the health of a community by providing counseling on healthy eating, counseling for smoking cessation, and other preventive services (KFF, 2011a) . In a national evaluation of WIC programs, Rush et al. (1988) found a reversal of low weight gain in early pregnancy and greater total weight gain during pregnancy among women enrolled in WIC compared with controls. The investigators also found greater intake of

protein, iron, calcium, vitamin C, and energy among WIC participants. Policies that increase food access to low-income women could have an important impact on dietary patterns and gestational weight gain.

Policies that do not directly affect pregnant women can also have an effect on gestational weight gain. For over 30 years, evidence-based nutrition information and advice has been provided to Americans to assist them with making healthy dietary selections (USDA, 2010). The *Dietary Guidelines for Americans* detail information about the nutritional value of foods and serve as the basis for Federal food and nutrition education programs. The guidelines should be standardized and competitive food and beverage companies should be both required to adhere to and provide proof that their products have been reformulated to meet the standards. Food retailers could also be encouraged to prominently display products that meet the guidelines making it easier for consumers to make healthier product choices. Policies such as these have the potential to alter the physical environments that influence dietary behaviors. They could also have an influence on the development of healthy eating habits which are important to women during their childbearing years.

Ensuring financing of and access to health care could have a particularly strong effect on women in need of assistance with achieving the appropriate weight gain. Women with health coverage are more likely to obtain needed preventive, primary, and specialty care services, and have better access to new advances in women's health (KFF, 2011b). More than 800,000 pregnant women in the U.S currently lack health insurance coverage (KFF, 2011b). Uninsured women are more likely to have poorer health outcomes, delay or skip important preventive care than their insured counterparts, and

receive a lower standard of care when they are in the health system (Wilper et al., 2009). Moreover, babies born to mothers who received no prenatal care are five times more likely to die than those whose mothers received prenatal care (DHHS, 2006).

Policies should be enacted that offer the most potential for health care coverage for women. The *Patient Protection and Affordable Care Act* (ACA) *of 2010* is one of those policies. The ACA has brought major changes to insurance coverage, including a new provision that ensures preventive health services will be covered with no out-of-pocket costs. The law requires nearly everyone carry health insurance by 2014, through a combination of changes in private and public coverage. Insurers will no longer be allowed to vary premium rates based on gender or health status. Individuals with very low incomes (< 138% of poverty) will also qualify for Medicaid.

Medicaid is one of the largest payers of pregnancy-related services, financing between an estimated 40% and 50% of all births in the U.S. (Elixhauser & Wier, 2008). In most states, Medicaid pays for prenatal services and supplies such as prenatal vitamins, ultrasound and amniocentesis screenings, and deliveries. However, coverage for other services, such as counseling and education, are more limited and vary considerably by state (KFF, 2009). Policies should ensure comprehensive nutrition counseling is covered for Medicaid recipients, particularly because this population is at a higher risk for adverse birth outcomes.

Another long-standing challenge with Medicaid has been limited participation by private physicians, particularly specialists, largely due to low payments to physicians relative to Medicare and private insurers (Zuckerman et al., 2009). The ACA requires states to raise Medicaid reimbursement rates for primary care providers up to at least

Medicare levels, with the federal government covering the costs through 2014. There are still, however, concerns about having a workforce large enough to care for the growing insured population. Policies should be enacted that address physician and nursing shortages and ensure quality health workers.

Although Medicaid already plays a large role in maternity care, the ACA also authorizes funding to implement new home visiting programs for expectant and new parents in at-risk communities. The *Maternal, Infant, and Early Childhood Home Visiting (Section 2951)* program reduces infant and maternal mortality by enhancing prenatal, maternal, and newborn health, child health and development, parenting skills, school readiness, and family economic self-sufficiency. The program is based on previous research on home visiting, which demonstrates positive social and health benefits for expectant and new parents (Olds et al., 2004). An intervention study using nutrition advice linked with home visits by nutritionists and supplemental food was also conducted (Bruce & Tchabo, 1989). The intervention group gained significantly more weight than the control group; however, the findings may be limited by the varying gestational age of the fetus when the intervention took place (IOM, 2009). The home visiting program is in need of additional studies to determine if its practices are capable of improving gestational weight gain.

Gestational weight gain policy development offers a number of opportunities to promote health and prevent infant mortality. Stronger advocacy efforts as well as scientific research is needed to educate policymakers about the benefits of implementing cost-effective prevention efforts.

Future Research

The results of the study identified the need for future research in several areas. First and foremost, there are only a small number of published studies examining gestational weight gain and infant survival**.** More research investigating inadequate gestational weight gain and infant mortality as well as other outcomes for underweight women who are at high risk is warranted.

The 2009 IOM guidelines are based on observational data, which consistently showed that infants of women who gained within the 1990 guidelines experienced better outcomes (IOM, 2009). The new guidelines require validation, but to be useful, such studies should include randomized controlled trials (RCT) that not only modify gestational weight gain, but also include follow-up. RCT's, however, might not always be feasible. Observational and experimental studies, should therefore when practical take into account maternal nutrient status starting in the peri-conceptional period and following it through the duration of the pregnancy period.

An additional area of research would be to study the rate and timing of gestational weight gain. There is evidence that the pattern of gestational weight gain may be as or more important than the total amount gained (IOM, 2009). Current studies indicate that gestational weight gain, particularly during the second and third trimesters, is an important determinant of fetal growth, birth weight, and preterm delivery (Abrams et al., 2000; Stotland et al., 2006). New research designs should help determine in what gestational age windows weight gain is most important. This might also help to address the question of the potential for reverse causality (i.e. where low weight gain is a result of adverse events before birth that lead to SGA or preterm birth).

The inclusion of contextual factors such as cultural norms, opportunities for physical activity, attitudes toward weight gain, and access to healthy foods would also elucidate information about additional health and behavioral factors that influence gestational weigh gain. Potential protective factors such as reproductive social capital, social cohesion, and paternal characteristics should also be incorporated. Most studies use a narrow clinical approach. Comprehensive conceptual models that address individual, interpersonal, community, environmental, cultural, and policy determinants of gestational weight gain should be investigated to identify effective clinical and population-based strategies that help women meet the gestational weight gain guidelines. Future research might also explore life course and intergenerational effects and whether protective processes differ between women of different racial and ethnic groups.

It is noteworthy that few intervention studies have evaluated ways to improve the nutritional choices of women during the childbearing period (IOM, 2009). Future research should establish the characteristics of interventions that reliably assist women in improving the quality of their diets and increasing physical activity.

Finally, there is a need for better research methods than the existing body of evidence reflects. Currently available data sources are inadequate for studying U.S. trends in gestational weight gain, coupled with the fact that many lack the data to precisely replicate the IOM guidelines. All states should adopt the revised version of the birth certificate, which includes fields for pre-pregnancy weight and height, maternal weight at delivery, and maternal age at the last measured weight (IOM, 2009). Building on the importance of collaborating across health departments, states should also create

mechanisms to easily share data, thereby allowing for the more rigorous documentation of national and regional surveillance information.

In addition, further investigation into the reliability of self-reported weight by age, race, parity, and BMI is also necessary. The degree of misreport of weight gain should be studied for women of varying pre-pregnancy BMI and relative to when it is asked in gestation (e.g., early first trimester, second trimester, or at delivery). Without a thorough understanding of the reliability of self-reported weights for all women, calculations for total weight gain may well lead researchers to conclusions supported by the data but not by actual weight changes.

Conclusion

These findings suggest that women with inadequate gestational weight gain should be counseled to maintain a moderate level of gestational weight gain in order to reduce their risk for infant mortality. Inadequate gestational weight gain was a significant predictor of infant death even after adjusting for gestational age and low birth weight. Further, the observation that underweight and overweight pre-pregnancy BMI was associated with infant mortality highlights the importance of pre-conceptional counseling for women—specifically the importance of women achieving or maintaining a normal weight status prior to pregnancy. Other factors that influenced infant mortality across all models were maternal age (older mothers had higher risks), maternal education (the greater the number of years of schools, the lower the risk), and maternal race (infants born to Black women were at higher mortality risk).

This study found a possible protective effect of weight gain beyond the recommended range on infant death among obese mothers. Although the study did not

find an association between high levels of maternal stress and inadequate gestational weight gain, it did find that attending at least 50% or more of expected prenatal care visits reduced the likelihood of a woman gaining an inadequate amount of weight suggesting support and resources can modify risk factors on the pathway to infant mortality.

These findings reinforce the need to keep studying the effects of inadequate gestational weight gain on infant mortality as data improves, not only because of the importance of the outcome, but also because of the potential implications for the literature on fetal growth and preterm birth.

Appendix A – IRB Approval from the University of Maryland

UNIVERSITY OF MARYLAND
INSTITUTIONAL REVIEW BOARD

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Date: October 25, 2010

To: Sandra L. Hofferth, PhD
Professor
Department of Family Science
University of Maryland College Park

Cc: Regina R. Davis
Student
Department of Family Science
University of Maryland College Park

From: Joseph M. Smith, MA, CIM
IRB Manager
University of Maryland, College Park

Re: Request for Human Subject Research Determination

Title: "The Association Between Inadequate Gestational Weight Gain and Infant Mortality Among U.S. Infants Born 2004-2008"

The request for determination of Non Human Subject Research for the above-cited project has been reviewed by the University of Maryland College Park Institutional Review Board Office. According to the information provided, it has been determined that this project does not meet one or both of the following definitions and therefore does not require further evaluation by the University of Maryland College Park Institutional Review Board.

§46.102 - (d) *Research* means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

§46.102 - (f) *Human subject* means a living individual about whom an investigator (whether professional or student) conducting research obtains:

(1) Data through intervention or interaction with the individual, or
(2) Identifiable private information.

If the scope of your project changes and meets one of the above definitions, an IRB protocol must be created and submitted to the UMCP IRB for approval. For further clarification, questions or concerns please contact the IRB Office at 301-405-0678.

References

Abrams, B., Altman, S., & Pickett, K. (2000). Pregnancy weight gain: Still controversial. *American Journal of Clinical Nutrition,* 71, 1233S–1241S.

Abrams, B., Newman, V., Key, T., & Parker, J. (1989). Maternal weight gain and preterm delivery. *Obstetrics & Gynecology,* 74, 577–583.

Abu-Saad, K, Fraser, D. (2010). Maternal Nutrition and Birth Outcomes. *Epidemiologic Reviews,* vol. 32, no. 1, pp. 5-25, 2010.

American Academy of Pediatrics and the American College of Obstetricians and Gynecologists.(2007). Guidelines for Perinatal Care; 6th ed. Elk Grove Village, Illinois: AAP; Washington, DC: ACOG.

American College of Obstetricians and Gynecologists (ACOG). (2009). Evaluation of stillbirths and neonatal deaths. *ACOG Committee Opinion,* 383.

American College of Obstetricians and Gynecologists (ACOG). (2004). Neural tube defects. Clinical management guidelines for obstetrician-gynecologist. *ACOG Practice Bulletin*, 44: 1-11.

American College of Obstetricians and Gynecologists (ACOG). (2002). ACOG committee opinion. Exercise during pregnancy and the postpartum period. Number 267, January 2002. *International Journal of Gynaecology and Obstetrics,* 77(1): 79-81.

Bagby, S. (2007). Maternal nutrition, low nephron number, and hypertension in later life: pathways of nutritional programming. *Journal of Nutrition,* Apr; 137(4):1066-1072.

Baron, R., & Kenny, D. (1986). The moderator-mediator variable distinction in social psychological research. *Journal of Personality and Social Psychology,* 51(6), 1173–1182.

Barker, D. (2004). The Developmental Origins of Adult Disease. *Journal of the American College of Nutrition*, 23 (6): 588S-595S.

Barker, D. (1997). Maternal nutrition, fetal nutrition, and disease in later life. *Nutrition,* Sep; 13(9):807-13.

Bennett, T. (1992). Marital status and infant health outcomes. *Social Science & Medicine,* 35(9):1179-87.

Bjorntorp, P. (2001). Do stress reactions cause abdominal obesity and comorbidities? *Obesity Reviews,* 2:73–86.

Black. P.H., Garbutt, L.D. (2002). Stress, inflammation and cardiovascular disease. *Journal of Psychosomatic Research,* 52:1-23.

Bodnar, L., Catov, J., Klebanoff, M.A., Ness, R.B. & J. M. Roberts. (2007). Prepregnancy body mass index and the occurrence of severe hypertensive disorders of pregnancy. *Epidemiology,* 18(2): 234-239.

Bodnar, L., Siega-Riz, A., Simhan, H., Diesel, J., Abrams, B. (2010). The impact of exposure misclassification on associations between prepregnancy bmi and adverse pregnancy outcomes.*Obesity*, 18(11): 2184-2190.

Brawarsky, P., Stotland, N., Jackson, R., Fuentes-Afflick, E., Escobar, G., Rubashkin, N., Haas, J. (2005). Pre-pregnancy and pregnancy-related factors and the risk of excessive or inadequate gestational weight gain. *International Journal of Gynaecology and Obstetrics,* 91(2):125-31.

Bruce, L. and Tchabo, J. (1989). Nutrition intervention program in a prenatal clinic. *Obstetricsand Gynecology*, 74(3 Pt 1): 310-312.

Butte, N. (2000). Carbohydrate and lipid metabolism in pregnancy: Normal compared with gestational diabetes mellitus. *American Journal of Clinical Nutrition,* 71 (5 Suppl): 1256S-1261S.

Byrne, C., Phillips, D. (2000). Fetal origins of adult disease: epidemiology and mechanisms. *Journal of Clinical Pathology*, 53: 822–828.

Carmichael, S., Abrams, B. (1997). A critical review of the relationship between gestational weight gain and preterm delivery. *Obstetrics and Gynecology,*89: 865-73.

Carmichael S., Shaw, G.,Schaffer, D., Laurent, C. & Selvin, S. (2003). Dieting behaviors and risk of neural tube defects. *American Journal of Epidemiology,* 158(12): 1127-1131.

Catalano P., Thomas, A., Huston-Presley, L., Amini, S. (2003). Increased fetal adiposity: a very sensitive marker of abnormal in utero development. *American Journal of Obstetrics and Gynecology,* 189(6): 1698-1704.

Catalano, P., Tyzbir, E., Roman, N., Amini, S. , & Sims, E. (1991). Longitudinal changes in insulin release and insulin resistance in nonobese pregnant women. *American Journal of Obstetrics and Gynecology,* 165(6 Pt 1): 1667-1672.

Caulfield, L., Witter, F., & Stoltzfus, R., (1996). Determinants of gestational weight gain outside the recommended ranges among black and white women. *Obstetrics and Gynecology* 87(5 Pt 1): 760-766.

Chassan-Taber, Schmitd, Pekow, Sternfeld, Solomon, Markenson. (2008). Predictors of Execissive and Inadqueate Gestational Weight Gain in Hispanic Women. Obesity, 16:1657-1666.

Centers for Disease Control and Prevention. Division of Nutrition, Physical Activity and Obesity. National Center for Chronic Disease Prevention and Health Promotion. (2010a). Pregnancy nutrition surveillance system data table. Retrieved from http://www.cdc.gov/pednss/index.htm.

Centers for Disease Control and Prevention, Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion. (2010b). Pregnancy Risk Assessment Monitoring System (PRAMS): How are PRAMS data used? Retrieved from http://www.cdc.gov/prams.

Centers for Disease Control and Prevention, National Center for Health Statistics. (2009). Linked Birth and Infant Death Data. Retrieved from http://www.cdc.gov/nchs/linked.htm.

Centers for Disease Control and Prevention. (2008). Behavioral risk factor surveillance system survey data. Atlanta, Georgia: U.S. Department of Health and Human Services.

Centers for Disease Control and Prevention. (2005). PRAMS model surveillance protocol. CATI version.

Centers for Disease Control and Prevention, National Center for Health Statistics. (2003).Revision of the U.S. Standard Certificate of Live Birth.

Chen, A., Feresu, S., Fernandez, C., & Rogan, W. (2009). Maternal obesity and the risk of infant death in the United States. *Epidemiology*, 20(1), 74–81.

Chen, X., Wen, S., Fleming, N., Demissie, K., Rhoads, G., & Walker, M. (2007). Teenage pregnancy and adverse birth outcomes: a large population based retrospective cohort study. *International Journal of Epidemiology*, 36(2): 368-373.

Chuang, C., Weisman, C., Hillemeier, M., Schwarz, E., Camacho, F., Dyer, A. (2010). Pregnancy intention and health behaviors: results from the Central Pennsylvania Women's Health Study cohort. *Maternal and Child Health Journal*, Jul;14(4):501-10. Epub 2009 Feb 12.

Chu, S., Callaghan, W., Bish, C. & D'Angelo, D. (2009). Gestational weight gain by body mass index among US women delivering live births, 2004-2005: Fueling

future obesity. *American Journal of Obstetrics and Gynecology,* 200(3): 271 e271-e277.

Cleary-Goldman, J., Malone, F., Vidaver, J., Ball, R., Nyberg, D., Comstock, C., Saade, G., Eddleman, K., Klugman, S., Dugoff, L., Timor-Tritsch, I., Craigo, S., Carr, S., Wolfe, H., Bianchi, D.,& D'Alton, M. (2005). Impact of maternal age on obstetric outcome. *Obstetrics and Gynecology,* 105(5 Pt 1):983-90.

Cnattingius, S., Bergström, R., Lipworth, .L, & Kramer, M. (1998). Prepregnancy weight and the risk of adverse pregnancy outcomes. *New England Journal of Medicine,* 15;338(3):147-52.

Cogswell, M., Scanlon, K., Fein, S. & Schieve, L. (1999). Medically advised, mother's personal target, and actual weight gain during pregnancy. *Obstetrics and Gynecology,* 94(4): 616-622.

Cohern, S., Kamarck, T., Memelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior,* 24, 386-396.

Copper, R., Goldenberg, R., Das, A., Elder, N., Swain, M., Norman, G., Ramsey, R., Cotroneo, P., Collin, B., & Johnson, F. (1996). The preterm prediction study: maternal stress is associated with spontaneous preterm birth at less than 35 weeks' gestation. *American Journal of Obstetrics and Gynecology,* 175:1286-92.

Cwikel, J. (2006). A history of public health and medicine. In: *Social Epidemiology: Strategies for Public Health Activism.* New York, NY: Columbia University Press, 95-122.

Dallman, M., Pecoraro, N., La Fleur, S. (2005). Chronic stress and comfort foods: self-medication and abdominal obesity. *Brain, Behavior, and Immunity,* Jul;19(4):275-80.

De Boo, H. and Harding, J. (2006). The developmental origins of adult disease (Barker) hypothesis. *The Australian New Zealand Journal of Obstetrics Gynaecology,* 46 (1): 4-14.

DeCherney, A., Pernoll, M., eds. (1996). *Obstetric and Gynecologic Diagnosis and Treatment*. 8th ed. Stamford, Conn: Appleton & Lange, 689-712.

Desai, M, Hales, C (1997) Role of fetal and infant growth in programming metabolism in later life. *Biological Reviews*. Cambridge Philos. Soc. 72 (2):329–348.

DeVader, S., Neeley, H., Myles, T., Leet, T. (2007). Evaluation of gestational weight gain guidelines for women with normal prepregnancy body mass index. *Obstetrics and Gynecology,*110:745–51.

Dietz, P., Callaghan, W., Cogswell, M., Morrow, B., Ferre, C., & Schieve, L. (2006). Combined effects of prepregnancy body mass index and weight gain during \ pregnancy on the risk of preterm delivery. *Epidemiology*, 17, 170–177.

Dietz, P., Callaghan, W., & Sharma, A. (2009a). High pregnancy weight gain and risk of excessive fetal growth. *American Journal of Obstetrics and Gynecology*, 201(1), 51.e1– 51.e6.

Dietz, P., Callaghan, W., Sharma, A., & Smith, R. (2009b). Low pregnancy weight gain and small for gestational age: a comparison of the association using three different measures of small for gestational age. *American Journal of Obstetrics and Gynecology*, 201(1), 53.e1–53.e7.

Dombkowski K., Leung, S., Gurney, J. (2008). Prematurity as a predictor of childhood asthma among low-income children. *Annals of Epidemiology*, 18(4): 290-297.

Drewnowski, A. (2004). Obesity and the food environment: Dietary energy density and diet costs. *American Journal of Preventative Medicine, 27* (3) 154-162.

Durlach J. (2004). New data on the importance of gestational Mg deficiency. *Jounal of American College of Nutrition*, 23(6):694S-700S.

Ehrenberg, H., Dierker, L., Milluzzi, C., & Mercer, B. (2003). Low maternal weight, failure to thrive in pregnancy, and adverse pregnancy outcomes. *American Journal of Obstetrics and Gynecology*, 189, 1726–1730.

Engel, G.L. (1997). The Need for a New Medical Model: A Challenge for Biomedicine. *Science.*1977;196(4286):129-136.

Engel, G.L. (1980). The clinical application of the biopsychosocial model. *American Journal of Psychiatry*, 137:535-544.

Epel, E., Lapidus, R., McEwen, B., Brownell, K.(2001). Stress may add bite to appetite in women: a laboratory study of stress-induced cortisol and eating behavior. *Psychoneuroendocrinology*,26:37-49.

Elixhauser A., Wier, L. (2008).Complicating Conditions of Pregnancy and Childbirth, *Healthcare Cost and Utilization Project*, Agency for Healthcare Research and Quality.

Frederick , I., Williams, M., Sales, A., Martin, D., Killien, M. (2007). Pre-pregnancy body mass index, gestational weight gain, and other maternal characteristics in relation to infant birth weight. *Maternal and Child Health Journal*, 12:557–67.

Gabbe, S., Graves, C. (2003). Management of diabetes mellitus complicating pregnancy. *Obstetrics and Gynecology,* 102:857-68.

Geronimus, A. (1992). The weathering hypothesis and the health of African-American women and infants: evidence and speculations. *Ethnicity and Disease,* 2:207-221.

Gillman, M. (2005). Developmental origins of health and disease. *New England Journal of Medicine,* 353(17): 1848-1850.

Glanz K., Rimer, B., Lewis, F., Eds. (2002). *Health Behavior and Health Education: Theory, Research, and Practice, 3rd Ed.* San Francisco, CA: Jossey-Bass.

Goldfrey, K, Barker, D. (2000). Fetal nutrition and adult disease. *American Journal of Clinical Nutrition,* 71:1344–1352.

Hamilton, B., Martin, J., Ventura, S. (2010). Births: Preliminary Data for 2009. *National Vital Statistics Report,* vol 59 no 3, supp 2. Hyattsville, Maryland: National Center for Health Statistics.

Harris, H., Ellison, G., Holliday, M. (1997). Is there an independent association between parity and maternal weight gain? *Annual of Human Biology,* Nov-Dec. 24: (6) 507-19.

Hart, N. (1993). Famine, maternal nutrition and infant mortality: a re-examination of the Dutch Hunger Winter. *Population Studies,* Vol. 47, Issue 1.

Hediger, M., Scholl, T., Ances, I., Belsky, D. & Salmon, R. (1990). Rate and amount of weight gain during adolescent pregnancy: associations with maternal weight for-height and birth weight. *American Journal of Clinical Nutrition,* 52(5): 793-799.

Hellerstedt, W., Himes, J., Story, M., Alton, I., Edwards, L. (1997). The effects of cigarette smoking and gestational weight change on birth outcomes in obese and normal-weight women. *American Journal of Public Health,* 87:591–6.

Herrmann, T., Siega-Riz, A., Hobel, C., Aurora, C., Dunkel- Schetter, C. (2001). Prolonged periods without food intake during pregnancy increase risk for elevated maternal corticotropin-releasing hormone concentrations. *American Journal of Obstetrics and Gynecology,* 185:403-12.

Hickey, C. (2000). Sociocultural and behavioral influences on weight gain during pregnancy. *American Journal of Clinical Nutrition,* 71(suppl):1364S-1370S.

Hickey, C., Cliver, S., Goldenberg, R., McNeal, S., Hoffman, H. (1995). Relationship of psychosocial status to low prenatal weight gain among nonobese black and white women delivering at term. *Obstetrics and Gynecology,* 86(2):177 – 83.

Hickey, C., Kreuter, M., Bronstein, J., Johnson, V., McNeal, S., Harshbarger, D., et al. (1999). Low prenatal weight gain among adult WIC participants delivering term singleton infants: variation by maternal and program participation characteristics. *Maternal and Child Health Journal*, 3(3):129– 40.

Hogue, C., Hoffman, S., Hatch, M. (2001). Stress and preterm delivery: a conceptual framework. *Paediatric and Perinatal Epidemiology*, 15(s2):30-40.

Howie, L., Parker, J. & Schoendorf, K. (2003). Excessive maternal weight gain patterns in adolescents. *Journal of the American Dietetic Association,* 103(12): 1653-1657.

Hytten, F., Chamberlain, G. (1991). *Clinical Physiology in Obstetrics.* Oxford: Blackwell Scientific Publications.

Institute of Medicine (IOM). (1990). Nutrition during pregnancy, weight gain and nutrient supplements. Report of the subcommittee on nutritional status and weight gain during pregnancy, subcommittee on dietary intake and nutrient supplements during pregnancy, committee on nutritional status during pregnancy and lactation, food and nutrition board. *The National Academies Press*, 1–233.

Institute of Medicine (IOM). (1996). WIC Nutrition Risk Criteria: A Scientific Assessment**.** *The National Academies Press,* 1-680.

Institute of Medicine (IOM). (2001). Crossing the Quality Chasm: A New Health System for the 21st Century .

Institute of Medicine (IOM) & National Research Council (NRC). (2009). Weight gain during pregnancy: Reexamining the guidelines. *The National Academies Press*, 1–263.

Jekel, J. (1998). The Coming Revolution in Health Care. *Journal of the American Scientific Affiliation,* 30: 116-123.

Jeffery, R. (1996).Bias in reported body weight as a function of education, occupation, health and weight concern. *Addictive Behaviors*,21:217–22.

Joint Center for Political and Economic Studies Health Policy Institute (2007). Infant Mortality Fact Sheets. The courage to love: Maternal nutrition and infant mortality in the context of relationality. *Infant Mortality Commission. Implications for Care, Research, and Public Policy to Reduce Infant Mortality Rates.* Washington, DC:1-5.

Jones, L., Lu, M., Ferre, C., Norris, K., Lucas-Wright, A., Maidenberg, M., Dillon-Brown, N., Broussard, M. (2010). One hundred intentional acts of kindness toward a pregnant woman: Building reproductive social capital in Los Angeles. *Ethnicity and Disease,* 20(1 Suppl 2):S2-36-40.

Johnson, K., Posner, S., Biermann, J., Cordero, J., Atrash, H., Parker, C., Boulet, S., Curtis, M. (2006). Recommendations to improve preconception health and health care—United States. A report of the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. *MMWR Recommendations and Reports*, 55: 1–23.

Joseph K., Allen, A., Dodds, L. Turner, A., Scott, H., Liston, R.. (2005). The perinatal effects of delayed childbearing. *Obstetrics and Gynecology,* 105(6): 1410-1418.

Kaiser Family Foundation. (2011a, December 27). Most Social Welfare Programs Closed to Undocumented Immigrants**.** *Kaiser's January Update on Health Disparities*. Retrieved from http://www.kff.org/minorityhealth/

Kaiser Family Foundation. (2011b, December). Women's Health Insurance Coverage. Women's Health Policy Fact Sheet.

Kaiser Family Foundation (2009, November). State Medicaid Coverage of Perinatal Services: Summary of State Findings**,** Kaiser Family Foundation and The George Washington University Medical Center School of Public Health and Health Services.

Kamau-Mbuthia, E., Elmadfa, I. (2007). Diet quality of pregnant women attending an antenatal clinic in Nakuru, Kenya. *Annals of Nutrition and Metabolism, 51(4):324-330.*

Keen, C., Clegg, M., Hanna, L., Lanoue, L., Rogers, J., Daston, G., Oteiza, P., Uriu-Adams, J. (2003). The plausibility of micronutrient deficiencies being a significant contributing factor to the occurrence of pregnancy complications. *Journal of Nutrition*, 133:1597S-1605S.

Kiel, D., Dodson, E., Artal, R., Boehmer, T., Leet, T. (2007). Gestational weight gain and pregnancy outcomes in obese women. *Obstetrics and Gynecology*,110: 752–8.

Kim, S., Dietz, P., England, L., Morrow, B., Callaghan. W. (2007). Trends in prepregnancy obesity in nine states, 1993-2003. *Obesity*, 15(4): 986-993.

King, J. (2006). Maternal obesity, metabolism, and pregnancy outcomes. *Annual Review of Nutrition,* 26: 271-291.

Kleinman, J.C. (1990). National Center for Health Statistics. Maternal weight gain during pregnancy: determinants and consequences. Hyattsville, MD: Public Health Service. (NCHS working paper series no. 33.

Kleinman, J., Fingerhut, L., Prager, K. (1991). Differences in infant mortality by race, nativity status, and other maternal characteristics. *American Journal of Diseases of Children,* 145(2): 194-199.

Kirchengast, S. & Hartmann ,B. (2003). Impact of maternal age and maternal somatic characteristics on newborn size. *American Journal of Human Biology,* Mar-Apr. 15: (2) 220-8.

Kochanek, K., Xu, J., Murphy ,S., Miniño, A., & Kung, H. (2011 March) National Center for Health Statistics. 2010 December. Deaths: Preliminary data for 2009. *National Vital Statistic Report.* Volume 59, Number 04. 69 pp.

Kochanek, K., Martin, J. (2006). Supplemental analyses of recent trends in infant mortality. *Health E-stats*. Hyattsville, MD: National Center for Health Statistics. Available from: http://www.cdc.gov/nchs/products/pubs/pubd/hestats/infantmort/infantmort.htm.

Korenbrot, C., Steinberg, A., Bender, C., Newberry, S. (2002). Preconception care: a systematic review. *Maternal and Child Health Journal*,6:75-88.

Kotelchuck, M. (1994). An evaluation of the Kessner adequacy of prenatal care index and a proposed adequacy of prenatal care utilization index. *American Journal of Public Health*, 84(9), 1414–1420.

Kramer M. (2003). The epidemiology of adverse pregnancy outcomes: an overview. *Journal of Nutrition,*133:1592S-96S.

Kramer, M., Kakuma, R. (2003). Energy and protein intake in pregnancy. *Cochrane Database of Systematic Reviews,* (4): CD000032.

Kramer, M., Seguin, L., Lydon, J., Goulet, L. (2000). Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly? *Paediatric and Perinatal Epidemiology*, Jul;14(3):194-210.

Krieger, N. (1994). Epidemiology and the web of causation: has anyone seen the spider? *Social Science and Medicine,* 39:887-903.

Kuczmarski ,R., Flegal, K., Campbell, S., Johnson, C. (1994). Increasing prevalence of overweight among US adults: the National Health and Nutrition Examination Surveys, 1960 to 1991. *Journal of the American Medical Association*, 272:205-11.

Kyrou, I., Chrousos, G., Tisgos, C. (2006). Stress, visceral obesity, and metabolic complications. *Annals of the New York Academy of Sciences,* 1083:77–110.

Lackland, D. (2005) Mechanisms and fetal origins of kidney disease. *Journal of the American Society of Nephrology,* Sep; 16(9):2531-2532.

Lamounier-Zepter, V., Ehrhart-Bornstein, M., Bornstein, S. (2006). Metabolic syndrome and the endocrine stress system. *Hormone and Metabolic Research,* 38: 437–441.

Langford, A., Joshu, C., Chang, J., Myles, T., Leet, T. (2011). Does gestational weight gain affect the risk of adverse maternal and infant outcomes in overweight women? *Maternal and Child Health Journal*, 15(7):860-5.

Laraia, B., Messer, L., Evenson, K., Kaufman, J. (2007). Neighborhood factors associated with physical activity and adequacy of weight gain during pregnancy. *Journal of Urban Health,* Nov; 84(6):793-806.

Laraia, B., Siega-Riz, A., Gundersen, C., Dole, N. (2006). Psychosocial factors and socioeconomic indicators are associated with household food insecurity among pregnant women. *Journal of Nutrition,* Jan;136(1):177-82.

Lu, M., Halfon, N. (2003). Racial and ethnic disparities in birth outcomes: a life-course perspective. *Maternal and Child Health Journal,* 7(1):13-30.

Lu M, Lu J. (2007 July). Maternal Nutrition and Infant Mortality in the Context of Relationality: The Courage to Love: Infant Mortality Commission Implications for Care, Research, and Public Policy to Reduce Infant Mortality Rates. Joint Center for Political and Economic Studies Health Policy Institute. Washington, DC:1-76.

Lucas, A. (1991). Programming by early nutrition in man. In *The Childhood Environment and Adult Disease* (ed. G. R. Bock and J. Whelan), pp. 38-55. John Wiley, Ciba Foundation symposium, number 156, Chichester.

Luke, B. (2005). The evidence linking maternal nutrition and prematurity. *Journal of Perinatal Medicine*, 33:500–5.

MacDorman, M., Menacker, F., Declercq, E. (2008 June). Cesarean birth in the United States: epidemiology, trends, and outcomes. *Clinics in Perinatology,* 35(2): 293-307.

Magee, L., Helewa, M., Moutquin. J-M., et al. (2008). Diagnosis, Evaluation, and Management of the Hypertensive Disorders of Pregnancy. *Journal of Obstetrics and Gynaecology Canada*, 30:S1-S48.

March of Dimes. (2011). What is late-preterm birth Q&A., Retrieved from http://www.marchofdimes.com/research/faq_researchlatepreterm.html.

March of Dimes (2010). “Quick Reference: Premature Birth”., Retrieved from http://www.marchofdimes.com/printableArticles/14332_1157.asp

Martin, J., Hamilton, B., Sutton, P., et al.(2010) Births: Final data for 2007. National vital statistics reports; vol 58 no 24. Hyattsville, MD: National Center for Health Statistics.

Martin, J., Kochanek, K., Strobino, D., Guyer, B., MacDorman, M. (2005). Annual summary of vital statistics— 2003. *Pediatrics,* 115:619–634.

Martin, J. Kung, H., Mathews, T., Hoyert, D., Strobino, D., Guyer, B., Sutton, S. (2008). Annual summary of vital statistics. *Pediatrics,* 121(4): 788-801.

Martin-Gronert, M., Ozanne, S. (2006). Maternal nutrition during pregnancy and health of the offspring. *Biochemical Society Transactions,* 34:779–782.

Matthews, T.J., Menacker, F. & MacDorman, M.F. (2005). Infant mortality statistics from the 2002 period linked birth/infant death data set. National Vital Statistics Reports, 53(10). Atlanta: U.S. Centers for Disease Control and Prevention

McLanahan, S. (1995). The consequences of nonmarital childbearing for women, children, and 4. society. In: *National Center for Health Statistics. Report to Congress on Out-of-Wedlock Childbearing*. Hyattsville, MD: National Center for Health Statistics.

Moore, V., Davies, M., Willson, K., Worsley, A., Robinson, J. (2004). Dietary composition of pregnant women is related to size of the baby at birth. *Journal of Nutrition,* 134: 1820– 1826.

Naeye, R. (1979). Weight gain and the outcome of pregnancy. *American Journal of Obstetrics and Gynecology,* 135(1): 3-9.

National Center for Health Statistics. (2011). Health, United States, 2010: With Special Feature on Death and Dying. Hyattsville, Maryland. 2011.

National Center for Health Statistics.(2010a). December Births: Final Data for 2008. *National Vital Statistics Reports,* 59(1): 105 pp. (PHS) 2011-1120.

National Center for Health Statistics. (2010b). Births preliminary data 2009 *National Vital Statistics Reports,* 59(3): 1-29.

National Center for Health Statistics.(2004). National Center for Health Statistics linked birth/infant death data set, 2002 cohort data. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Health Statistics.

National Center for Health Statistics. (1986). Maternal weight gain and the outcome of pregnancy, United States, 1980. Vital health and statistics. Series 21, No. 44.

DHHS Pub. No. (PHS) 86–1922. Public Health Service. Washington, DC: Government Printing Office.

National Research Council and Institute of Medicine. (2007). Influence of pregnancy weight on maternal and child health: workshop report. Committee on the impact of pregnancy weight on maternal and child health. Washington, DC: National Academy Press.

Newton, E. (2007), Maternal Nutrition. In: Queenan J, Spong C, Lockwood C , 5 ed. Management of High-Risk Pregnancy: An Evidence-based Approach. Malden, MA: Wiley-Blackwell; 12-24.

Newton, R., Hunt, L. (1984). Psychosocial stress in pregnancy and its relation to low birth weight. *British Medical Journal*, 288:1191-1194.

Newton, R., Webster, P., Binu, P., Maskrey, N., Phillips, A. (1979). Psychosocial stress in pregnancy and its relation to the onset of premature labour. *British Medical Journal* , J7;ii:411-3.

Nohr, E., Vaeth, A., Baker, J., Sorensen, T., Olsen, J., Rasmussen, K. (2009). Pregnancy outcomes related to gestational weight gain in women defined by their body mass index, parity, height, and smoking status. *American Journal of Clinical Nutrition*, 90(5): 1288-1294.

Nohr, E., Bech, B., Vaeth, M., Rasmussen, K., Henriksen, T., & Olsen, J. (2007). Obesity, gestational weight gain and preterm birth: A study within the Danish National Birth Cohort. *Paediatric and Perinatal Epidemiology*, 21, 5–14

Oken, E., Kleinman, K. P., Belfort, M. B., Hammitt, J. K., & Gillman, M. W. (2009). Associations of gestational weight gain with short- and longer-term maternal and child health outcomes. *American Journal of Epidemiology*, 170(2), 173–180.

Olds, D., Kitzman, H., Cole, R., Robinson, J., Sidora, K., Luckey, D., Henderson, C., Hanks, C., Bondy, J., Holmberg, J. (2004). Effects of nurse home-visiting on maternal life course and child development: Age 6 follow-up results of a randomized trial P*ediatrics*,114(6):1550-1559.

Oliveti J. F., C. M. Kercsmar and S. Redline. (1996). Pre- and perinatal risk factors for asthma in inner city African-American children. *American Journal of Epidemiology*, 143(6):570- 577.

Olson, C. & Strawderman, M. (2003). Modifiable behavioral factors in a biopsychosocial model predict inadequate and excessive gestational weight gain. *Journal of the American Dietetic Association*, 103(1): 48-54.

Olson, C. (2008). Achieving a healthy weight gain during pregnancy. *Annual Review of Nutrition* 28: 411-423.

Olson, C. & Strawderman, M. (2003). Modifiable behavioral factors in a biopsychosocial model predict inadequate and excessive gestational weight gain. *Journal of the American Dietetic Association,* 103(1): 48-54.

Orr, S., James, S., Miller, C. *et al*. (1996). Psychosocial stressors and low birthweight in an urban population. *American Journal of Preventive Medicine,*12:459–466.

Osmond, C, Barker, D. (2000). Fetal, infant, and childhood growth are predictors of coronary heart disease, diabetes, and hypertension in adult men and women. *Environmental Health Perspectives,* 108 (suppl 3):545–553.

Paul, A. (2010). Origins: How the Nine Months Before Birth Shape the Rest of Our Lives. New York; Simon and Schuster.

Phillips, D. I. W. (2006). External influences on the fetus and their long-term consequences. *Lupus,* 15, 794–800.

Picone, T., Allen, L., Schramm, M. Olsen, P. (1982). Pregnancy outcome in North American women. I. Effects of diet, cigarette smoking, and psychological stress on maternal weight gain. *American Journal of Clinical Nutrition,* 36(6): 1205-1213.

Potti, S., Sliwinski, C., Jain, N., Dandolu, V. (2010). Obstetric outcomes in normal weight and obese women in relation to gestational weight gain: comparison between Institute of Medicine guidelines and Cedergren criteria. *American Journal of Perinatology,* 27(5):415-20.

Pryor, J., Silva, P., Brooke, M. (1995). Growth, development and behaviour in adolescents born small-for-gestational-age. *Journal of Paediatrics and Child Health,* 31(5): 403-407.

Raatikainen, K., Heiskanen, N., Heinonen, S.(2004). Marriage still protects pregnancy. *BJOG An International Journal of Obstetrics and Gynaecology,* 112(10):1411-6.

Ross, M. (2011). Fetal growth restriction. *Medscape eMedicine.* Retrieved from http://www.emedicine.com/med/topic3247.htm.

Rush D. (2001). Maternal nutrition and perinatal survival. *Journal of Health, Population and Nutrition,*19:S217-64.

Rush D., Horvitz, D., Seaver, W., Leighton, J., Sloan, N., Johnson, S., Kulka, R., Devore, J., Holt, M., Lynch, J. (1988). The National WIC Evaluation: evaluation

of the Special Supplemental Food Program for Women, Infants, and Children. IV. Study methodology and sample characteristics in the longitudinal study of pregnant women, the study of children, and the food expenditures study. *American Journal of Clinical Nutrition* ,48(2 Suppl): 429-438.

Rydhström, H., Tyden, T., Herbst, A., Ljungblad, U., Walles, B. (1994). No relation between maternal weight gain and stillbirth. *Acta Obstetricia et Gynecologica Scandinavica*,73:779-81.

Samuelsson A., Matthews, P., Argenton, M., Christie, M., McConnell, J., Jansen, E., Piersma, A., Ozanne, S., Twinn, D., Remacle, C., Rowlerson, A., Poston, L., Taylor, P. (2008). Diet-induced obesity in female mice leads to offspring hyperphagia, adiposity, hypertension, and insulin resistance: a novel murine model of developmental programming. *Hypertension,* 51(2): 383-392.

Sapolsky, R. (1995). Social subordinance as a marker of hypercortisolism. Some unexpected subtleties. *Annals of the New York Academy of Sciences,* 771: 626-639.

Scholl, T., Hediger, M., Ances, I., Belsky, D., Salmon, R. (1990). Weight gain during pregnancy in adolescence: predictive ability of early weight gain. *Obstetrics and Gynecology* 75(6): 948-953.

Scholl, T., Hediger, M., Schall, J., Khoo, C., & Fischer, R. (1994). Maternal growth during pregnancy and the competition for nutrients. *American Journal of Clinical Nutrition,* 60(2): 183-188.

Schulz, L. (2010). The Dutch Hunger Winter and the developmental origins of health and disease. *Proceedings of the National Academy of Sciences of the United States of America,* Sep 28;107(39):16881-6.

Shapiro, C., Sutija, V., Bush, J. (2000). Effect of maternal weight gain on infant birth weight. *Journal of Perinatal Medicine,* 28: (6) 428-31.

Shaw G., Todoroff, K., Carmichael, S., Schaffer, D. & Selvin, S. (2001). Lowered weight gain during pregnancy and risk of neural tube defects among offspring. *International Journal of Epidemiology,* 30(1): 60-65.

Siega-Riz, A., Herrmann, T., Savitz, D., Thorp, J. (2000). The frequency of eating during pregnancy and its effect on preterm delivery. *American Journal of Epidemiology,* 153:647-52.

Siega-Riz, A., King, J. (2009). American Dietetic Association; American Society of Nutrition. Position of the American Dietetic Association and American Society

for Nutrition: obesity, reproduction, and pregnancy outcomes. *Journal of the American Dietetic Association*,109(5):918-27.

Siega-Riz, A. & Hobel, C. (1997). Predictors of poor maternal weight gain from baseline anthropometric, psychosocial, and demographic information in a Hispanic population. *Journal of the American Dietetic Association*, 97(11): 1264-1268.

Stevens-Simon, C. & McAnarney, E. (1992). Determinants of weight gain in pregnant adolescents. *Journal of the American Dietetic Association*, 92(11): 1348-1351.

Stotland, N., Haas, J., Brawarsky, P., Jackson, R., Fuentes-Afflick, E. & Escobar, G. (2005). Body mass index, provider advice, and target gestational weight gain. *Obstetrics and Gynecology*, 105(3): 633-638.

Stotland, N., Caughey, A., Lahiff, M., & Abrams, A. (2006). Weight gain and spontaneous preterm birth: The role of race or ethnicity and previous preterm birth. *Obstetrics & Gynecology*, 108:1448–1455.

Stotland, N., Hopkins, L., & Caughey, A. (2004). Gestational weight gain, macrosomia, and risk of cesarean birth in nondiabetic nulliparas. *Obstetrics and Gynecology*, 104, 671– 677.

Sullivan, F., Barlow, S. (2001). Review of risk factors for sudden infant death syndrome. *Paediatric and Perinatal Epidemiology*,15(2):144- 200.

Szklo, M. (2007). Epidemiology: Beyond the Basics. 2nd ed. Sudbury, MA: Jones and Bartlett Publishers.

Taffel, S. (1986). National Center for Health Statistics. Maternal weight gain and the outcome of pregnancy, United States, 1980. *Vital Health Statistics*, 21 1986;44. [DHHS publication no. (PHS) 86-1922.

Taffel, S. (1980). Maternal weight gain and the outcome of pregnancy. *Vital and Health Statistics*, U.S. Department of Health and Human Services, Publication (PHS) 86-1922.

Taggart, N., Holliday, r., Billewicz, W., Hytten, F. & Thomson, A. (1967). Changes in skinfolds during pregnancy. *British Journal of Nutrition*, 21(2): 439-451.

Teitler J. (2001). Father involvement, child health and maternal health behavior. *Children and Youth Services Review*,23:403-425.

Tovar, A., Must, A., Bermudez, O. I., Hyatt, R. R., & Chasan- Taber, L. (2009). The impact of gestational weight gain and diet on abnormal glucose tolerance during

pregnancy in Hispanic women. *Maternal and Child Health Journal*, 13(4), 520–530.

U.S. Department of Agriculture and U.S. Department of Health and Human Services. (2010). *Dietary Guidelines for Americans.* 7th Edition, Washington, DC: U.S. Government Printing Office.

U.S. Department of Commerce .(1993). We the American Women. Retrieved from http://www.census.gov/apsd/wepeople/we-8.pdf.

U.S. Department of Health and Human Services, National Center for Health Statistics. (2011). Linked Birth/Infant Death Data, 2005 Birth Cohort: United States. Hyattsville, MD: U.S. Dept. of Health and Human Services, National Center for Health Statistics.

U.S. Department of Health and Human Services. (2006). Preventing Infant Mortality Factsheet. Retrieved from http://www.hhs.gov/news/factsheet/infant.html

Ventura, S. (2009). Changing patterns of nonmarital childbearing in the United States. *NCHS data brief*, no 18. Hyattsville, MD: National Center for Health Statistics.

Ventura, S. (1994). Recent trends in teenage childbearing in the United States. *Statistical Bulletin/Metropolitan Insurance Companies,* 75(4): 10-17.

Ventura, S., Martin, J., Curtin, S., Mathews, T. (1998). Report of final natality statistics, *Monthly vital statistics report*; vol 46, no.11 (suppl). Hyattsville, Maryland: National Center for Health Statistics.

Villamor, E., Dreyfuss, M. L., Baylı´n, A., Msamanga, G., & Fawzi, W. W. (2004). Weight loss during pregnancy is associated with adverse pregnancy outcomes among HIV-1 infected women. *Journal of Nutrition,* 134, 1424–1431.

Viswanathan M., Siega-Riz,A., Moos, M., Deierlein, A., Mumford, S., Knaack, J., Thieda, P., Lux, L., & Lohr, K. (2008). Outcomes of Maternal Weight Gain, Evidence Report/Technology Assessment No. 168 . (Prepared by RTI International-University of North Carolina Evidence-based Practice Center under contract No. 290-02-0016.) AHRQ Publication No. 08-E-09. Rockville, MD: Agency for Healthcare Research and Quality.

Walker, L., Minseong, K. (2002). Psychosocial thriving during late pregnancy: Relationship to ethnicity, gestational weight gain, and birth weight. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*,31:263–274.

Webb, J., Siega-Riz, A., Dole, N. (2009). Psychosocial determinants of adequacy of gestational weight gain. *Obesity*, 17(2): 300–309.

Wells, C., Schwalberg, R., Noonan, G., Gabor, V. (2006). Factors influencing inadequate and excessive weight gain in pregnancy: Colorado, 2000-2002. *Maternal and Child Health Journal*, 10(1): 55-62.

Widdowson, E, McCance R. (1975). A review: new thought on growth. *Pediatric Research*, 9:154-6.

Willwerth, B., Schaub, B., Tantisira, K., Gold, D., Palmer, L., Litonjua, A., Perkins, D., Schroeter, C., Gibbons, F., Gillman, M., Weiss, S., Finn, P. (2006). Prenatal, perinatal, and heritable influences on cord blood immune responses. *Annals of Allergy, Asthma,and Immunology*, 96(3): 445-453.

Wilper, A., Woolhandler, S., Lasser, K., McCormick, D., Bor, D., Himmelstein, D. (2009). Health Insurance and Mortality in U.S. Adults. *American Journal of Public Health*, 99(12):2289-95.

Winikoff , Debrovnec, C. (1981). Anthropometric determinants of birth weight. *Obstetrics and Gynecology*, 58(6), Dec.

Zandi-Nejad, K., Luyckx, V., Brenner, B. (2006). Adult hypertension and kidney disease: the role of fetal programming. *Hypertension*, Mar; 47(3):502-508.

Zuckerman, A., Williams, A., Stockley, K. (2009). Trends in Medicaid Physician Fees, 2003- 2008, *Health Affairs*, 28(3):w510-9.