DETERMINANTS OF GESTATIONAL DIABETES MELLITUS: PREPREGNANCY WEIGHT STATUS AND DIETARY PATTERNS DURING PREGNANCY

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ABSTRACT

DETERMINANTS OF GESTATIONAL DIABETES MELLITUS:
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Modifiable determinants for gestational diabetes mellitus (GDM) include high prepregnancy body mass index (BMI), inadequate or excessive gestational weight gain, diet during pregnancy, cigarette smoking and physical inactivity during pregnancy. To date, few studies examined the independent associations of each of these modifiable determinants with GDM risk. For these reasons, no recommendations on diet, weight or weight gain during pregnancy could be established in efforts to reduce the risk for GDM. The overarching aim of this doctoral dissertation research was to investigate if GDM risk is associated with modifiable determinants, in particular, prepregnancy weight status and dietary patterns during pregnancy in U.S. representative pregnant women.

Four hypotheses of this research are: 1) prepregnancy weight status, independent from gestational weight gain, is a determinant for GDM; 2) prepregnancy weight status is associated with diet quality during pregnancy; 3) dietary patterns during pregnancy are associated with gestational weight gain; and 4) dietary patterns during pregnancy are associated with increased GDM risk in conjunction with an inflammatory marker.

For hypothesis 1, we used the data of 219,868 pregnant women from 2004 to 2011 Pregnancy Risk Assessment Monitoring System (PRAMS). Multivariable logistic regression analyses were performed to examine the effect of prepregnancy BMI on GDM risk after controlling for the adequacy of gestational weight gain. For hypothesis 2, we analyzed the data of 795 U.S. pregnant women in the National Health and Nutrition Examination Survey (NHANES) 2003-2012. Multivariable logistic regression analyses were used to estimate the adjusted odds

ratio (AOR) and 95% CIs for the association of prepregnancy weight status with dietary patterns during pregnancy assessed by the Healthy Eating Index (HEI)-2010 after controlling for confounders. For hypothesis 3, a total of 391 pregnant women in the NHANES 2003-2006 were included. Multivariable logistic regression analyses were performed to investigate the association between dietary patterns during pregnancy derived by factor analysis and the adequacy of gestational weight gain. For hypothesis 4, a total of 253 pregnant women were included in the NHANES 2003-2012. Multivariable logistic regression models were used to examine the relationship between dietary patterns using reduced rank regression and the risk of GDM.

Women who were overweight or obese based on prepregnancy BMI compared to normal prepregnancy BMI had higher odds for GDM (AOR=1.79; 95% CI=1.68-1.92, AOR=2.78; 95% CI=2.60-2.96, respectively). Regardless of the adequacy of gestational weight gain, women who were overweight or obese before pregnancy had higher odds for GDM (hypothesis 1). Women who were obese before pregnancy had increased odds for being in the lowest tertile of HEI-2010 compared to those with normal prepregnancy BMI (AOR 5.50; 95% CI 2.05-14.77) after controlling for maternal sociodemographic variables, and physical activity (hypothesis 2). Women in the middle tertile of a 'mixed' dietary pattern had significantly lower odds of excessive gestational weight gain compared to those in the lowest tertile (AOR 0.39; 95% CI 0.15-0.99) (hypothesis 3). Multivariable AOR (95% CIs) for GDM comparing the highest with lowest tertiles of 'added sugar, low fruits and vegetables' dietary pattern was 12.61 (4.08-38.97), after controlling for maternal sociodemographic variables, prepregnancy BMI, gestational weight gain, energy intake, and log-transformed CRP (hypothesis 4). In conclusion, GDM risks are associated independently with prepregnancy weight status, gestational weight gain and a specific dietary pattern during pregnancy in U.S. representative pregnant women. These findings may provide scientific bases to establish recommendations on diet, weight or weight gain during pregnancy in efforts to reduce the risk for GDM.

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Chapter One: Introduction

Women with gestational diabetes mellitus (GDM) have increased risks for short-term and long-term adverse health outcomes for both themselves and their offspring. Women with GDM face increased risks for cesarean deliveries (Langer et al., 2005), preeclampsia (Montoro et al., 2005), hypertension complications during pregnancy (Bellamy et al., 2009), and developing type 2 diabetes in their later lives (Kim et al., 2002; Bellamy et al., 2009) with insulin resistance syndrome (Verma et al., 2002). Infants born to mothers with GDM were associated with a high risk to be large-for-gestational-age (LGA) and for developing metabolic syndrome (Boney et al., 2005), autism spectrum disorder (Xiang et al., 2015) and childhood obesity (Kubo et al., 2014).

GDM is defined as when any degree of glucose intolerance is first recognized between 24 and 28 weeks of pregnancy, regardless of whether the condition may have predated the pregnancy or persists after the pregnancy (Expert Committee on the and Classification of Diabetes, 2003). In the U.S., approximately 7% of all pregnancies were reported to be complicated by GDM in 2014, which accounts for more than 200,000 cases annually (American Diabetes Association, 2014). This rate in the literature ranges from 1 to 14%, depending on the population studied and the diagnostic criteria used. There has been a steady increase in the prevalence of GDM in recent decades from 3.1% in 1993 to 7% in 2014 (Correa et al., 2015). The upward prevalence has been consistent when either diagnostic criteria of the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) or the National Institutes of Health (NIH) was used. The American Diabetes Association (ADA) concluded that the decision of GDM diagnostic tests must be based on cost-benefit estimation (American Diabetes Association, 2014). The economic burden associated with GDM in the U.S. reached $1.3 billion in 2012 (Dall et al., 2014) with an estimated GDM health care cost of $5,800 per case (Dall et al., 2014).

Factors associated with GDM have not yet been fully elucidated. Currently, we do not have recommendations to reduce the risk of GDM based on interventions with modifiable determinants. Determinants for GDM reported in the literature to date are advanced maternal age (Xiong et al., 2001; Solomon et al., 1997), family history of diabetes mellitus (Ben-Haroush et al., 2004), non-white ethnicity (Solomon et al., 1997), prepregnancy weight status (Chung et al., 2012; Doherty et al., 2006; Li et al., 2013), gestational weight gain (Hedderson et al., 2010; Nohr et al., 2008), diet before and during pregnancy (Bo et al., 2001; Radesky et al., 2008; Saldana et al., 2004; Wang et al., 2000; Zhang et al., 2008; Zhang et al., 2004), and inflammation during pregnancy (Qiu et al., 2004). The first three of these determinants are non-modifiable, whereas the rest of the determinants are modifiable. Of the modifiable determinants, prepregnancy weight status, gestational weight gain and diet before and during pregnancy are highly connected as reported in various studies on GDM as an outcome (Shin et al., 2014a; Bowers et al., 2011; Tobias et al., 2012; Bowers et al., 2012; Bao et al., 2013; Bao et al., 2014a). Consequently, the extent to which each of these determinants influence the GDM risk independently or collectively, and how the information on modifiable determinants can be effective in reducing the GDM risk remains unknown. This obscurity in the current body of knowledge on modifiable determinants for GDM is attributed further to differences among studies in diagnostic criteria and screening strategies used, and study populations in different countries.

Several researchers (Doherty et al., 2006; Chung et al., 2012; Li et al., 2013; Al-Obaidly et al., 2014) reported prepregnancy obesity as a risk factor for GDM. These studies (Doherty et al., 2006; Chung et al., 2012; Li et al., 2013; Al-Obaidly et al., 2014), however, did not control for gestational weight gain which is known to be highly associated with prepregnancy weight status. One Danish study (Nohr et al., 2008) partitioned gestational weight gain from prepregnancy weight status in their associations with GDM risk. In the Danish National Birth Cohort study (Nohr et al., 2008), prepregnancy Body Mass Index (BMI) ≥25 kg/m^2 and gestational weight gain

<10 kg were independently associated with increased risks for GDM. The independent effect of prepregnancy BMI on the development of GDM has not yet been established in U.S. pregnant women. Furthermore, it has not been investigated whether or not the gestational weight guidelines of the Institute of Medicine (Institute of Medicine, 2009), which aims to optimize "not only the welfare of the infant, but also the health of the mother," would be effective in lowering GDM prevalence. The positive association of prepregnancy overweight and obesity with excessive gestational weight gain has been documented (Institute of Medicine, 2009). However, it is not well understood how prepregnancy weight status is associated with gestational weight gain through diet during pregnancy. Insufficient evidence exists regarding the role of dietary patterns during pregnancy in relation to prepregnancy weight status and gestational weight gain.

At the time of positive diagnosis of GDM, one of the most commonly asked questions by pregnant women is whether poor diet might have caused their GDM (Moses and Brand-Miller, 2009). Although improved diet quality during pregnancy may have a favorable effect, uncertainty remains as to which dietary factors or patterns during pregnancy may be associated with GDM. Currently, insufficient evidence exists to base any firm dietary advice, whether with single nutrient or specific dietary pattern, on how to reduce the risk for GDM. Intake of dietary elements during pregnancy such as saturated and n-3 fatty acids, dietary heme iron, and processed meat (Wang et al., 2000; Bo et al., 2001; Saldana et al., 2004; Radesky et al., 2008; Zhang et al., 2008; Zhang et al., 2004) have also been reported to be associated with GDM risk. To date, dietary patterns have been under-studied among pregnant women (Tobias and Bao, 2014) in relation to the risk of GDM.

Pregnancy is physiologically characterized by systemic inflammatory responses which have been hypothesized to be associated with GDM (Romero et al., 2007). Specifically, elevation of C-reactive protein (CRP), an inflammatory marker, during the first trimester of pregnancy has been reported as a risk factor for GDM (Wolf et al., 2003; Qiu et al., 2004). CRP has been reported to increase during pregnancy in obese women in association with maternal

diet during pregnancy (Scholl et al., 2011). Because the relationship between maternal diet during pregnancy and GDM risk can be influenced by inflammation, it is questionable whether the maternal diet influences the risk for GDM through inflammation.

Previous researchers reported that collinearity among non-modifiable and modifiable determinants for GDM including maternal age, race/ethnicity, prepregnancy weight status, gestational weight gain, dietary patterns during pregnancy, and inflammation is high (Solomon et al., 1997; Scholl et al., 2011). However, previous studies have not consistently addressed collinearity among the determinants in identifying its independent role for GDM. To date, few studies examined the independent associations of each of these modifiable determinants with GDM risk. For these reasons, no recommendations on diet, weight or weight gain could be established in order to reduce the risk for GDM. The overarching aim of this doctoral dissertation research was to investigate if GDM is independently associated with selected modifiable determinants, in particular, prepregnancy weight status and dietary patterns during pregnancy in U.S. representative pregnant women (Figure 1). Additionally, this research examined the relationship of dietary patterns during pregnancy to prepregnancy weight status and gestational weight gain.

Four hypotheses of this research are: 1) prepregnancy weight status, independent from gestational weight gain, is a determinant for GDM; 2) prepregnancy weight status is associated with diet quality during pregnancy; 3) dietary patterns during pregnancy are associated with gestational weight gain; and 4) dietary patterns during pregnancy are determinants of GDM risk in conjunction with an inflammatory marker.

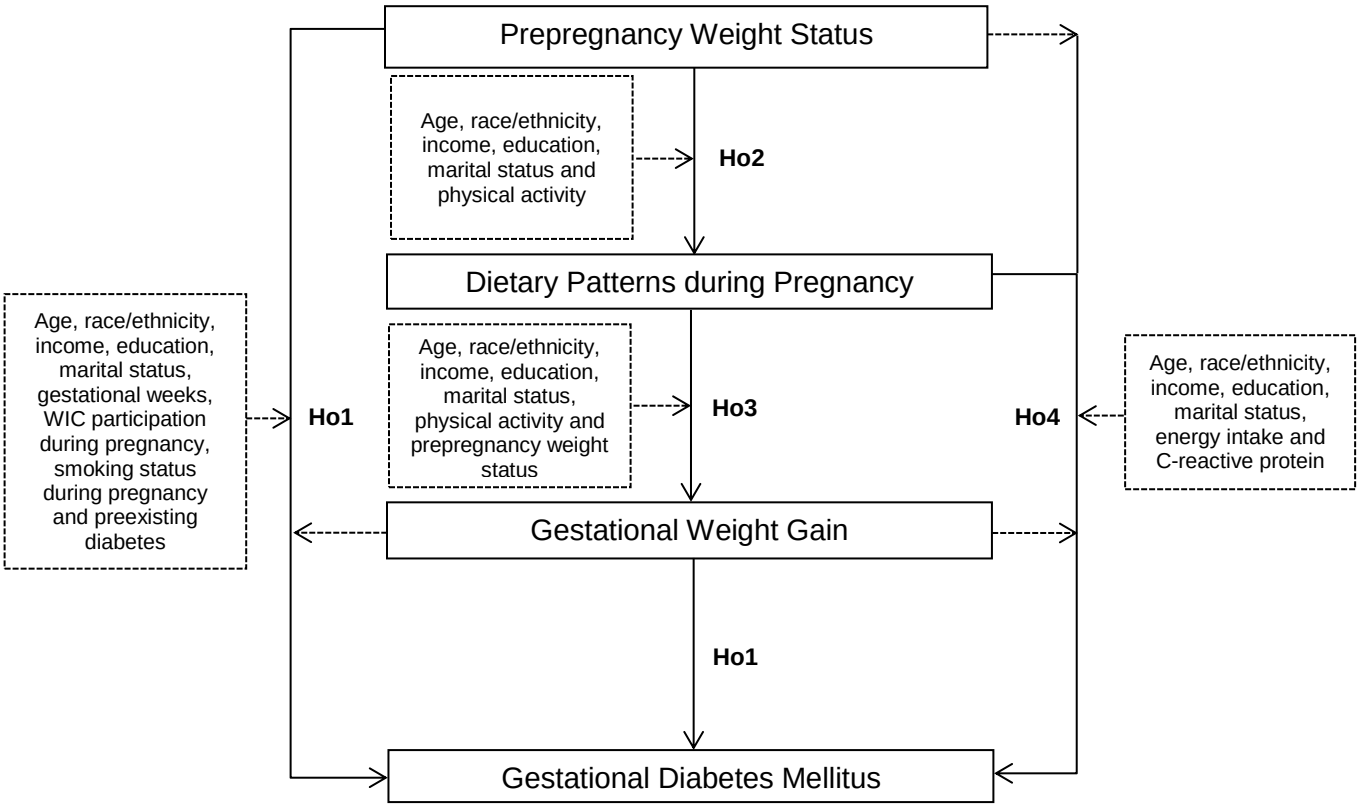

Figure 1. Overall research framework with specific hypotheses

1.1 Significance

The increasing prevalence and numerous consequences of GDM underscore the urgent need to investigate ways to decrease the risk of GDM. Ultimately identifying the most significant modifiable determinants such as prepregnancy weight status and dietary patterns during pregnancy for GDM can be used in establishing the public health recommendations.

Recognizing that prepregnancy weight status is a predictor for gestational weight gain (Chu et al., 2009), we cannot differentiate which of the two maternal weight statuses play a more critical role, or how they interact to explain the increased risk for GDM associated with maternal weight status. Previous studies established obese prepregnancy BMI as a determinant

for GDM (Li et al., 2013; Chung et al., 2012; Doherty et al., 2006) without controlling for gestational weight gain as a covariate. Our study aimed to provide the evidence for the effect of prepregnancy BMI on the development of GDM after controlling for gestational weight gain based on the Institute of Medicine's 2009 guidelines in U.S. pregnant women.

The importance of diet during pregnancy in relation to pregnancy weight status and gestational weight gain is unclear. If evidence-based public health strategies are to be developed to improve health outcomes for pregnant women who were obese in their prepregnancy stages and who gain excessive gestational weight during pregnancy, it would be critical to understand first the relationship of dietary patterns during pregnancy with prepregnancy weight status and gestational weight gain.

Currently, insufficient evidence exists to base any dietary advice, whether with a single nutrient or dietary patterns in association with inflammation, on how to reduce the risk for GDM. Available data have predominantly focused on macro- or micro-nutrients, not dietary patterns in relation to the risk of GDM (Hu, 2002). Meals consumed habitually consist of a variety of foods containing complex combinations of nutrients that are likely to be interactive or synergistic (National Research Council - Committee on Diet and Health, 1989). Studying dietary patterns may have important public health implications because overall patterns of dietary intake might be simpler than nutrients or food components for the public to translate into diets (National Reserach Council, 1989). Previous literature (Uusitalo et al., 2009; Shin et al., 2014a; Hillesund et al., 2014) does not provide strong enough evidence to make specific recommendations of dietary patterns in order to reduce the risk of inadequate or excessive gestational weight gain and thus possibly GDM risk (Zhang and Ning, 2011). Our study aimed to fill eventually in the missing linkages between maternal dietary patterns during pregnancy, GDM risk, and inflammation.

The aim of this doctoral dissertation research was to investigate if GDM is independently associated with selected modifiable determinants, in particular, prepregnancy weight status and

dietary patterns during pregnancy in U.S. representative pregnant women. Our aim was to help to make consolidated recommendations incorporating prepregnancy weight status, gestational weight gain, and dietary patterns during pregnancy relative to inflammation to reduce the risk of GDM. Reducing the risk for GDM is critically important to lower the adverse metabolic consequences in both mothers and their offspring. Identification of the role of each of the modifiable determinants for GDM by addressing collinearity among determinants would be important in formulating recommendations, which are prerequisite to prevention and management of GDM in public health interventions.

The committee to reexamine Institute of Medicine (IOM) Pregnancy Weight Guidelines (Institute of Medicine, 2009) issued gestational weight gain guidelines for not only the welfare of the infant, but also that of the mother. The dietary reference intakes (DRIs) for pregnancy set by the Food and Nutrition Board of the IOM (Institute of Medicine, 2005) emphasize the importance of diet quality and nutritional adequacy at each trimester of pregnancy to facilitate favorable birth outcomes. Both gestational weight gain guidelines and DRIs for pregnant women aim to minimize adverse birth outcomes and reduce pregnancy complications. Eventually, these two recommendations need to be merged into one message. It was important to cross-examine the two recommendations by examining the relationship between dietary patterns during pregnancy and gestational weight gain in the study.

More than 50% of the pregnancies in the U.S. are reported to be unplanned (Finer and Zolna, 2011; Finer and Zolna, 2014). Capturing the window of strategic intervention periods during both prepregnancy and prenatal states need simplified and yet effective evidence-based messages. Increased health-consciousness such as maintaining a healthy weight and adopting healthy dietary behaviors from preconception through pregnancy may continue to long-term lifestyle changes and impact on positive health outcomes in mothers and their immediate offspring. Our findings aimed to contribute to establishing a consolidated recommendation for pregnant and reproductive aged women to reduce the risk for GDM.

1.2 Innovation

There is strong collinearity among modifiable determinants for GDM including prepregnancy weight status, gestational weight gain, dietary patterns during pregnancy, and inflammation. However, previous literature has not addressed collinearity among modifiable determinants when identifying independent modifiable determinants for GDM. Our study clarified the independent associations of each of these modifiable determinants with GDM risk.

In assessing diet-disease relations, the reduced rank regression method has been proven to be better than the classic principal component analysis approach (Hoffmann et al., 2004a). We chose to use the reduced rank regression method in order to identify dietary patterns that explain the maximum variation of GDM-related biomarkers as response variables in women with GDM. Previously the reduced rank regression method has been applied to derive dietary patterns in pregnant women in relation to spina bifida (Vujkovic et al., 2009) and congenital heart defects (Obermann-Borst et al., 2011) in Netherlands. Risk for GDM has been assessed in relation to prepregnancy dietary patterns derived by factor analysis (Zhang et al., 2006b) or index analysis (Tobias et al., 2012) in the Nurses' Health Study II. To the best of our knowledge, no studies have reported dietary patterns during pregnancy examined by the reduced rank regression method in relation to GDM risk. Our study used the U.S. representative population, and the results could be generalizable and applicable for further recommendations for reproductive aged women in the U.S.

Chapter Two: Review of Literature

In the U.S., approximately 7% of all pregnancies are complicated by gestational diabetes mellitus (GDM) (American Diabetes Association, 2014). More than 200,000 cases are affected by GDM annually (American Diabetes Association, 2014). Diagnostic criteria for GDM vary significantly in terms of the amount of glucose used (75 or 100 g) during oral glucose tolerance test, the cut-off values of fasting glucose levels and the number of abnormal values required to make the diagnosis (Holt et al., 2011). These wide variations may be due to the lack of reliable evidence regarding the effects of hyperglycemia for the fetus (Holt et al., 2011).

Women with GDM have increased risks for short-term and long-term adverse health outcomes for both themselves and their offspring. Women with GDM face increased risks for cesarean deliveries (Langer et al., 2005), preeclampsia (Montoro et al., 2005), hypertension complications during pregnancy (Bellamy et al., 2009), and developing type 2 diabetes in their later lives (Kim et al., 2002; Bellamy et al., 2009) with insulin resistance syndrome (Verma et al., 2002). Infants born to mothers with GDM were associated with a high risk to be large-for-gestational-age (LGA) and for developing metabolic syndrome (Boney et al., 2005), autism spectrum disorder (Xiang et al., 2015), and childhood obesity (Kubo et al., 2014).

Identifying an independent role of modifiable determinants for the development of GDM could give the opportunity to intervene before and during pregnancy with behavioral modifications in order to reduce the burden of adverse maternal and neonatal outcomes. This review provides the overview of both non-modifiable and modifiable determinants for the development of GDM that have been reported in the literature. This information could be useful for prepregnancy counseling, and for better prediction and control of a woman's risk for developing GDM.

Determinants for GDM

2.1 Sociodemographics and lifestyle as determinants for GDM

Determinants for GDM reported in the literature include advanced maternal age (Xiong et al., 2001; Solomon et al., 1997), family history of diabetes mellitus (Ben-Haroush et al., 2004), non-white ethnicity (Solomon et al., 1997), low education level (Bo et al., 2002), cigarette smoking (Solomon et al., 1997), a prior history of neonatal death, preterm delivery or cesarean section (Xiong et al., 2001), physical inactivity before pregnancy (Baptiste-Roberts et al., 2011), polycystic ovary syndrome (PCOS) (Lo et al., 2006), and multiple pregnancies (Sivan et al., 2002; Schwartz et al., 1999). In the Nurses' Health Study II (Solomon et al., 1997), women aged >40 years had a 2-fold increased risk for GDM, compared with women aged 25-29 years. Women with a family history of diabetes mellitus in a first-degree relative had an increased risk for GDM than those without family history of type 2 diabetes (Relative Risk (RR) 1.68; 95% CI 1.39-2.04). Women who were African-Americans, Hispanics, or Asian ethnicity had significantly higher age-adjusted RRs for GDM as compared with white women (Solomon et al., 1997). Women who smoked 5 to 14 cigarettes per day before pregnancy compared to a never-smoker had a higher risk for GDM (RR 1.65; 95% CI 1.05-2.58) (Solomon et al., 1997). Women who had a history of having had neonatal death (Odds Ratio (OR) 2.09; 95% CI 1.50-2.92), preterm delivery (OR 1.25; 95% CI 1.03-1.51) and/or cesarean section (OR 1.55; 95% CI 1.39-1.72) had a higher risk for GDM, compared to those who did not (Xiong et al., 2001). In a prospective study of Parity, Inflammation, and Diabetes (PID) with a racially diverse urban-based sample of 152 U.S. pregnant women in the first trimester, physical inactivity before pregnancy was associated with an increased risk for GDM (Baptiste-Roberts et al., 2011). Pregnant women who had a prepregnancy leisure activity score ≥2.75 were 70% less likely to have a 1-hour glucose challenge test response >140 mg/dL compared to those women with a prepregnancy

leisure activity score <2.75 after adjusting for age, race, parity, gestational weight gain, and prepregnancy BMI (OR 0.32; 95% CI 0.12-0.86).

Low maternal education level was found to be associated with a high GDM rate in a population-based cohort study in Netherlands (Bouthoorn et al., 2014; Bo et al., 2002). Women with the lowest education level had three times higher odds of developing GDM than women with the highest education level (OR 3.07; 95% CI 1.37-6.89) after controlling for ethnicity, age, family history of diabetes and parity (Bouthoorn et al., 2014). Pregnant women diagnosed with PCOS have been reported to have a two-fold increased odds for developing for GDM compared to women without PCOS (Lo et al., 2006). Multiple pregnancies have also been reported to increase the incidence of GDM, possibly because of the increased placental mass and the increase in diabetogenic hormones such as cortisol, glucagon and epinephrine (Ben-Haroush et al., 2004). Compared to the singleton birth group, both twin delivery group (Schwartz et al., 1999) and triplet birth group (Sivan et al., 2002) had higher rate of GDM with (7.7% vs. 4.1%) and (22.3% vs. 5.8%), respectively.

These previous studies that used different diagnostic criteria for GDM vary across study populations and designs. Furthermore, these studies did not address potential collinearity among risk factors including socioeconomic status, physical activity, and smoking status. Although these concerns make it difficult to compare findings across different studies, advanced maternal age, non-white ethnicity, a family history of type 2 diabetes seem to be the common risk factors for GDM.

Table 1. Determinants for the development of gestational diabetes mellitus (GDM) reported in the literature

Modifiable determinants for GDM	Diet[1] Physical activity[2] Prepregnancy BMI[3] Gestational weight gain[4] Cigarette smoking[5]
Non-modifiable determinants for GDM	Advanced age[5;6] Non-white ethnicity[5] Family history of type 2 diabetes[7] Prior history of neonatal death[6] Preterm delivery or cesarean section[6] PCOS[8] Multiple pregnancies[9;10]

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2.2 Prepregnancy weight status as a determinant for GDM

Previous researchers reported that obese prepregnancy weight status was associated with increased risk for GDM (Torloni et al., 2009; Chu et al., 2007; Li et al., 2013; Chung et al., 2012; Nohr et al., 2008; Hedderson et al., 2008; Doherty et al., 2006; Al-Obaidly et al., 2014). Each of these studies used different cut-off points to categorize prepregnancy weight status and sampling schemes.

Li et al. (Li et al., 2013) used health care records of 33,973 Chinese pregnant women to assess whether prepregnancy weight status was a risk factor for GDM. From their retrospective study, women who were underweight prepregnancy (BMI<18.5 kg/m^2) had a lower risk for GDM regardless of gestational weight gain compared to those with a normal prepregnancy BMI (18.5-23.9 kg/m^2) (Li et al., 2013). Women with overweight (24.0-27.9 kg/m^2) and obese (≥28.0 kg/m^2) prepregnancy weight status had higher risks for GDM even after controlling for maternal age, maternal height, maternal education, smoking, family income, maternal occupation, and gestational age (OR (95% CI), 1.97 (1.70-2.14); 2.46 (2.09-2.90), respectively) (Li et al., 2013).

In the Danish National Birth Cohort study with 60,892 women, women in the overweight (BMI 25-29.9 kg/m^2) or obese (≥30 kg/m^2) prepregnancy BMI group had higher risk for GDM compared to the normal prepregnancy weight group (OR 2.5; 95% CI 2.1-3.0, OR 5.9; 95% CI 4.8-7.3, respectively) (Nohr et al., 2008). The increased risk persisted even after controlling for gestational weight gain, age, parity, smoking, alcohol consumption, and other sociodemographic variables (Nohr et al., 2008). In a multi-ethnic cohort of 14,235 U.S. women who delivered live births between 1996 and 1998, women with overweight (BMI 25-29.9 kg/m^2) and obese (BMI ≥30 kg/m^2) prepregnancy weight had increased risks for GDM with OR 2.44 (95% CI 1.53-3.89) and OR 3.89 (95% CI 2.35-6.43), respectively. These associations persisted after adjusting for age, race/ethnicity, and parity (Hedderson et al., 2008). Obese prepregnancy BMI (BMI 30-39.9 kg/m^2) increased the risk for GDM nearly 3 times (OR 2.83; 95% CI 2.74-2.92) compared to

normal prepregnancy BMI (BMI 18.5-24.9 kg/m^2) in a retrospective cohort study in California (Chung et al., 2012). In Australian women, those with overweight or obese prepregnancy weight status had at least three times higher odds for GDM (OR 2.71; 95% CI 1.32-5.55, OR 6.50; 95% CI 3.32-12.74, respectively) after adjusting for maternal age and parity (Doherty et al., 2006).

A meta-analysis of seventy studies (Torloni et al., 2009) assessed the relationship between prepregnancy BMI and the risk for GDM using the adjusted pooled OR. Overweight (BMI 25-29.9 kg/m^2), moderately obese (BMI 30-34.9 kg/m^2), and morbidly obese (BMI ≥35 kg/m^2) prepregnancy weight groups, in reference to normal prepregnancy weight group had incrementally higher risks for developing GDM (OR 1.83; 95% CI 1.58-2.12, OR 3.22; 95% CI 2.68-3.87, OR 4.71; 95% CI 2.89-7.67, respectively). The study controlled for demographic variables and previous history of GDM. A meta-analysis of twenty studies (Chu et al., 2007) used age-adjusted pooled OR. In the study, overweight (BMI 25-29.9 kg/m^2), obese (BMI 30-39.9 kg/m^2), and severely obese (BMI ≥40 kg/m^2) prepregnancy women, in reference to normal prepregnancy weight women (BMI 19.8-24.9 kg/m^2), also had incrementally increased risks for developing GDM (OR (95% CI), 1.86 (1.22-2.78) 3.34 (2.43-4.55), 5.77 (3.60-9.39), respectively). Although these two meta-analysis studies (Torloni et al., 2009; Chu et al., 2007) used different criteria for selection of articles such as inclusion of cohort, case-control and cross-sectional studies (Torloni et al., 2009) vs. cohort studies only (Chu et al., 2007), after classification of weight status and confounders were controlled, the results seem to support that prepregnancy weight is an important risk factor for GDM. These findings underscore the importance of maintaining a healthy weight prior to conception by all childbearing age women to control the extended public health issues associated with GDM and subsequent type 2 diabetes and intergenerational health consequences.

Except for one Danish study (Nohr et al., 2008), none of the above studies investigated gestational weight gain as a covariate in examining prepregnancy weight status as a GDM risk.

Evidence for an effect of prepregnancy BMI after controlling for the adequacy of gestational weight gain on GDM has been limited in U.S. pregnant women. Most of these studies (Nohr et al., 2008; Li et al., 2013; Ovesen et al., 2011) were conducted in European or Asian countries, and few studies inadequately addressed the interactions between prepregnancy BMI and gestational weight gain.

Since prepregnancy weight status is highly associated with gestational weight gain, we cannot yet clearly discern if prepregnancy weight, gestational weight gain or their interactions explain the increased risk for GDM. The answer to this important question may enhance the efficacy of educational interventions through gestational counseling, and nutrition and health education to all childbearing age women in an effort to reduce GDM for better public health.

Table 2. Previous studies that examined prepregnancy weight status as a determinant for GDM

Authors (year)	Title	Subjects (description, n)	Prepregnancy weight status (Y/N)	GWG as a covariate (Y/N)	Conclusion	Other Covariates
Al-Obaidly et al. (2014)	Maternal pre-gravid body mass index and obstetric outcomes in twin gestations	Canadian women who delivered twins after 23 weeks of gestation (n=1,228)	Y	N	There was an increased risk for GDM in overweight and obese women (OR 3.3; 95% CI 1.52-7.3) and (OR 3.2; 95% CI 1.41-7.1), respectively.	None
Li et al. (2013)	Maternal prepregnancy body mass index and gestational weight gain on pregnancy outcomes	Pregnant women in Tianjin, China (n=33,973)	Y	N	The adjusted ORs for developing GDM were 1.91 (95% CI 1.70-2.14) and 2.46 (95% CI 2.09-2.90) for overweight and obese women, respectively, compared with normal-weight pregnant women.	Maternal age, maternal height, maternal education, smoking, family income, maternal occupation, and gestational age
Chung et al. (2012)	Increasing pre-pregnancy body mass index is predictive of a progressive escalation in adverse pregnancy outcomes	Retrospective cohort study of California (n=436,414)	Y	N	Obese women were nearly 3 times more likely to have gestational diabetes (OR 2.83; 95% CI 2.74-2.92) when compared to normal prepregnancy BMI women.	BMI categories, race-ethnicity, parity, chronic hypertension, gestational hypertension /preeclampsia, and chronic preeclampsia
Torloni et al. (2009)	Prepregnancy BMI and the risk of gestational diabetes: a systematic review of the literature with meta-analysis	Meta-analysis (70 studies)	Y	N	The ORs of GDM for overweight, moderately obese and morbidly obese women were 1.97 (95% CI 1.77-2.19), 3.01 (95% CI 2.34-3.87) and 5.55 (95% CI 4.27-7.21), respectively.	n/a
Nohr et al. (2008)	Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy	Term pregnancies in the Danish National Birth Cohort (n=60,892)	Y	Y	Compared to women with normal prepregnancy weight, women categorized as overweight (OR 2.5; 95% CI 2.1-3.0) or obese (OR 5.9; 95% CI 4.8-7.3) had increased risk for GDM.	Gestational weight gain (<10kg, 10-15 kg, 16-19 kg, ≥20 kg), age, parity, height, smoking, alcohol consumption, social status, exercise, and gestational age
Hedderson et al. (2008)	Body mass index and weight gain prior to pregnancy and risk of gestational diabetes mellitus	Kaiser Permanente Medical Care Program of Northern California (n=455)	Y	N	The adjusted ORs for developing GDM were 2.44 (95% CI 1.53-3.89) and 3.89 (2.35-6.43) for overweight and obese women, respectively, compared with normal-weight pregnant women.	Maternal age, race/ethnicity, and parity

Table 2. (cont'd)

Authors (year)	Title	Subjects (description, n)	Prepregnancy weight status (Y/N)	GWG as a covariate (Y/N)	Conclusion	Other Covariates
Chu et al. (2007)	Maternal obesity and risk of gestational diabetes mellitus	Meta-analysis of (20 studies)	Y	N	The unadjusted ORs for developing GDM were 2.14 (95% CI 1.82-2.53), 3.56 (95% CI 3.05-4.21), and 8.56 (95% CI 5.07-16.04) among overweight, obese, and severely obese compared with normal prepregnancy weight, respectively.	n/a
Doherty et al. (2006)	Pre-pregnancy body mass index and pregnancy outcomes	Australian pregnant women between 16 and 18 weeks (n=2,827)	Y	N	Compared to women with a normal prepregnancy BMI, women categorized as obese by their prepregnancy BMI were significantly more likely to have GDM (OR 6.50; 95% CI 3.32-12.74).	Maternal age and parity

n/a: Not applicable

2.3 Gestational weight gain as a determinant for GDM

Previous literature has shown inconsistent findings on gestational weight gain as a risk factor for GDM. The IOM report noted that there was “a lack of evidence” regarding the role of gestational weight gain in relation to GDM (Institute of Medicine, 2009). Several studies indicated excessive gestational weight gain as a risk for GDM (Hedderson et al., 2010; Herring et al., 2009; Carreno et al., 2012). In a randomized controlled trial of vitamins C and E supplementation in nulliparous low-risk women (Carreno et al., 2012), those who gained greater than the upper range of Institute of Medicine’s 2009 gestational weight guidelines had 43% higher risk of developing GDM compared to those with non-excessive gestational weight gains (OR 1.4; 95% CI 1.1-1.9). This association persisted after controlling for maternal age, smoking, race and treatment group (vitamins vs. placebo), not controlling for prepregnancy BMI (Carreno et al., 2012). In a nested case-control study of 345 U.S. pregnant women (Hedderson et al., 2010), women in the highest tertile of gestational weight gain (≥0.41 kg/week) before 24 weeks of gestation had higher risk for GDM compared to women with the lowest tertile of gestational weight gain (<0.27 kg/week) (OR 1.74; 95% CI 1.16-2.60) after adjusting for age at delivery, race/ethnicity, parity, and prepregnancy BMI. The IOM recommends pregnant women to gain weight during pregnancy at 0.45 kg/week for women with underweight and normal prepregnancy BMI, 0.27 kg/week for women with overweight prepregnancy BMI, and 0.23 kg/week for women with obese prepregnancy BMI in the second and third trimesters of pregnancy (Institute of Medicine, 2009). Based on a prospective cohort study of 1,960 women, Herring et al. (Herring et al., 2009) reported that gestational weight gain was positively associated with odds of developing abnormal glucose intolerance during the third trimester of pregnancy (OR 2.14; 95% CI 1.04-4.42) after adjusting for age, race/ethnicity, prepregnancy BMI category, and history of GDM.

In contrast, other studies (Tanaka et al., 2014; Hackmon et al., 2007; Seghieri et al., 2005) reported no associations between gestational weight gain and the risk for GDM. From the

medical records of 1,883 Japanese women who delivered singleton infants (Tanaka et al., 2014), adequacy of gestational weight gain based on 2009 IOM's guidelines was not associated with the risk for GDM. Inadequate or excessive gestational weight gain was not associated with risks for GDM even after controlling for maternal age, parity, length of gestation, mode of delivery, and pregnancy-induced hypertension (OR 1.39; 95% CI 0.50-5.00, OR 2.84; 95% CI 0.61-12.8, respectively) (Tanaka et al., 2014). Overall, gestational weight gain had a smaller impact on GDM in Japanese women. This may partially due to the fact that the distribution of prepregnancy weight status and gestational weight gain among Asian women differed from that of Western women.

For this reason, there is ongoing debate regarding the definition of overweight and obesity in Asian populations: the World Health Organization proposed a BMI cut-off of 23.0 kg/m^2 for overweight among Asians, compared to a cut-off of 25.0 kg/m^2 for non-Asian populations (World Health Organization et al., 2000). Hackmon et al. (Hackmon et al., 2007) also reported that there was no difference in gestational weight gain between patients with abnormal vs. normal glucose challenge test values in a retrospective chart review of 75 U.S. pregnant women with singleton pregnancies. Seghieri et al. (Seghieri et al., 2005) reported that no association was found between gestational weigh gain and the risk for GDM in a study of a hospital records including 1,880 Italian women.

Several studies show inverse associations between gestational weight gain and risk of GDM. In the Danish Birth Cohort, Nohr et al. (Nohr et al., 2008) found that gestational weight gain <10 kg compared to those with 10-15 kg had a higher risk for GDM (OR 2.3; 95% CI 1.9-2.8) after controlling for prepregnancy BMI, maternal age, parity, height, smoking, alcohol consumption, socioeconomic status, exercise, and gestational age. The authors explained that the inverse relationship between gestational weight gain and the risk for GDM was due to the variation in prenatal care. The authors noted that screening was carried out more often among

obese than lower-weight women, and after diagnosis of GDM. Also, the obese women were often prescribed a diet that would restrict their total gestational weight gain (Nohr et al., 2008).

In summary, inconsistent relationships have been reported between gestational weight gain and the risk for GDM. The Institute of Medicine (Institute of Medicine, 2009) also reported "a lack of evidence" for the relation between gestational weight gain and the risk for GDM. We suspect that these inconclusive findings are due to substantial heterogeneity in the approach of analyzing the associations, different cut-off points used for categorizing gestational weight gain, total or weekly rate of gestational weight gain, and differences in study designs and populations. Future studies are warranted to examine gestational weight gain in different terms of total, weekly rate, changing patterns from first to third trimester of pregnancy to the development of GDM after controlling for prepregnancy BMI, age, parity, maternal height, smoking, alcohol consumption, physical activity, and gestational age.

Table 3. Previous studies that examined gestational weight gain as a determinant for gestational diabetes mellitus (GDM)

Author(s) (year)	Title	Subjects (description, n)	Gestational Weight Gain	Conclusion	Covariates
Positive associations					
Carreno et al. (2012)	Excessive early gestational weight gain and risk of gestational diabetes mellitus in nulliparous women	A randomized controlled trial of vitamins C and E in nulliparous low-risk women (n=7,985)	<IOM; Within IOM; ≥IOM	Excessive early gestational weight gain is associated with the development of GDM.	Maternal age, smoking, race, and treatment group (vitamins vs. placebo)
Herring et al. (2009)	Weight gain in pregnancy and risk of maternal hyperglycemia	A longitudinal cohort study of pregnant women in eastern Massachusetts 1999-2002, Project Viva (n=1,960)	-9.4-7.9 kg; 7.9-10.1 kg; 10.1-12.9 kg; 12.9-29.1 kg	Participants in the highest quartile had increased odds of impaired glucose tolerance in pregnancy, but not GDM.	Gestational age at glycemic screening, age, race/ethnicity, prepregnancy BMI, and history of GDM
Hedderson et al. (2008)	Gestational weight gain and risk for gestational diabetes mellitus	A nested case-control study (n=1,145)	<0.27 kg/week; 0.27-0.40 kg/week; ≥0.41 kg/week	High rates of gestational weight gain in the first trimester may increase a woman's risk for GDM.	Age at delivery, race/ethnicity, parity, and prepregnancy BMI
No association					
Tanaka et al. (2014)	Associations between the pre-prepregnancy body mass index and gestational weight gain with pregnancy outcomes in Japanese women	A retrospective study of Japanese women with singleton infants at Osaka-Minami Medical Center	<IOM; Within IOM; ≥IOM	Gestational weight gain did not show any significant association with the development of GDM.	Maternal age, parity, length of gestation, and mode of delivery, and pregnancy-induced hypertension
Seghieri et al. (2005)	Does parity increase insulin resistance during pregnancy?	Longitudinal study of pregnant women at the Outpatient Clinic of the Diabetes Unit of the Hospital of Pistoia, Italia (n=1,880)	Total gestational weight gain as a continuous variable	No association was found between gestational weight gain and the risk for GDM.	Maternal age, parity, prepregnancy BMI, and family history of diabetes
Hackmon et al. (2007)	The impact of maternal age, body mass index and maternal weight gain on the glucose challenge test in pregnancy	A retrospective chart review 75 consecutive singleton pregnancies (n=75)	Gestational weight gain at 24-28 weeks of gestation as a continuous variable	No significant difference was observed in gestational weight gain between patients with abnormal vs. normal glucose challenge test values.	None

Table 3 (cont'd)

Author(s) (year)	Title	Subjects (description, n)	Gestational Weight Gain	Conclusion	Covariates
Inverse associations					
Nohr et al. (2008)	Combined associations of prepregnancy body mass index and gestational weight gain with the outcome of pregnancy	Term pregnancies in the Danish National Birth Cohort (n=60,892)	<10kg; 10-15 kg; 16-19 kg; ≥20 kg	Gestational weight gain less than 10 kg had an increased risk for the development of GDM.	Prepregnancy BMI, age, parity, height, smoking, alcohol consumption, social status, exercise, and gestational age
Heude et al. (2012)	Pre-pregnancy body mass index and weight gain during pregnancy: relations with gestational diabetes	The EDEN study, an on-going mother-child cohort, with a follow-up of the child until their 5th birthday (n=1,884)	<3 kg; 3-12 kg; 12-16 kg; >16 kg	An inverse relation was observed between increased gestational weight gain and the risk for GDM.	Clinical center, maternal age and height, number of cigarettes smoked per week during pregnancy, and parity

n/a: Not applicable

2.4 Inflammation as a determinant for GDM

C-reactive protein (CRP) is an acute phase reactant, a biomarker for the inflammatory process. Elevated maternal CRP concentration in the first trimester of pregnancy has been reported to be positively associated with the risk for GDM in the third trimester (Qiu et al., 2004). In a prospective nested case-control study (n=137) (Wolf et al., 2003), first-trimester CRP levels were significantly increased among women who subsequently developed GDM in the third trimester compared with those without GDM.

In the Health Professionals Follow-up Study (n=466) (Fung et al., 2001), higher CRP concentrations were associated with a Western diet, characterized by high consumption of red meat, high-fat dairy products, and refined grains. Scholl et al. (Scholl et al., 2011) have suggested that diet during pregnancy was associated with circulating levels of CRP in lean pregnant women (prepregnancy BMI <25 kg/m^2). The authors noted that lean pregnant women with high CRP (range, 7.06-137.41 mg/L) at 28 weeks' gestation was associated with higher intakes of protein and cholesterol with lower intakes of carbohydrates. Inflammation may be one of the routes by which diet during pregnancy increases the risk for GDM. It is questionable whether the maternal diet influences the risk for GDM through inflammation after controlling for prepregnancy BMI. Limited studies are available as to the role of dietary factors during pregnancy in relation to GDM risk (Zhang and Ning, 2011; Zhang, 2010) in association with inflammation.

2.5 Dietary patterns before and during pregnancy as determinants for GDM

2.5.1 Dietary intake before pregnancy

Diet intake of women before pregnancy has been assessed by various approaches: dietary patterns derived by factor analysis (Zhang et al., 2006b), dietary intake by index analysis (Tobias et al., 2012; Bao et al., 2014a), individual nutrient intakes (Bao et al., 2013; Zhang et al.,

2006a; Bowers et al., 2011) or dietary intake of specific foods (e.g., fried foods) (Bao et al., 2014b). The large prospective Nurses' Health Study II (Zhang et al., 2006b; Tobias et al., 2012; Bao et al., 2013; Zhang et al., 2006a; Bao et al., 2014b; Bowers et al., 2011; Bao et al., 2014a) has been investigated to answer if dietary intake before pregnancy increases the risk for GDM.

In the Nurses' Health Study II (Zhang et al., 2006b), women whose diets before pregnancy were in the highest quintile of the "Western" dietary pattern (characterized by high intake of red meat, processed meat, refined grain products, sweets, French fries and pizza), had a higher risk for GDM (RR 1.63; 95% CI 1.20-2.21) compared to those in the lowest quintile. Conversely, women whose diets were in the lowest quintile of the "prudent" dietary pattern (characterized by a high intake of fruits, green leafy vegetables, poultry and fish) had an increased risk for GDM (RR 1.39; 95% CI 1.08-1.80) (Zhang et al., 2006b). From the study of the same cohort, Tobias et al. (Tobias et al., 2012) reported that women who adhered to healthful dietary patterns before pregnancy such as the Mediterranean Diet (aMED), Dietary Approaches to Stop Hypertension (DASH), and high score of alternate Heathy Eating Index (aHEI) had a lower risk of developing GDM after controlling for maternal age, total energy intake, gravidity, smoking status, physical activity, sedentary time, parental history of type 2 diabetes, and prepregnancy BMI (Tobias et al., 2012). This study suggests that a high consumption of fruits and vegetables and a low consumption of red and processed meats before pregnancy were associated with a decreased risk for GDM. In the same cohort of Nurses' Health Study II (Bao et al., 2014a), adherence to low-carbohydrate diet scores (reflecting higher intake of fat and protein and a lower intake of carbohydrates) was positively associated with the risk for GDM after controlling for maternal age, parity, race/ethnicity, family history of diabetes, cigarette smoking, alcohol intake, physical activity, total energy intake, and prepregnancy BMI.

From the same Nurses' Health Study II, Bao et al. (Bao et al., 2013) reported that GDM risks were positively associated with prepregnancy intake of animal protein, while inversely associated with prepregnancy vegetable protein intake. Women whose diets were in the highest

quintile for animal protein intake compared to the lowest quintile had an increased risk for GDM with RR 1.49 (95% CI: 1.03-2.17) after controlling for maternal age, parity, race/ethnicity, family history of diabetes, cigarette smoking, alcohol intake, physical activity, dietary factors, and prepregnancy BMI. Women whose diets were in the highest quintile of vegetable protein intake compared to the lowest quintile had a decreased risk for GDM (RR 0.69; 95% CI 0.50-0.97). In the same Nurses' Health Study II (Zhang et al., 2006a), prepregnancy consumption of total dietary fiber, cereal, and fruit fiber were significantly and inversely associated with the risk for GDM. When total, cereal and fruit dietary fiber intake were analyzed as continuous variables, each 10 g/day increase in total fiber intake before pregnancy was associated with 26% reduction (RR 0.74; 95% CI 0.51-0.91) in the development of GDM. Each 5 g/day increase in cereal or fruit fiber was associated with 23% (RR 0.77; 95% CI 0.64-0.91) or 26% reduced risk for GDM (RR 0.74; 95% CI 0.58-0.95). In the same Nurses' Health Study II, prepregnancy dietary iron intake was associated with the risk for GDM (Bowers et al., 2011). Women in the highest quintile of dietary heme iron intake were associated with an increased risk for GDM (OR 1.58; 95% CI 1.21-2.08) compared to the lowest quintile as a reference after controlling for maternal age, parity, prepregnancy BMI, physical activity, glycemic load, polyunsaturated fat intake, cereal fiber, smoking, alcohol, total calories, and family diabetes. Red meat, one of the major sources of dietary heme iron was found to be positively associated with GDM risk (Bowers et al., 2011). In the Nurses' Health Study II, women whose total fried foods consumption was ≥7 times/week had an increased risk for GDM (RR 1.88; 95% CI 1.34-2.64) compared to those women whose consumption was less than once/week in fully-adjusted model (Bao et al., 2014b). Frequent consumption of fried foods might have reflected unhealthy dietary habits with high total energy intake and poor diet quality, as assessed by alternate HEI-2010 (Bao et al., 2014b).

In summary, the findings from the Nurses' Health Study II indicate that several dietary factors before pregnancy are associated with risk of GDM. However, the Nurses' Health Study II

cohort does not represent a random sample of U.S. women, as the study population largely consisted of highly educated white American women. These findings may not be generalized to form dietary recommendations to reduce the risk of GDM.

2.5.2 Dietary intake during pregnancy

Several studies reported how macro- or micro-nutrient intakes during pregnancy are related to GDM risk (Wang et al., 2000; Bo et al., 2001; Saldana et al., 2004; Radesky et al., 2008; Zhang et al., 2008; Zhang et al., 2004). In 171 nulliparous Chinese pregnant women (Wang et al., 2000), macronutrient intakes estimated from a 24-hour recall at 24-28 weeks of pregnancy were associated with glucose tolerance in pregnancy. Chinese women with GDM had a significantly lower intake of polyunsaturated fat (% total fat) compared to women without GDM (28.2% vs. 31.6% of total fat) (Wang et al., 2000). Conversely, women with GDM had a significantly higher saturated fat intake compared to those without GDM (46.1% vs. 42.1% of total fat) (Wang et al., 2000). In a study of 504 Italian pregnant women, Bo et al. (Bo et al., 2001) investigated if the macronutrient compositions of diets during pregnancy were related to the risk for GDM. Every 10% increase in saturated fat (% total fat) at 24 to 28 weeks of gestation, the OR (95% CI) for GDM was 2.0 (1.2-3.2) after adjusting for maternal age, gestational age, and prepregnancy BMI. Every 10% increase in intake of polyunsaturated fat (% total fat) was associated with a 15% reduction of GDM risk (OR 0.85; 95% CI 0.77-0.92). Women's intakes of monounsaturated fat (as % of total fat) and percentages of total fat (as % kcal) were not associated with GDM risk (Bo et al., 2001). In a prospective cohort study entitled Pregnancy, Infection, and Nutrition (PIN), macronutrient intake during the second trimester was assessed by a FFQ in1,698 U.S. pregnant women to determine its relation to the development of glucose intolerance (Saldana et al., 2004). The intake of carbohydrates and fat as a percentage of energy significantly differed among normal, impaired glucose tolerance and GDM groups. Women with GDM consumed a lower percentage of energy from carbohydrates and a higher

percentage of energy from fat than women with normal glucose tolerance did (Saldana et al., 2004). In another prospective cohort study of 3,158 U.S. pregnant women, Qiu et al. (Qiu et al., 2011) evaluated if dietary heme iron intake in the first trimester assessed by a FFQ was associated with the development of GDM. Women who had the highest level of dietary heme iron intake compared with those who reported lower intake levels (≥1.52 vs. <0.48 mg per day) had a 3.31-fold increased risk for GDM (RR 3.31; 95% CI 1.02-10.72) after controlling for energy intake, maternal age, race/ethnicity parity, physical activity, prepregnancy BMI, dietary fiber, vitamin C, saturated fat, cholesterol, and red and processed meat intake (Qiu et al., 2011). In Project Viva, a prospective cohort study of pregnant women and their children in eastern Massachusetts, pregnant women's nutrient intake of the first trimester was assessed by a FFQ in relation to GDM risk (Radesky et al., 2008). The only nutrient that had a significant association with GDM risk was total n-3 fatty acids. Each 300 mg/day intake of n-3 fatty acids was associated with increased risk for GDM after controlling for maternal age, prepregnancy BMI, race/ethnicity, previous history of GDM, history of diabetes in participant's mother, and smoking during pregnancy (OR: 1.11; 95% CI 1.02-1.22). In another prospective cohort study of 755 U.S. pregnant women, low maternal plasma ascorbic acid concentrations at an average of 13 weeks' gestation were associated with increased risks for GDM (Zhang et al., 2004). Women with plasma ascorbic acid concentrations <55.9 μmol/L (lowest quartile) had a 3.1-fold increased odds for GDM (OR 3.1; 95% CI 1.0-9.7) compared with those with ≥74.6 μmol/L (upper quartile) after controlling for maternal age, race, prepregnancy adiposity, parity, family history of type 2 diabetes, and household income. From a nested case-control study in a prospective cohort study of 953 U.S. pregnant women, maternal plasma 25-hydroxyvitamin D concentrations at an average of 16 weeks of gestation was also associated with the risk for GDM (Zhang et al., 2008). Women classified as being vitamin D deficient (<20 ng/ml) had a 2.66-fold increased GDM risk after controlling for maternal age, race/ethnicity, family history of type 2 diabetes, and prepregnancy BMI compared to those women of vitamin D sufficient (≥30

ng/ml) (OR 2.66; 95% CI 1.01-7.02). Each 5 ng/ml decrease in 25-hydroxyvitamin D concentrations was related to a 1.29-fold increased odds for GDM risk (OR 1.29; 95% CI 1.05-1.60). In summary, high in intake of high saturated fat, n-3 fatty acids, and dietary heme iron and low levels of plasma vitamin C and vitamin D during pregnancy were associated with increased risk for GDM, whereas polyunsaturated fat intake was associated with decreased risk for GDM.

In literature on dietary patterns in the pregnant population, factor analysis or principal component analysis (Zhang et al., 2006b; Brantsaeter et al., 2009; Englund-Ogge et al., 2014; Rasmussen et al., 2014; Jacka et al., 2013) were used to derive dietary patterns and related to pregnancy complications or birth outcomes. Reduced rank regression methods have been introduced to assess better the diet-disease relations (Hoffmann et al., 2004a), but the method has been underutilized. The reduced rank regression method has only been reported in the studies that assessed dietary patterns during pregnancy in relation to spina bifida (Vujkovic et al., 2009) and congenital heart defect (Obermann-Borst et al., 2011) in Netherlands. Dietary patterns derived using the reduced rank regression method are expected to explain the maximum variation of GDM-related maternal nutrients and biomarkers as response variables in women with GDM.

A better understanding of the modifiable dietary factors during pregnancy using dietary patterns approach in U.S. representative pregnant women that lead to the development of GDM is imperative to improving the health of women and their infants. This is also critical for researchers, clinicians and health professionals, in order to develop public health interventions for the prevention and management of GDM.

Chapter Three: Prepregnancy weight status, independent from gestational weight gain, is a determinant for GDM.

3.1 Abstract

Previous studies established obese prepregnancy body mass index (BMI) as a determinant for gestational diabetes mellitus (GDM) without controlling for gestational weight gain as a covariate. This study aimed to examine if prepregnancy BMI is an independent determinant for GDM with consideration of gestational weight gain, to document the importance of preconception vs. prenatal stage. We used the data of 219,868 pregnant women from the 2004 to 2011 Pregnancy Risk Assessment Monitoring System (PRAMS). Multivariable logistic regression analyses were used to examine the effect of prepregnancy BMI for GDM after controlling for the adequacy of gestational weight gain. Women who had overweight or obese prepregnancy BMI in reference to normal prepregnancy BMI had higher odds for GDM (adjusted odds ratio (AOR)=1.79; 95% CI=1.68-1.92, AOR=2.78; 95% CI=2.60-2.96, respectively). Women who had underweight prepregnancy BMI in reference to normal prepregnancy BMI had lower odds for GDM (AOR=0.85; 95% CI=0.74-0.97). Regardless of the adequacy of gestational weight gain, if women were overweight or obese before pregnancy, they all had higher odds for GDM. Prepregnancy weight status is an independent determinant for GDM.

3.2 Introduction

Several researchers (Doherty et al., 2006; Chung et al., 2012; Li et al., 2013; Al-Obaidly et al., 2014) reported prepregnancy obesity as a risk factor for GDM. These studies (Doherty et al., 2006; Chung et al., 2012; Li et al., 2013; Al-Obaidly et al., 2014), however, did not control gestational weight gain which is known to be highly associated with prepregnancy weight status. One Danish study (Nohr et al., 2008) partitioned gestational weight gain from prepregnancy weight status in their associations with GDM risk. In the Danish National Birth Cohort (Nohr et

al., 2008), prepregnancy BMI ≥25 kg/m^2 and gestational weight gain <10 kg were independently associated with increased risks for GDM. Independent effects of prepregnancy BMI on the development of GDM have not yet been established in U.S. pregnant women. Furthermore, it has not been investigated whether the gestational weight guidelines of the Institute of Medicine (Institute of Medicine, 2009), which aims to optimize the health of both mothers and their offspring would be effective in lowering GDM prevalence.

Except for a Danish study (Nohr et al., 2008), most of the studies did not consider the effect of gestational weight gain as a covariate when examining the association of prepregnancy weight status with GDM risk. Evidence for an effect of prepregnancy BMI after controlling for the adequacy of gestational weight gain based on the Institute of Medicine's 2009 guidelines on GDM has been limited in U.S. pregnant women. Most of the previous studies (Nohr et al., 2008; Li et al., 2013; Heude et al., 2012) were conducted in European or Asian countries, and few studies adequately addressed the interactions between prepregnancy BMI and gestational weight gain.

Recognizing that prepregnancy weight status is a predictor of gestational weight gain (Chu et al., 2009), we cannot differentiate which of the two maternal weight statuses played a more critical role, or how they interacted to explain the increased risk for GDM associated with maternal weight status. Previous studies established obese prepregnancy BMI as a determinant for GDM (Li et al., 2013; Chung et al., 2012; Doherty et al., 2006) without controlling for gestational weight gain as a covariate. We aimed to examine if prepregnancy weight status, independent from gestational weight gain is a determinant for GDM. Study findings would provide the evidence for the effect of prepregnancy BMI on the development of GDM after controlling for gestational weight gain based on the Institute of Medicine's 2009 guidelines in the U.S. representative pregnant women.

3.3 Material and Methods

3.3.1 Study Population

The sample for this study was derived from the respondents of the Pregnancy Risk Assessment Monitoring System (PRAMS). PRAMS is an ongoing surveillance project of the Centers for Disease Control and Prevention (CDC) and state health departments of 40 states and New York City in the U.S. PRAMS is designed to collect state-specific, population-based maternal health data before, during, and shortly after pregnancy (Centers for Disease Control and Prevention, 2014). The most recent dataset that was attainable at the beginning of this project was the dataset of 2004 to 2011 at phase 5 (2004-2008) and 6 (2009-2011).

The PRAMS sample was chosen from all women who had recent live births, so findings can be applied to the state's entire population of women who have recently delivered live-born infants. PRAMS provides state-specific data, and also allows for comparisons among participating states because the same data collection methods are used in all states. PRAMS collects data based on the state’s birth certificate file, a stratified systematic sample of 100-300 new mothers who delivered live-born infants in the preceding 2-4 months. The medical information in the state’s birth certificate files are collected through the state's vital records system and submitted electronically to the State Department of Health by the healthy facility where the respondent gave birth. A self-administered questionnaire is mailed to each mother to obtain information on prepregnancy BMI and GDM. If the mother fails to respond, a second and usually a third questionnaire is mailed to each mother. If the mother does not respond to the mailings, telephone interviews are made to follow-up with her. Each completed questionnaire is then linked to information from the state’s birth certificate file. The state’s birth certificate files include information on total gestational weight gain.

The initial PRAMS 2004-2011 cohort includes 313,735 women at the national level from Alaska, Arkansas, Colorado, Delaware, Florida, Georgia, Hawaii, Illinois, Louisiana,

Massachusetts, Maryland, Maine, Michigan, Minnesota, Missouri, Mississippi, North Carolina, Nebraska, New Jersey, New Mexico, New York, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Texas, Utah, Vermont, Washington, Wisconsin, West Virginia, Wyoming, and New York City.

Approval was obtained for the data usage from the PRAMS Working Group at the CDC for this analysis. After excluding women with missing information on prepregnancy BMI, gestational weight gain, gestational diabetes or preexisting diabetes, and maternal characteristic variables, the final analytic sample size for the present study consisted of 219,868 pregnant women.

3.3.2 Exposure Variable

Prepregnancy BMIs were calculated from weight in kilograms divided by height in meters squared. Prepregnancy BMIs were then grouped into four categories based on the WHO criteria (WHO Expert Committee on Physical Status, 1995) and adopted by the NHLBI that are widely used in the U.S. and elsewhere: underweight (<18.5 kg/m^2), normal (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), and obese (≥30.0 kg/m^2).

3.3.3 Outcome Variable

From the PRAMS questionnaire, GDM was defined as any woman who answered “yes” to the question, “did you have GDM during your most recent pregnancy?”

3.3.4 Covariates

Analyses were adjusted for gestational weight gain, maternal age, race/ethnicity, education, annual household income, gestational age, marital status, Women, Infants, and Children (WIC) status during pregnancy, and smoking status during pregnancy. Adequacy of

gestational weight gain status (inadequate, adequate, excessive gain) was determined by comparing the actual gestational weight gain on the birth certificate file in reference to the Institute of Medicine's gestational weight gain guidelines (2009) (Institute of Medicine, 2009) using the prepregnancy weight status. The inadequate gestational weight gain status group consisted of pregnant women whose gestational weight gain is less than the minimum weight gain recommended for each prepregnancy weight status. The adequate gestational weight gain group consisted of pregnant women whose gestational weight gain was between minimum and maximum recommended gestational weight gain. The excessive gestational weight gain group consisted of pregnant women whose gestational weight gain exceeded the maximum recommended gestational weight gain. Maternal age was divided into three groups (≤24, 25-34, ≥35 years). The study group consists of non-Hispanic white, non-Hispanic black, Hispanic, and other non-Hispanic races. Maternal education was grouped by the number of completed years of school (less than high school, high school diploma, more than high school). Annual house income was classified into five categories (<$15,000, $15,000-$35,000, $35,000-$50,000, ≥$50,000). Gestational weeks were categorized into five groups (≤27, 28-33, 34-36, 37-42, ≥43 weeks). History of preexisting diabetes was divided into two groups (yes or no). Marital status was divided into two groups (married or other). WIC status during pregnancy was divided into two groups (yes or no). Lastly, smoking status during pregnancy was divided into two groups (yes or no).

3.3.5 Statistical Analyses

Participants' characteristics were described using weighted frequency distributions and consistent with survey sampling. Tests of associations between prepregnancy BMI categories and maternal characteristics were conducted using the chi-square statistics. The independent variable of interest was prepregnancy BMI stratified into the standard BMI categories as defined by the WHO (WHO Expert Committee on Physical Status, 1995): underweight (<18.5 kg/m^2),

normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), obese (≥30 kg/m^2), with normal weight as the reference. Multivariable logistic regression was used to examine the relationship of prepregnancy BMI with GDM risk after controlling for gestational weight gain, maternal age, race, education level, household income level, history of preexisting diabetes, marital status, gestational weeks, WIC status during pregnancy, and smoking status. To obtain the findings that are applicable to all women of the PRAMS participating states in the U.S., sample weights were applied to account for unequal probability of selection and response probabilities of the survey design. SAS version 9.3 (SAS Institute, Cary, NC, U.S.) was used to conduct all statistical analyses. Significance was declared at a *P*-value < 0.05.

3.4 Results

Table 4 shows the characteristics of the study population by prepregnancy BMI (underweight, normal, overweight, and obese). Distributions in maternal age, race, maternal education, income, marital status, gestational weeks, WIC participation during pregnancy, smoking status during pregnancy by prepregnancy BMI categories were all significant (p<0.0001). Overweight and obese women were slightly older, unmarried, WIC participants, and more likely to be less educated compared to underweight women.

Table 5 depicts the distribution of women in GDM by prepregnancy BMI. Distribution of GDM significantly differed by each prepregnancy BMI category, respectively (p<0.0001). The lowest rate of GDM was observed in women who had underweight prepregnancy BMI compared to those women who had normal, overweight or obese prepregnancy BMI (2.9% vs. 35.9%, 27.0%, 34.2%, respectively).

Women who had overweight or obese prepregnancy BMI in reference to normal prepregnancy BMI had higher odds for GDM (adjusted odds ratio (AOR) 1.79; 95% CI 1.68-1.92, AOR 2.78; 95% CI 2.60-2.96, respectively). Women who had underweight prepregnancy BMI in

reference to normal prepregnancy BMI had lower odds for GDM (AOR 0.85; 95% CI 0.74-0.97) (Table 6).

Women in the inadequate gestational weight gain group in reference to adequate gestational weight gain group had higher odds for GDM (AOR 1.31; 95% CI 1.22-1.41). Women in excessive gestational weight gain group in reference to the adequate gestational weight gain group had lower odds for GDM (AOR 0.84; 95% CI 0.79-0.89) (Table 7).

Regardless of the adequacy of gestational weight gain, if women were overweight or obese before pregnancy, they all had higher odds for GDM in comparison to those women with normal prepregnancy BMI and adequate gestational weight gain. Women who had normal prepregnancy BMI and inadequate gestational weight gain had higher odds for GDM (AOR 1.42; 95% CI 1.28-1.58). Women who had normal prepregnancy BMI and excessive gestational weight gain had lower odds for GDM (AOR 0.90; 95% CI 0.81-0.99) (Table 8).

Table 4. Maternal characteristics by prepregnancy weight status (n=219,868)

	Prepregnancy BMI[1]												
	Underweight (n=11,865; Wt'd[2] %=4.6%)			Normal (n=113,523; Wt'd %=52.4%)			Overweight (n=51,517; Wt'd %=23.7%)			Obese (n=42,963; Wt'd %=19.2%)			
	n	Wt'd % (Row)	Wt'd % (Col)	N	Wt'd % (Row)	Wt'd% (Col)	n	Wt'd % (Row)	Wt'd % (Col)	n	Wt'd % (Row)	Wt'd % (Col)	*P*[3]
Maternal Age (y)													
≤24	5998	47.8	7.1	38927	31.7	53.1	15999	29.8	22.5	12530	28.1	17.3	<0.0001
25-34	4782	43.2	3.7	57513	53.9	52.2	26944	54.7	23.9	23360	56.7	20.1	
≥35	1085	9.1	2.9	17083	14.4	51.8	8574	15.5	25.2	7073	15.2	20.1	
Maternal Race													
Non-Hispanic white	7107	65.2	4.6	68900	68.3	54.8	28310	62.5	22.6	23188	60.9	17.9	<0.0001
Non-Hispanic black	1490	11.5	4	13843	10.5	41	9093	15.5	27.3	9231	19.5	27.7	
Hispanic	1148	11.9	3.9	13349	13.0	48.6	7436	16.1	27	5623	15.0	20.5	
Other non-Hispanic	2120	11.4	7.5	17431	8.1	60.2	6678	5.9	19.8	4921	4.6	12.5	
Maternal Education (y)													
Less than high school	2672	21.1	7	15582	13.0	48.8	7240	14.5	24.5	6012	14.3	19.6	<0.0001
High school diploma	3882	31.1	5.3	29796	24.5	47.2	15123	28.0	24.4	14496	32.6	23.1	
Some college	2547	21.9	3.9	27468	23.9	48.5	14394	27.2	24.9	13267	30.6	22.7	
More than college	2764	26.0	3.7	40677	38.6	61.4	14760	30.3	21.8	9188	22.4	13.1	
Income													
Less than $15,000	5176	40.9	6.9	32338	25.3	48.3	15114	27.2	23.4	13926	30.4	21.3	<0.0001
$15,000-$34,999	2850	23.4	4.6	24865	21.1	47.1	13115	24.8	25	12517	28.5	23.3	
$35,000-$50,000	1017	9.1	3.9	12027	10.2	49.6	5894	11.2	24.7	5222	12.3	21.8	
≥$50,000	2822	26.5	3.2	44293	43.3	59.5	17394	36.8	22.8	11298	28.8	14.5	
Marital Status													
Married	6429	55.3	4	74095	67.2	54.5	32501	63.8	23.4	26062	61.0	18.1	<0.0001

Table 4 (cont'd)

	Prepregnancy BMI												
	Underweight (n=11,865; Wt'd[2] %=4.6%)			Normal (n=113,523; Wt'd %=52.4%)			Overweight (n=51,517; Wt'd %=23.7%)			Obese (n=42,963; Wt'd %=19.2%)			
	n	Wt'd % (Row)	Wt'd % (Col)	N	Wt'd % (Row)	Wt'd% (Col)	n	Wt'd % (Row)	Wt'd % (Col)	n	Wt'd % (Row)	Wt'd % (Col)	*P*[3]
Other	5436	44.7	5.9	39428	32.8	48.6	19016	36.2	24.3	16901	39.0	21.2	
Gestational age at birth (weeks)													
≤27	259	0.5	4.7	2029	0.3	39.6	1240	0.5	26.6	1462	0.7	29.1	<0.0001
28-33	862	2.0	6.3	6295	1.3	46.5	3145	1.4	23.5	3274	1.8	23.7	
34-36	1812	7.6	6.2	12633	5.4	49.8	5444	5.6	23.1	5037	6.3	20.9	
37-42	8923	89.8	4.5	92485	92.9	52.8	41636	92.4	23.7	33143	91.2	19	
≥43	9	0.1	7.2	81	0.1	38.7	52	0.1	31.2	47	0.1	22.9	
WIC during pregnancy													
Yes	6378	49.9	5.6	45371	63.4	45.9	23615	56.5	24.6	23256	48.1	23.9	<0.0001
No	5487	50.1	4	68152	36.6	57.1	27902	43.5	23	19707	51.9	15.9	
Smoking status during pregnancy													
Yes	2614	17.9	7.8	13923	9.6	47.3	6432	10.4	23	5994	12.2	21.9	<0.0001
No	9251	82.1	4.3	99600	90.4	53.1	45085	89.6	23.8	36969	87.8	18.8	
Total	11865			113523			51517			42963			

[1] BMI (kg/m2) categories according to the World Health Organization: underweight (<18.5), normal weight (18.5-24.9), overweight (25-29.9), and obese (≥30).
[2] Wt'd: Based on weighted percentage.
[3] Chi-square tests for differences in prepregnancy BMI by maternal age, race, education, income, marital status, gestational weeks, WIC participation during pregnancy, and smoking status during pregnancy.
Numbers may not sum up to 100.0 due to rounding.

Table 5. Distribution of gestational diabetes mellitus (GDM) by prepregnancy weight status

	Prepregnancy BMI[1]												P^3
	Underweight (n=11,865)			Normal (n=113,523)			Overweight (n=51,517)			Obese (n=42,963)			
	n	Wt'd[2] % (Row)	Wt'd % (Col)	n	Wt'd % (Row)	Wt'd % (Col)	n	Wt'd % (Row)	Wt'd % (Col)	n	Wt'd % (Row)	Wt'd % (Col)	
GDM													
Yes	714	5.3	2.9	7,433	5.8	35.9	5,479	9.7	27.0	6,978	15.1	34.2	<0.0001
No	11,151	94.7	4.8	106,090	94.2	54.0	46,038	90.3	23.4	35,985	84.9	17.8	

[1] BMI (kg/m^2) categories according to the World Health Organization: underweight (<18.5), normal weight (18.5-24.9), overweight (25-29.9), and obese (≥30).
[2] Wt'd: Based on weighted percentage.
[3] Chi-square tests for differences in prepregnancy BMI by the status of GDM.
Numbers may not sum up to 100.0 due to rounding.

Table 6. Adjusted odds ratios (AOR) and 95% CI for gestational diabetes mellitus (GDM) across categories of prepregnancy weight status

	Prepregnancy BMI[1]												
	Normal (n=113,523)		Underweight (n=11,865)			Overweight (n=51,517)			Obese (n=42,963)				*P trend*
	OR	AOR[2]	95% CI		*P*	AOR	95% CI	*P*	AOR	95% CI		*P*	
GDM	1 (ref)	0.85	0.74	0.97	0.018	1.79	1.68 1.92	<0.0001	2.78	2.60	2.96	<0.0001	<0.0001

[1] BMI (kg/m^2) categories according to the World Health Organization: underweight (<18.5), normal weight (18.5-24.9), overweight (25-29.9), and obese (≥30).

[2] Adjusted for gestational weight gain (inadequate, adequate, excessive), maternal age (≤24, 25-34, ≥35), race (non-Hispanic White, non-Hispanic Black, Hispanic, other non-Hispanic), education level (less than high school, high school diploma, some college, more than college), income level (<$15,000, $15,000 $34,999, $35,000-$50,000, ≥$50,000), marital status (Married or other), gestational weeks (≤27, 28-33, 34-36, 37-42, ≥43), WIC during pregnancy (yes or no), smoking status during pregnancy (yes or no), and preexisting diabetes (yes or no).

Table 7. Adjusted odds ratios (AOR) and 95% CI for gestational diabetes mellitus (GDM) across gestational weight gain categories

	Gestational Weight Gain[1]									
	Adequate (n=64,272; Wt'd[2] %=18.4%)	Inadequate (n=49,377; Wt'd %=28.9%)				Excessive (n=106,219; Wt'd %=52.7%)				*P* trend
	OR	AOR[3]	95% CI		*P*	AOR	95% CI		*P*	
GDM	1 (ref)	1.31	1.22	1.41	<0.0001	0.84	0.79	0.89	<0.0001	<0.0001

[1] Gestational weight gain was divided inadequate, adequate, and excessive groups according to Institute of Medicine's 2009 guidelines.
[2] Wt'd: Based on weighted percentage.
[3] Adjusted for prepregnancy BMI (underweight, normal, overweight, obese), maternal age (≤24, 25-34, ≥35), race (non-Hispanic White, non-Hispanic Black, Hispanic, other non-Hispanic), education level (less than high school, high school diploma, some college, more than college), income level (<$15,000, $15,000 $34,999, $35,000-$50,000, ≥$50,000), marital status (Married or other), gestational weeks (≤27, 28-33, 34-36, 37-42, ≥43), WIC during pregnancy (yes or no), smoking status during pregnancy (yes or no), and preexisting diabetes (yes or no).

Table 8. Adjusted odds ratios (AOR) and 95% CI for gestational diabetes mellitus (GDM) across categories of prepregnancy weight status and gestational weight gain

	Prepregnancy BMI[1]															
	Underweight (n=11,865)				Normal (n=113,523)				Overweight (n=51,517)				Obese (n=42,963)			
	AOR[3]	95% CI		*P*	AOR	95% CI		*P*	AOR	95% CI		*P*	AOR	95% CI		*P*
Gestational weight gain[2]																
Inadequate (n=64,272)	0.94	0.76	1.17	0.5698	1.42	1.28	1.58	<.0001	2.26	1.95	2.63	<.0001	3.93	3.44	4.48	<.0001
Adequate (n=49,377)	0.87	0.69	1.10	0.2361	1.00 (ref)				2.04	1.81	2.28	<.0001	2.99	2.64	3.38	<.0001
Excessive (n=106,219)	1.14	0.88	1.48	0.3138	0.90	0.81	0.99	0.0330	1.56	1.42	1.72	<.0001	2.41	2.20	2.65	<.0001

[1] BMI (kg/m^2) categories according to the World Health Organization: underweight (<18.5), normal weight (18.5-24.9), overweight (25-29.9), and obese (≥30).
[2] Gestational weight gain was divided inadequate, adequate, and excessive groups according to Institute of Medicine's 2009 guidelines.
[3] Adjusted for maternal age (≤24, 25-34, ≥35), race (non-Hispanic White, non-Hispanic Black, Hispanic, other non-Hispanic), education level (less than high school, high school diploma, some college, more than college), income level (<$15,000, $15,000 $34,999, $35,000-$50,000, ≥$50,000), marital status (Married or other), gestational weeks (≤27, 28-33, 34-36, 37-42, ≥43), WIC during pregnancy (yes or no), smoking status during pregnancy (yes or no), and preexisting diabetes (yes or no).

3.5 Discussion

The results of our study suggest that prepregnancy BMI is independently associated with the risk for GDM even after adjustment of maternal sociodemographic characteristics and gestational weight gain. The risk of GDM increased in women with overweight and obese prepregnancy BMI. In parallel with our findings, previous researchers found that overweight and obese prepregnancy weight status was associated with increased risks for GDM (Chu et al., 2007; Li et al., 2013; Chung et al., 2012; Nohr et al., 2008; Hedderson et al., 2008; Doherty et al., 2006; Torloni et al., 2009) at varying degrees across studies with different BMI categorization and sampling schemes. In a retrospective cohort study of California, obese women before pregnancy were nearly 3 times more likely to have GDM (OR 2.83; 95% CI 2.74-2.92) in comparison to those who had normal prepregnancy BMI (Chung et al., 2012). Except for a Danish study (Nohr et al., 2008), majority of the studies did not consider the effect of gestational weight gain as a covariate when examining the association of prepregnancy weight status with GDM risk. In the Danish National Birth Cohort (Nohr et al., 2008), compared to women of normal prepregnancy BMI, women who were overweight or obese all had increased risks for GDM (OR 2.5; 95% CI 2.1-3.0, OR 5.9; 95% CI 4.8-7.3, respectively).

Women who had inadequate gestational weight gain had increased risk for GDM. Consistent with our finding, pregnant women who had a total gestational weight gain of less than 10 kg had increased risk for GDM (OR 2.3; 95% CI 1.9-2.8) compared to those women with 10-15 kg (Nohr et al., 2008). The authors explained that the inverse relationship between gestational weight gain and the risk for GDM was due to the variation in prenatal care. Screening is carried out more often among obese than lower-weight women, and after diagnosis of GDM, the obese women are often prescribed a diet that will restrict their total gestational weight gain (Nohr et al., 2008). In a mother-child cohort study of 1,884 French pregnant women (Heude et al., 2012), as the categories of gestational weight gain moved from normal (3-12 kg)

to high (>16 kg), the risk of GDM decreased at the margin of significance (p=0.06). In contrast, in a randomized controlled trial of vitamins C and E supplementation in nulliparous low-risk women (Carreno et al., 2012), women who had excessive gestational weight gain, greater than the upper range of Institute of Medicine's 2009 guidelines had 43% higher risk of developing GDM compared to the non-excessive gestational weight gain group (OR 1.4; 95% CI 1.1-1.9). In a retrospective cohort study, gestational weight gain through 24 weeks was significantly higher in the women with GDM compared to those women without GDM (14.8 lb vs. 11.2 lb) (Gibson et al., 2012). Research findings to date have been inconsistent (Institute of Medicine, 2009). Some failed to find the association between gestational weight gain and GDM (Hackmon et al., 2007; Seghieri et al., 2005), whereas other study found both excessive and inadequate gestational weight gain was associated with the risk of GDM (Nohr et al., 2008; Heude et al., 2012; Carreno et al., 2012; Gibson et al., 2012).

Our findings demonstrate that regardless the adequacy of gestational weight gain, women of overweight and obese prepregnancy BMI, they all had increased risks for GDM. In parallel with our finding, from the analysis of health care records of 33,973 Chinese pregnant women (Li et al., 2013), women with prepregnancy obesity (BMI ≥28.0 kg/m^2), regardless of the adequacy of gestational weight gain had all increased risks for GDM. This addresses the importance of preventing prepregnancy overweight or obesity for pregnant women to lower the risk of GDM. Counseling about nutrition and physical activity, and appropriate contraceptive use may help women achieve a healthy weight before pregnancy (DeSisto et al., 2014). However, lack of obstetrician/gynecologists offering advice on weight loss, physical activity, or behavioral modifications may indicate significant obstacles for reproductive aged women to achieve a healthy weight before pregnancy (Cogswell et al., 2010).

Half of the U.S. pregnancies were unintended in 2008 (Finer and Zolna, 2014). Unintended pregnancy was associated with a wide range of adverse prenatal behaviors such as smoking and drinking during pregnancy, and attending later for the first prenatal appointment

(McCrory and McNally, 2013). Possibly, unintended pregnancy may be one of the determinants for GDM since women who do not plan their pregnancies would not receive adequate prenatal care screening and counseling compared to those who plan their pregnancies ahead of time.

It has been reported that women with GDM may have a higher risk of glucose intolerance in their offspring (Crowther et al., 2005) than healthy women, partially due to shared genetic factors or similar dietary and physical activity in their families (Gillman et al., 2003). Recently, in a retrospective longitudinal cohort study at Kaiser Permanente Southern California hospitals, women with GDM were at risk for their child being born with autism spectrum disorder (Xiang et al., 2015). Moreover, GDM increased U.S. medical costs by $636 million in 2007 (Chen et al., 2009b). Given the long-term adverse health consequence of GDM on future generations and its economic burden to the society, it is of great importance to reduce the risk of GDM through preventing overweight or obesity for women of childbearing age.

Strengths of this study include that PRAMS is a population-based study with the overall response rate of over 70%. The extensive information on maternal sociodemographic and lifestyle factors including physical activity could be matched with state birth records, and thus a number of important confounders could be controlled in the present study. Prepregnancy BMI used in this study are self-reported, and we (Shin et al., 2014b) previously demonstrated that prepregnancy weight status classified based on self-reported prepregnancy height and weight was valid in U.S. pregnant women. This study may have limitations as the retrospective cross-sectional study design may not establish a cause-effect relationship. Second, mothers who were surveyed 2-4 months postpartum could have had some recall bias with memory lapse. Third, no information was available on family history of type 2 diabetes.

In conclusion, prepregnancy BMI was an independent predictor for GDM after controlling for gestational weight gain. This confirms that weight status before the start of pregnancy is critically important and thus special attention needs to be given to preconception care and counseling for all reproductive aged women, particularly those with overweight or obesity.

Chapter Four: Prepregnancy weight status is associated with diet quality during pregnancy.

4.1 Abstract

Although the positive association of prepregnancy overweight and obesity with excessive gestational weight gain has been well-known, it is not clear how prepregnancy weight status is associated with gestational weight gain through diet during pregnancy. This study aimed to examine the relationship between prepregnancy weight status and diet quality during pregnancy. Our study included 795 U.S. pregnant women of the National Health and Nutrition Examination Survey (NHANES) 2003-2012. Prepregnancy body mass index (BMI) was calculated based on self-reported prepregnancy weight and height. The cut-off points of <18.5 (underweight), 18.5–24.9 (normal), 25.0–29.9 (overweight), and 30 kg/m^2 (obese) were used to categorize pregnant women's weight status. Diet quality during pregnancy was assessed by the Healthy Eating Index (HEI)-2010 based on a 24-hour recall. Multivariable logistic regressions were used to estimate the odds ratios (OR) and 95% confidence intervals (CI). For all pregnant women included in this study, the mean HEI-2010 was 50.7 (± 0.9). Women with obese prepregnancy BMI demonstrated significantly lower HEI-2010 compared to those with underweight and normal prepregnancy BMI, respectively. In an unadjusted model, women with prepregnancy obesity BMI had increased odds for being in the lowest tertile of HEI-2010 compared to those with normal prepregnancy BMI (OR 4.99; 95% CI 2.19-11.37). The inverse association between prepregnancy overweight and obesity status and diet quality during pregnancy persisted even after we controlled for physical activity levels (adjusted OR (AOR) 4.30; 95% CI 1.44-12.86, AOR 5.50; 95% CI 2.05-14.77). An inverse association was found between prepregnancy weight status and diet quality during pregnancy. Nutrition education and interventions need to be provided to those women entering pregnancy as overweight and obese.

4.2 Introduction

Maternal diet before and during pregnancy may play an important role in maternal, neonatal and child health outcomes (Ramakrishnan et al., 2012; Bloomfield, 2011). Overweight and obesity status before pregnancy has been found to be associated with excessive gestational weight gain (Chu et al., 2009), which in turn is associated with postpartum weight retention (Kac et al., 2004). Prepregnancy weight status has also been reported as an independent determinant for gestational diabetes mellitus (GDM), gestational hypertension, preterm birth, and small- and large-for gestational age births in U.S. pregnant women (Shin and Song, 2015). Diet during pregnancy may partially mediate the relationship between prepregnancy overweight and obesity and pregnancy complications and birth outcomes (Tomedi et al., 2013). Laraia et al. (Laraia et al., 2007) firstly demonstrated that prepregnancy BMI was inversely associated with diet quality as measured by the Diet Quality Index for Pregnancy (DQI-P) in pregnant women in North Carolina. In a cross-sectional study of Greek women, Tsigga et al. (Tsigga et al., 2011) also reported that pregnant women who were underweight or normal weight before pregnancy demonstrated a better diet quality as assessed by the Healthy Eating Index (HEI)-2005 compared to women with obese prepregnancy BMI. However, the majority of the study population in these studies (Laraia et al., 2007; Tsigga et al., 2011) were low- to middle- income non-Hispanic white women. Thus, this may not be representative of the entire population of U.S. pregnant women.

It has been reported that pregnant women rarely change their dietary patterns before and during pregnancy using principal component analysis (Crozier et al., 2009). The authors reported that there were overall small decreases in applied diet scores in pregnancy compared with before pregnancy and a small increase in applied high-energy diet scores in late pregnancy, indicating little overall change from before to during pregnancy. The little diet changes before to during pregnancy may be due to the fact that the majority of pregnancies are unplanned, and women do not have adequate time to adapt to the new nutritional recommendations for

pregnancy (Inskip et al., 2009). Pregnant women's dietary behaviors and intake during pregnancy may reflect those of prior to their pregnancy.

Gestational weight gain guidelines were established based on prepregnancy weight status (Institute of Medicine, 2009). However, it is unclear how prepregnancy weight status is associated with gestational weight gain through maternal diet during pregnancy. Diet during pregnancy may play a significant role linking the association between prepregnancy weight status and gestational weight gain. It is important to examine the relationship between prepregnancy weight status and diet quality during pregnancy in U.S. representative pregnant women.

4.3 Material and Methods

4.3.1 Study Population

We used public domain data from the continuous National Health and Nutrition Examination Survey (NHANES) 2003-2004, 2005-2006, 2007-2008, 2009-2010, and 2011-2012 for this study. NHANES is a program of studies cross-sectionally designed to assess the health and nutritional status of civilian, non-institutionalized population in the U.S. conducted by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC). The NHANES used a stratified multistage probability sample that was based on the selection of counties, blocks, households, and finally persons within households. The NHANES survey is unique in that it combines interviews and physical examinations. The participants were interviewed for the information of age, race/ethnicity, education level, marital status, family poverty income ratio, and physical activity. Reproductive health interviews obtained information on month of gestation at the time of the survey. Pregnancy status was based on a positive urine pregnancy test or self-reported pregnancy. A complete description of data-collection procedures

and analytic guidelines has been provided elsewhere (Centers for Disease Control and Prevention, 2013a; Centers for Disease Control and Prevention, 2013b).

The 2003-2012 NHANES dataset included 856 pregnant women. Subjects were excluded if they reported unreliable dietary data, as defined by the NCHS (Centers for Disease Control and Prevention and National Center for Health Statistics, 2014b). Included in the present study were participants with complete data for all variable of our interest: pregnancy urine test, age, race/ethnicity, family poverty income ratio, education, marital status, trimester of pregnancy, self-reported prepregnancy weight, and measured height and weight. The final analytic sample size was 795 pregnant women.

4.3.2 Exposure Variable

Self-reported prepregnancy weight and measured height were used to calculate prepregnancy BMI. We have previously demonstrated that prepregnancy weight status classified based on self-reported prepregnancy height and weight was valid (Shin et al., 2014b). Self-reported prepregnancy weight status were stratified into four categories based on the WHO criteria (WHO Expert Committee on Physical Status, 1995): <18.5 kg/m^2 (underweight), 18.5–24.9 kg/m^2 (normal), 25.0–29.9 kg/m^2 (overweight), and ≥30 kg/m^2 (obese).

4.3.3 Outcome Variables

Dietary intake was measured via an in-person 24-hour recall collected by trained personnel of National Center for Health Statistics (NCHS) using the USDA's Automated Multiple-Pass Method (Moshfegh et al., 2008). The HEI is a measure of diet quality in terms of conformance to the Dietary Guidelines for Americans, which are the basis of nutrition policy for the U.S. government and the foundation of all federal nutrition guidance (Guenther et al., 2013). The HEI-2010 is made up of 12 components: 9 adequacy components (total fruit; whole fruit; total vegetables; greens and beans; whole grains; dairy; total protein foods; seafood and plant protein; and fatty acids) and 3 moderation components (refined grains; sodium; and empty calories) (Table 9) (Guenther et al., 2013). For the adequacy component, a higher score corresponds to a higher intake. For the moderation component, a higher score corresponds to lower intake. The total HEI-2010 scores range from 0 (non-adherence) to 100 (perfect adherence). The MyPyramid Equivalent Database (MPED) 2.0, Food Patterns Equivalents Database (FPED) 2005-2006, FPED 2007-2008, FPED 2009-2010, and FPED 2011-2012 with the addendum from the Center for Nutrition Policy and Promotion was used for food grouping (U.S. Department of Agriculture Center for Nutrition Policy and Promotion, 2013). The scoring method of the HEI-2010 is described and elsewhere (Guenther et al., 2013) and summarized in Table 9. In our study, a categorical variable was created using the HEI-2010 tertiles as cut-off points to compare the lowest with the highest tertile as a reference.

Daily energy intake, percent energy from carbohydrates, protein and intakes of fat, folate, iron, and calcium from one-day 24-hour recall were calculated. Diet-related biomarkers including total calcium and total iron levels were obtained from the NHANES standard biochemistry profile dataset. Detailed descriptions and instructions can be found in the NHANES Laboratory/Medical Technologists Procedures Manual (Centers for Disease Control and Prevention and National Center for Health Statistics, 2009c). Briefly, serum levels of total calcium and total iron were

measured by the DxC800 System (Centers for Disease Control and Prevention and National Center for Health Statistics, 2013a). Serum folate and ferritin were also assessed in relation to prepregnancy weight status. Serum folate was measured by using the Quantaphase II (Bio-Rad Laboratories) radioassay kit during NHANES 2003-2006 (Centers for Disease Control and Prevention and National Center for Health Statistics, 2006a), by the microbiologic growth assay during NHANES 2007-2010 (Centers for Disease Control and Prevention and National Center for Health Statistics, 2011), and by the isotope-dilution high performance liquid chromatography coupled to tandem mass spectrometry during NHANES 2011-2012 (Centers for Disease Control and Prevention and National Center for Health Statistics, 2014a). Ferritin was measured by the immune-turbidimetry using the Roche/Hitachi 912 clinical analyzer (Centers for Disease Control and Prevention and National Center for Health Statistics, 2009b).

Table 9. The Healthy Eating Index (HEI)-2010 components and standards

Component	Max. Points	Standard for Max. Score	Standard for Min. Score of Zero
HEI-2010[a]			
Adequacy:			
Total Fruit[b]	5	≥0.8 cup equivalent/1,000kcal	No Fruit
Whole Fruit[c]	5	≥0.4 cup equivalent/1,000kcal	No Whole Fruit
Total Vegetables[d]	5	≥1.1 cup equivalent/1,000kcal	No Vegetables
Greens and Beans[d]	5	≥0.2 cup equivalent/1,000kcal	No Dark Green Vegetables or Beans or Peas
Whole Grains	10	≥1.5 oz equivalent/1,000kcal	No Whole Grains
Dairy[e]	10	≥1.3 cup equivalent/1,000kcal	No Dairy
Total Protein Foods[f]	5	≥2.5 oz equivalent/1,000kcal	No Protein Foods
Seafood and Plant Proteins[fg]	5	≥0.8 oz equivalent/1,000kcal	No Seafood or Plant Proteins
Fatty Acids[h]	10	(PUFAs+MUFAs)/SFAs >2.5	(PUFAs+MUFAs)/SFAs ≤1.2
Moderation:			
Refined Grains	10	≤1.8 oz equivalents/1,000kcal	≥4.3 oz equivalent/ 1,000 kcal
Sodium	10	≤1.1 g/1,000 kcal	≥2.0 g per 1,000 kcal
Empty Calories[i]	20	≤19% of energy	≥50% of energy

Source: Adapted from: Guenther PM et al. (2013) Update of the Healthy Eating Index: HEI-2010. J Acad Nutr Diet. 2013;113:569-580.

[a] Intakes between the minimum and maximum standards are scored proportionately.

[b] Includes fruit juice

[c] Includes all forms except juice.

[d] Includes any beans and peas not counted as Total Protein Foods.

[e] Includes all milk products, such as fluid milk, yogurt, and cheese, and fortified soy beverages.

[f] Beans and peas are included here (and not with vegetables).

[g] Includes seafood, nuts, seeds, soy products (other than beverages) as well as beans and peas counted as Total Protein Foods.

[h] Ratio of polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs) to saturated fatty acids (SFAs).

[i] Calories from solid fats, alcohol, and added sugars; threshold for counting alcohol is >13g/1,000 kcal.

4.3.4 Covariates

Analyses were adjusted for maternal age, race/ethnicity, family poverty income ratio, education, marital status, and physical activity level. Maternal age was divided into three groups: ≤24, 25-34 and ≥35 years. The study group consisted of Mexican-American or other Hispanic, non-Hispanic White, non-Hispanic Black, or other races. Family poverty income ratio was divided into three categories: ≤1.85, 1.85-4 and >4. Maternal education was grouped by the

number of completed years of school: less than high school, high school diploma and more than high school. Marital status was divided into three groups: married, widowed/divorced/ separated/living with a partner and single. Physical activity level was divided into four groups: no activity, 0-500 MET-minutes/week, 500-1000 MET-minutes/week and ≥1,000 MET-minutes/week.

4.3.5 Statistical Analyses

Descriptive statistics for main variables of interest were generated. Analysis of variance with Bonferroni correction was conducted for each of the twelve HEI-2010 components and overall HEI-2010 scores across the categories of prepregnancy weight status.

A multivariable linear regression model was used to examine the association of maternal sociodemographic factors and physical activity levels with HEI-2010 as a continuous variable. The overall HEI-2010 scores were categorized into tertiles using the highest tertile as a reference group. A multivariable logistic regression model was used to estimate the association of prepregnancy weight status with the lowest tertile of the HEI-2010. We ran models in three ways: (1) crude; (2) adjusted for age, race/ethnicity, family poverty income ratio, education, and marital status; and (3) adjusted for model 2 + physical activity.

To analyze the magnitude of collinearity among covariates, the variance inflation factor (VIF) was used to test with VIF <5 set as the acceptable level (O'Brien, 2007). We calculated *P*-value for trend by modeling the dietary pattern score as a continuous variable. We accounted for the stratified, multi-stage probability design used in NHANES 2003–2012. Appropriate sample weights were applied in all statistical analyses to produce estimates of means and percentiles that can be generalized to the healthy U.S. adult population. All analyses were carried out using SAS software (version 9.3; SAS Institute, Cary, NC). A *P*-value <0.05 was declared as statistically significant.

4.4 Results

Pregnant women included in this study were 52% non-Hispanic white, 23% Mexican American or other Hispanic, 18% non-Hispanic black and 8% other race; 64% were married; and 91% had between 1 to 5 previous live births. Forty-four percent had an income of <185% of the poverty level (the income eligibility criterion for the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC)). Fifty-nine percent had more than a college level education, 39% were in their third trimester of pregnancy, and 35% engaged in light leisure-time physical activities during pregnancy (Table 10).

For all pregnant women included in this study, the mean HEI-2010 was 50.7 (± 0.9). The mean HEI-2010 score varied significantly by maternal sociodemographic characteristics (Table 10). Significantly higher mean HEI-2010 scores were found for pregnant women who were older than 35, other race including multi-racial groups, family poverty income ratio above 4, and married. Multi-collinearity between age, race/ethnicity, family poverty income ratio, education, marital status, parity number, trimester of pregnancy, and physical activity were assessed. The VIF for all the confounding variables ranged from 1.04 to 1.59. These findings suggest that collinearity between these confounding variables was not significant.

Multivariable predictors of HEI-2010 for pregnant women are presented in Table 11. There was no significant association between race/ethnicity, education level, marital status, parity number or physical activity level during pregnancy in relation to HEI-2010. Maternal age, family poverty income ratio, and trimester of pregnancy were significant determinants for HEI-2010 (Table 11).

Table 12 shows unadjusted and covariate-adjusted mean HEI across all the prepregnancy weight status groups. The overall HEI-2010 significantly varied by prepregnancy weight status. Women of obese prepregnancy BMI had significantly lower HEI-2010 compared to underweight and normal weight women, respectively (45.8 ± 1.6 vs. 52.4 ± 1.7, 52.3 ± 1.6).

After adjusting for maternal age, race/ethnicity, family poverty income ratio, education, marital status, and physical activity, women with obese prepregnancy BMI had significantly lower overall HEI-2010 compared to those with normal prepregnancy BMI (48.8 ± 2.0 vs. 55.2 ± 1.6). Women with obese prepregnancy BMI had significantly lower scores for the sodium component compared to normal weight women (3.7 ± 0.6 vs. 5.4 ± 0.4) (Table 12).

Table 13 represents mean values for dietary intake and diet-related biomarkers across prepregnancy weight status groups. Intakes of folate (mcg)/1,000 kcal and iron (mg)/1,000 kcal significantly differed by prepregnancy weight status. Women of obese prepregnancy BMI had significantly lower intake of both folate and iron per 1,000 kcal compared to women of underweight prepregnancy BMI. Serum folate (ng/mL) and iron (ug/dL) values were significantly differed by prepregnancy weight status groups. Serum folate level was significantly higher in underweight women compared to overweight women. Serum iron level was significantly higher in normal weight women compared to obese women. None of supplement intake differed by prepregnancy weight status (Table 13).

Multivariable logistic regression analysis results show that women with prepregnancy overweight and obese BMI had increased odds of falling into the lowest vs. the highest HEI-2010 tertile compared with underweight BMI (OR 2.60; 95% CI 1.06-6.36, OR 4.99; 95% CI 2.19-11.37, respectively) (Table 14). We then compared two models controlling first for maternal age, race/ethnicity, family poverty income ratio, education level, marital status. In the second model, we controlled for the covariates controlled in the first model as well as leisure-time physical activity level during pregnancy. The inverse association between prepregnancy overweight and obesity and diet quality during pregnancy remained significant after we adjusted for maternal characteristics (adjusted OR (AOR) 3.08; 95% CI 1.30-7.29, AOR 3.87; 95% CI 1.78-8.41). The inverse association between prepregnancy overweight and obesity and diet quality persisted even after we controlled for physical activity levels (AOR 4.30; 95% CI 1.44-12.86, AOR 5.50; 95% CI 2.05-14.77) (Table 14).

Table 10. The mean Healthy Eating Index (HEI)-2010 scores by maternal characteristics (n=795)

	n	Wt'd[1] %	Mean HEI-2010	SEM
Age				
≤25 (reference)	355	37.9	45.7	0.9
26-35	377	48.4	52.0*	1.4
≥35	63	13.7	59.5*	2.3
Race/ethnicity				
Mexican American or other Hispanic	272	22.6	53.5*	1.2
Non-Hispanic white	317	51.7	50.6*	1.4
Non-Hispanic black (reference)	152	17.7	43.1	1.2
Other including multi-racial	54	8.0	59.8*	2.7
Family Poverty Income Ratio				
≤1.85 (reference)	427	43.6	47.7	1.1
1.85-4	185	26.1	50.3	1.5
>4	183	30.3	55.1*	1.9
Education Level				
≤11th grade (reference)	288	23.4	46.2	1.3
High school grade	143	17.8	48.5	1.4
Above college	364	58.7	53.1*	1.4
Marital Status (n=794)				
Married	466	63.9	53.5*	1.3
Widowed/divorced/separated/living with a partner	152	15.9	47.7	1.6
Single (reference)	176	20.2	44.1	1.5
Parity (n=488)				
None (reference)	37	7.0	43.8	2.7
1-5	446	91.3	50.2	1.3
≥6	5	1.7	50.1	1.2
Trimester of Pregnancy (n=640)				
1st trimester (reference)	136	26.6	48.4	2.6
2nd trimester	257	34.6	52.6	2.0
3rd trimester	247	38.8	51.6	1.6
Physical activity (n=526)				
No activity	107	30.8	51.6	1.5
0 to <500 MET[2]-min/week	217	34.6	52.0	2.1
500 to <1,000 MET-min/week	91	17.4	54.2	2.8
≥1,000 MET-min/week (reference)	111	17.2	50.9	2.5
Total	795	100.0	50.7	0.9

[1] Wt'd %: Weighted %. Sample weights are created in NHANES to account for the complex survey design (including oversampling of some subgroups), survey non-responses, and post-stratification. When a sample is weighted in NHANES, it is representative of the U.S. civilian non-institutionalized Census population.

[2] Total MET-min/week from self-reported leisure-time physical activities

* Significant at *P*<0.001, using analysis of variance with Bonferroni correction.

Table 11. Factors associated with the Healthy Eating Index (HEI)-2010

	Slope (ß)	SE ß	*P* value
Age			
≤25 (reference)	0		
26-35	2.6	1.2	0.04
≥35	5.0	1.7	0.006
Race/ethnicity			
Mexican American or other Hispanic	3.9	2.4	0.11
Non-Hispanic white	2.2	2.2	0.33
Non-Hispanic black (reference)	0		
Other including multi-racial	1.8	3.9	0.64
Family Poverty Income Ratio			
≤1.85 (reference)	0		
1.85-4	2.2	1.9	0.24
>4	8.0	2.0	0.0002
Education Level			
≤11th grade (reference)	0		
High school grade	1.6	2.1	0.45
Above college	0.1	1.9	0.96
Marital Status (n=794)			
Married	1.9	1.8	0.28
Widowed/divorced/separated/living with a partner	1.8	2.2	0.43
Single (reference)	0		
Parity (n=488)			
None (reference)	0		
1-5	1.9	3.2	0.56
≥6	9.8	5.7	0.09
Trimester of Pregnancy (n=640)			
1st trimester (reference)	0		
2nd trimester	3.8	1.7	0.03
3rd trimester	5.1	1.7	0.004
Physical activity (n=526)			
No activity	2.1	1.8	0.26
0 to <500 MET[1]-min/week	1.0	1.8	0.60
500 to <1,000 MET-min/week	2.9	2.0	0.16
≥1,000 MET-min/week (reference)	0		

[1] Total MET-min/week from self-reported leisure-time physical activities

Table 12. The Healthy Eating Index (HEI)-2010 scores across categories of prepregnancy weight status (n=795)

		Prepregnancy Weight Status				
	Max. Pts	Underweight (n=124)	Normal (n=343)	Overweight (n=173)	Obese (n=155)	*P* trend
			Unadjusted			
Overall HEI-2010	100	52.4 ± 1.7[b]	52.3 ± 1.6[b]	50.4 ± 2.4[ab]	45.8 ± 1.6[a]	0.002
Total Vegetables	5	3.3 ± 0.3	3.3 ± 0.1	3.2 ± 0.2	2.7 ± 0.2	0.09
Greens and Beans	5	1.3 ± 0.3	1.8 ± 0.2	1.2 ± 0.2	1.1 ± 0.3	0.27
Total Fruit	5	3.2 ± 0.3	3.0 ± 0.2	2.6 ± 0.3	2.3 ± 0.2	0.003
Whole Fruit	5	2.8 ± 0.3	2.8 ± 0.2	2.5 ± 0.3	1.6 ± 0.3	0.004
Whole Grains	10	2.5 ± 0.5	2.5 ± 0.3	2.3 ± 0.5	1.6 ± 0.4	0.21
Dairy	10	6.3 ± 0.5	5.9 ± 0.3	5.9 ± 0.4	6.1 ± 0.5	0.90
Total Protein Foods	5	4.1 ± 0.2	3.9 ± 0.2	4.1 ± 0.2	4.1 ± 0.2	0.64
Seafood and Plant Proteins	5	1.3 ± 0.2	2.0 ± 0.2	1.5 ± 0.3	1.5 ± 0.2	0.79
Fatty Acids	10	4.1 ± 0.5	3.8 ± 0.4	4.4 ± 0.7	3.9 ± 0.4	0.86
Sodium	10	4.5 ± 0.5	5.6 ± 0.3	4.6 ± 0.4	4.8 ± 0.4	0.70
Refined Grains	10	5.8 ± 0.5	5.9 ± 0.3	5.4 ± 0.5	5.5 ± 0.4	0.33
Empty Calories	20	13.4 ± 0.7	11.9 ± 0.6	12.7 ± 0.7	10.6 ± 0.8	0.03
			Adjusted[1]			
Overall HEI-2010	100	54.7 ± 2.1[ab]	55.2 ± 1.6[b]	52.3 ± 2.8[ab]	48.8 ± 2.0[a]	0.0074
Total Vegetables	5	3.4 ± 0.3	3.2 ± 0.2	3.2 ± 0.3	2.9 ± 0.4	0.28
Greens and Beans	5	1.3 ± 0.3	2.0 ± 0.3	1.3 ± 0.3	1.6 ± 0.4	0.71
Total Fruit	5	3.2 ± 0.3	3.1 ± 0.3	2.5 ± 0.4	2.4 ± 0.3	0.02
Whole Fruit	5	2.9 ± 0.4	2.8 ± 0.3	2.4 ± 0.4	2.0 ± 0.3	0.01
Whole Grains	10	2.2 ± 0.5	2.4 ± 0.4	2.3 ± 0.7	1.6 ± 0.5	0.66
Dairy	10	6.2 ± 0.5	6.0 ± 0.4	5.6 ± 0.6	6.5 ± 0.5	0.98
Total Protein Foods	5	4.3 ± 0.3	4.0 ± 0.2	4.3 ± 0.2	4.2 ± 0.3	0.64
Seafood and Plant Proteins	5	1.6 ± 0.3	2.2 ± 0.2	1.7 ± 0.4	1.8 ± 0.4	0.99
Fatty Acids	10	4.2 ± 0.7	4.2 ± 0.5	4.9 ± 0.9	3.9 ± 0.6	0.91
Sodium	10	4.3 ± 0.6[ab]	5.4 ± 0.4[b]	4.0 ± 0.5[ab]	3.7 ± 0.6[a]	0.04
Refined Grains	10	6.1 ± 0.6	6.3 ± 0.4	5.6 ± 0.5	5.7 ± 0.5	0.53
Empty Calories	20	14.9 ± 1.2	13.7 ± 0.8	14.5 ± 1.0	12.4 ± 0.9	0.07

Values are weighted mean ± SEM. Labeled means in a row without a common letter differ, $P<0.05$ (Bonferroni-adjusted $P<0.0125$).

[1] Adjusted for maternal age, race/ethnicity, family poverty income ratio, education, marital status, and physical activity

Table 13. Dietary intake and diet-related biomarkers during pregnancy across categories of prepregnancy weight status

	Prepregnancy Weight Status							
	Underweight		Normal		Overweight		Obese	
	n	Mean (SEM)	n	Mean (SEM)	n	Mean (SEM)	n	Mean (SEM)
Dietary Intake								
Energy Intake (kcal/d)	124	2139.5 (99.8)	343	2245.6 (82.9)	173	2153.8 (55.5)	155	2326.6 (88.0)
%Energy Carbohydrate	124	54.6 (1.4)	343	53.3 (1.0)	173	52.6 (1.3)	155	50.6 (1.4)
%Energy Protein	124	15.4 (0.6)	343	14.5 (0.4)	173	15.8 (0.5)	155	15.3 (0.4)
%Energy Fat	124	31.5 (1.4)	343	33.5 (0.8)	173	32.8 (1.1)	155	34.8 (1.1)
Folate, DFE (mcg/d)	124	659.0 (69.3)	343	627.6 (40.3)	173	675.7 (70.8)	155	558.2 (36.6)
Folate, DFE (mcg)/1,000 kcal	124	319.5 (27.4)[b]	343	282.2 (15.0)[ab]	173	319.4 (36.1)[ab]	155	246.1 (15.9)[a]
Iron (mg/d)	124	18.1 (1.2)	343	17.2 (0.9)	173	19.4 (1.6)	155	15.8 (0.8)
Iron (mg)/1,000 kcal	124	8.9 (0.5)[b]	343	7.8 (0.3)[ab]	173	9.1 (0.8)[ab]	155	6.9 (0.3)[a]
Calcium (mg/d)	124	1139.8 (63.2)	343	1132.2 (62.2)	173	1060.1 (63.6)	155	1131.9 (89.1)
Calcium (mg)/1,000 kcal	124	568.4 (41.4)	343	507.6 (22.4)	173	516.6 (42.0)	155	489.3 (30.6)
Biomarkers								
Serum folate (ng/mL)	115	23.4 (1.7)[b]	321	19.1 (0.7)[ab]	158	17.0 (0.8)[a]	143	17.4 (1.8)[ab]
Ferritin (ng/mL)	72	44.5 (9.2)	321	34.7 (3.8)	158	35.1 (3.7)	143	44.5 (6.4)
Calcium (mg/dL)	72	9.2 (0.1)	322	9.1 (0.03)	158	9.1 (0.05)	143	9.1 (0.04)
Iron (ug/dL)	72	79.4 (9.4)[ab]	322	86.2 (5.0)[b]	158	68.9 (3.0)[a]	143	72.2 (5.5)[ab]
Dietary Supplement Intake[1]								
Folic acid (mcg)	29	838.8 (90.3)	40	781.8 (36.8)	13	1186.2 (181.7)	15	922.7 (105.0)
Folate, DFE (mcg)	29	1426.0 (153.5)	40	1329.0 (62.5)	13	2016.6 (308.9)	15	1568.5 (178.6)
Iron (mg)	28	29.3 (2.6)	37	41.1 (5.4)	12	81.7 (28.0)	17	30.2 (1.8)
Zinc (mg)	28	19.5 (2.1)	38	19.9 (1.2)	11	22.9 (4.8)	12	16.4 (2.8)
Calcium (mg)	28	346.7 (77.5)	38	294.5 (53.9)	10	253.0 (61.9)	17	544.0 (170.1)

Values are weighted mean ± SEM. Labeled means in a row without a common letter differ, P <0.05 (Bonferroni-adjusted P <0.0125).

[1] NHANES 2007-2012 included.

Table 14. Associations between the lowest Healthy Eating Index (HEI)-2010 tertile and prepregnancy weight status categories

	HEI-2010 Scores Tertile[1] 3 vs. Tertile 1 (Reference)		
	Model 1	Model 2	Model 3
Prepregnancy Weight Status			
Obese	4.99 (2.19-11.37)*	3.87 (1.78-8.41)*	5.50 (2.05-14.77)*
Overweight	2.60 (1.06-6.36)*	3.08 (1.30-7.29)*	4.30 (1.44-12.86)*
Normal weight	1.91 (0.87-4.21)	1.76 (0.87-3.56)	2.01 (0.84-4.82)
Underweight	1.00	1.00	1.00
Age			
≤25		3.43 (1.04-11.33)*	3.31 (0.75-14.54)
26-35		2.19 (0.75-6.42)	2.37 (0.63-8.94)
≥35		1.00	1.00
Race/ethnicity			
Mexican American or other Hispanic		0.18 (0.08-0.40)*	0.21 (0.07-0.57)*
Non-Hispanic white		1.00	1.00
Non-Hispanic black		0.82 (0.34-1.96)	0.64 (0.22-1.92)
Other including multi-racial		0.19 (0.07-0.52)*	0.16 (0.04-0.63)*
Family Poverty Income Ratio			
≤1.85		2.30 (0.88-5.99)	3.39 (1.17-9.86)*
1.85-4		1.16 (0.48-2.80)	0.81 (0.28-2.39)
>4		1.00	1.00
Education Level			
≤11th grade		2.54 (1.16-5.57)*	1.78 (0.75-4.22)
High school grade		1.43 (0.63-3.20)	1.12 (0.38-3.28)
Above college		1.00	1.00
Marital Status			
Married		1.00	1.00
Widowed/divorced/separated/ living with a partner		1.21 (0.57-2.61)	0.97 (0.38-2.49)
Single		2.04 (0.80-5.17)	1.79 (0.64-4.98)
Physical activity (n=526)			
No activity			1.00
0 to <500 MET[2]-min/week			1.25 (0.59-2.68)
500 to <1,000 MET-min/week			0.90 (0.32-2.55)
≥1,000 MET-min/week			1.40 (0.47-4.19)

Model 1: Crude association between prepregnancy weight status and HEI-2010 (n=795)

Model 2: Adjusted for age, race/ethnicity, family poverty income ratio, education level, marital status (n=794)

Model 3: Adjusted for model 2 + physical activity level (n=526)

[1] Tertiles 1, 2 and 3 represent pregnant women in the lowest, intermediate and highest thirds of the HEI-2010 score, respectively. Mean (SEM) of tertiles 1, 2 and 3 are 33.4 (0.5), 48.5 (0.3), and 66.5 (0.9), respectively.

[2] Total MET-min/week from self-reported leisure-time physical activities

*P<0.05

4.5 Discussion

Recently, HEI-2010 was found to be valid and reliable to measure overall diet quality of an individual (Guenther et al., 2014). However, the food-based HEI-2010 possesses limitations such as not capturing key micronutrient intake from diet for pregnant women (Pick et al., 2005). To overcome this issue, we examined folate, iron and calcium from both a dietary recall and their biomarker values across prepregnancy weight status. Serum folate level decreased as prepregnancy BMI increased, as others have found (Derbyshire et al., 2006). Serum folate level was significantly higher in underweight women compared to overweight women in our study. In a case-control study in South Carolina of 179 women with or without neural tube defect-affected pregnancies, high intakes of dietary folate from 3 months before pregnancy to the first 3 months of pregnancy was associated with decreased neural tube defect risk that was stronger in overweight and obese women compared to underweight or normal women (McMahon et al., 1998). In parallel with this finding, in the Nurses' Health Study II, high intake of folate from supplements before pregnancy was associated with a reduced risk of spontaneous abortion, and the authors concluded that women should use supplemental folate to prevent the risk of spontaneous abortion and stillbirth (Gaskins et al., 2014).

The study showed that diet quality during pregnancy measured using HEI-2010 was inversely associated with increasing prepregnancy BMI. Our study findings are in an agreement with previous research results in Greece (Tsigga et al., 2011) and the U.S. (Laraia et al., 2007). In a cross-sectional study of Greek women (Tsigga et al., 2011), those who were underweight or normal prepregnancy BMI had a better diet quality assessed by HEI-2005 compared to those who were obese prepregnancy BMI. Consistent with this finding, in a prospective cohort study in North Carolina, U.S., prepregnancy BMI was inversely associated with diet quality assessed by the DQI-P (Laraia et al., 2007). Women who were obese before pregnancy had 76% increased odds of falling into the lowest diet quality tertile of the DQI-P than those who were underweight before pregnancy. The major difference in our study compared to these two studies (Tsigga et

al., 2011; Laraia et al., 2007) is that we used the most current index (HEI-2010) while others used old versions, HEI-2005 and DQI-P. The updated HEI-2010 was chosen to assess diet quality of pregnant women in the present study, for it reflects the most current 2010 Dietary Guidelines for Americans with key changes, such as the additional recommendations for seafood (fish and shellfish) and limitations on refined grains (McGuire, 2011). The DQI-P (Laraia et al., 2007) includes three components, percentage of recommended servings per day of grains, vegetables and fruits based upon previous version of the 2000 Dietary Guidelines for Americans, which may not fully reflect current dietary recommendations for Americans.

In our study, the three most lacking components based on HEI-2010 scores for pregnant women's diets were whole fruit, whole grains, and seafood and plant proteins. Strategies are needed to recommend greater consumption of whole fruit, whole grains, and seafood and plant proteins among pregnant women to increase overall diet quality. In 2004, pregnant women or women likely to become pregnant are advised to restrict their overall consumption of seafood to 340g per week by two U.S. Federal Government agencies, the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA) (U.S. Food and Drug Administration and U.S. Environmental Protection Agency, 2004). Supporting evidence for this advice was that maternal fish consumption during pregnancy might increase the exposure to mercury that may harm child development (Oken and Bellinger, 2008). However, in a prospective birth cohort study in Spain (Mendez et al., 2009), more than 2-3 times/week of fish intakes during pregnancy, were beneficial for neurodevelopment among children breastfed for less than 6 months. Future studies are warranted to examine the long-term health consequences of maternal seafood consumption during pregnancy on their children.

In our study, pregnant women who were older, other race including the multi-racial group, married, and/or who had high income and high education levels had better diet quality. Our results confirm previous findings that pregnant women with advanced maternal age (Bodnar and Siega-Riz, 2002; Rifas-Shiman et al., 2009; Arkkola et al., 2006), high income (Bodnar and

Siega-Riz, 2002), and high education (Rifas-Shiman et al., 2009; Arkkola et al., 2006) consumed diets of better quality. There are inconsistent findings for the association between race/ethnicity and diet quality during pregnancy. In our study, we found that non-Hispanic black pregnant women demonstrated the lowest HEI-2010 score compare to other race groups. Rifas-Shiman et al. (Rifas-Shiman et al., 2009) reported that African-American pregnant women had similar Alternate HEI-Pregnancy score assessed in the second trimester of pregnancy compared to other race/ethnicity groups (59.4 ± 10.7 vs. 61.0 ± 10.0, respectively) in the prospective cohort study, Project Viva after controlling for education and age. Bodnar et al. (Bodnar and Siega-Riz, 2002) also found that no significant ethnic/race differences in mean DQI-P score measured in the second trimester of pregnancy among pregnant women who participated in the Pregnancy, Infection, and Nutrition study. This contradictory finding may be due to a different categorization of race/ethnicity groups. The Pregnancy, Infection, and Nutrition study (Bodnar and Siega-Riz, 2002) categorized race/ethnicity into white and black only, and Project Viva study (Rifas-Shiman et al., 2009) categorized race/ethnicity into black/African American, other, and white as the majority of the study population (72%). Our study stratified race/ethnicity into Mexican American or other Hispanic, non-Hispanic white, non-Hispanic Black, and other including multi-racial groups with even-distributions across the race/ethnicity categories.

There are several limitations of this study. Due to cross-sectional study design in the NHANES, the cause-effect relation cannot be made. The study focused on generating snapshots of the diet quality derived from foods and nutrients, and this information may not be adequate to represent usual dietary intake of pregnant women. Despite these limitations, the study has several strengths. First, we used a validated and reliable index, HEI-2010 (Guenther et al., 2013) to assess diet quality of U.S. representative pregnant women in addition to various maternal diet-related biomarkers and intake of supplement across the categories of prepregnancy weight status. Second, the study was based on U.S. representative pregnant

women incorporating diverse groups of pregnant women in the different month of pregnancy. Third, although the study used self-reported prepregnancy weight status, we previously validated self-reported prepregnancy weight status based on self-reported height and weight before pregnancy, and it was found to be valid (Shin et al., 2014b). Lastly, we were able to control for important maternal sociodemographic characteristics, such as gestational weight gain and physical activity level that may influence the relationship between prepregnancy weight status and diet quality.

In conclusion, prepregnancy weight status was inversely associated with diet quality during pregnancy. The association of prepregnancy weight status and diet quality remained significant even after controlling for maternal sociodemographic characteristics and physical activity during pregnancy. Given the increasing prevalence of overweight and obesity of reproductive aged women in the U.S. (Flegal et al., 2012), nutrition education and interventions need to be targeted towards those women entering pregnancy as overweight and obese.

Chapter Five: Dietary patterns during pregnancy are associated with gestational weight gain.

5.1 Abstract

The role of diet during pregnancy on gestational weight gain is unclear. This study aimed to evaluate the hypothesis that dietary patterns during pregnancy are differentially associated with the amount of gestational weight gain at different stages of pregnancy. A total of 391 pregnant women in the National Health and Nutrition Examination Survey (NHANES) 2003-2006 were included. Dietary intake was obtained using a National Cancer Institute's food-frequency questionnaire. Three dietary patterns were identified by factor analysis with 36 food groups among pregnant women, and they were named according to food group factor loadings as follows: 'mixed', 'healthy', and 'western'. The 'mixed' pattern was characterized by a high intake of meat, dairy products, fruits, potatoes, nuts and seeds and sweets. After adjusting for maternal sociodemographic variables and physical activity level, women in the highest tertile of 'mixed' pattern score had significantly greater odds of being in the inadequate gestational weight gain compared to those in the lowest tertile (adjusted odds ratio (AOR) 4.72; 95% CI 1.07-20.94). Women in the middle tertile of the 'mixed' pattern had significantly lower odds of excessive gestational weight gain compared to those in the lowest tertile (AOR 0.39; 95% CI 0.15-0.99). The other two dietary patterns, 'healthy' and 'western,' were not associated with the adequacy of gestational weight gain across different trimesters of pregnancy. Our findings suggest that a diet high in meat, dairy products, fruits, potatoes, and nuts and seeds during pregnancy might be associated with reducing excessive gestational weight gain.

5.2 Introduction

Excessive gestational weight gain is associated with adverse health outcomes for both the mother and the offspring. Gestational weight gain is associated with postpartum weight

retention at 1 year (Vesco et al., 2009), large-for-gestational-age infants (Ferraro et al., 2012), cesarean section (Langford et al., 2011), and child adiposity at age 3 years (Oken et al., 2007). Of 869,531 pregnancies in the 2006-2012 birth certificate data from the Ohio Department of Health (Chen et al., 2015), more than half of normal weight, 70% of overweight, and 60% of obese women before pregnancy had gestational weight gain exceeding the Institute of Medicine's 2009 guidelines (Institute of Medicine, 2009). This alarmingly high rate of excessive gestational weight gain and its subsequent adverse health consequences on the mother and offspring suggest urgent needs to reduce the number of women gaining excessive gestational weight.

Diet plays an important role in weight management during pregnancy (Tobias and Bao, 2014) while providing extra nutrients required during pregnancy. Thornton et al. (Thornton et al., 2009) conducted a randomized study of 257 pregnant women examined the effect of nutritional counseling with or without nutritional monitoring on gestational weight gain. Patients were divided into either the control group (without nutritional monitoring), consisting of conventional prenatal dietary management or to the study group (with nutrition monitoring) with prescribed a balanced nutritional regiment and were asked to record in a diary all of the foods eaten during each day. The group with the nutritional monitoring intervention had a significantly lower mean gestational weight gain compared to the group without nutritional monitoring (mean difference -9.07, 95% confidence interval [CI] -10.90 to -7.24). In a systematic review conducted by Skouteris et al. (Skouteris et al., 2010), the effect of modifiable risk factors were evaluated in relation to excessive gestational weight gain in pregnant women through diet and/or physical activity interventions. Among ten intervention studies that focused on behavioral changes including physical activity and/or diet to reduce excessive gestational weight gain, six studies reported significantly less gestational weight gain in the diet and physical activity intervention groups compared to control groups (Skouteris et al., 2010). However, the independent role of dietary factors in relation to gestational weight gain remains unclear, due to the high collinearity

among lifestyle behavior factors including physical activity, diet, medications and sociodemographic variables.

Identifying and evaluating the role of diet, with an adequate amount and balance of extra nutrients during pregnancy on gestational weight gain, would provide meaningful information for establishing dietary guidelines for pregnant women. In 2009, the Institute of Medicine published gestational weight gain guidelines for how much a pregnant woman should gain during pregnancy to optimize health outcomes for both the mother and offspring (Institute of Medicine, 2009). However, these guidelines focused on ranges of weight gain that women need to achieve during pregnancy without offering dietary recommendations on how to gain weight. It is of great importance to cross-examine diet during pregnancy and gestational weight gain for providing dietary recommendations to help pregnant women to achieve recommended gestational weight gain. This study aimed to examine the relationship between dietary patterns during pregnancy and the adequacy of gestational weight gain.

5.3 Materials and Methods

5.3.1 Study Population

Data from National Health and Nutrition Examination Survey (NHANES) 2003–2006 represented the total civilian, non-institutionalized population in the U.S. for those years. NHANES is a program of studies cross-sectionally designed to assess the health and nutritional status of the civilian, non-institutionalized population in the U.S. and is conducted by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC). The NHANES uses a stratified multistage probability sample that was based on the selection of counties, blocks, households, and finally persons within households. The NHANES 2003–2006 was conducted in 2-year cycles. For the purpose of the current study, we pooled data for all 4 years to obtain a maximal sample size of pregnant women. The NHANES 2003–

2006 dataset was used for the present study as the survey during those years oversampled pregnant women of all ages from the U.S. representative population (Centers for Disease Control and Prevention and National Center for Health Statistics, 2009d). The NHANES survey is unique in that it combines interviews and physical examinations. The participants were interviewed to obtain information on age, race/ethnicity, education level, marital status, family poverty income ratio, parity, the month of pregnancy and physical activity. Reproductive health interviews obtained information on the month of gestation at the time of the survey. Pregnancy status was based on a positive urine pregnancy test.

The 2003-2006 NHANES dataset included 674 pregnant women. Subjects were excluded if they reported unreliable dietary data, as defined by the NCHS. Included in the present study were participants with complete data for all variable of our interest: pregnancy urine test, age, race/ethnicity, family poverty income ratio, education, marital status, trimester of pregnancy, self-reported prepregnancy weight, and measured height and weight. The final analytic sample size was 391 pregnant women.

5.3.2 Dietary Assessment

In the NHANES 2003-2006, a food frequency questionnaire (FFQ) was administered to participants older than 2 years who provided at least one 24-hr dietary recall, in order to collect information on the frequency of food consumption during the past 12 months. The FFQ was developed by National Cancer Institute based on a 216-item food frequency instrument without portion size information (Subar et al., 2006). Participants were asked to choose from eleven possible frequency responses, ranging from never to 6 or more times per day, for each food. The selected frequency category for each food item was converted to a daily intake based on algorithms within Diet*Calc software (Centers for Disease Control and Prevention and National Center for Health Statistics, 2008d). For example, a response of ‘1 time per week’ was converted to 0.14 times per day.

5.3.3 Outcome Variable

Gestational weight gain was calculated by subtracting the self-reported prepregnancy weight from the measured weight at the specific month of pregnancy (1-10 months) during the survey. Adequacy of gestational weight gain status (inadequate, adequate, excessive gain) was determined by comparing the actual gestational weight gain of each pregnant woman in reference to the Institute of Medicine's 2009 gestational weight gain guidelines by using the self-reported prepregnancy weight status (underweight, normal, overweight, obese) (Table 15). The inadequate gestational weight gain status group consisted of pregnant women whose gestational weight gain was less than the minimum recommended weight gain for the month of pregnancy for each prepregnancy weight status. The adequate gestational weight gain status group consisted of pregnant women whose gestational weight gain was between the minimum and maximum recommended gestational weight gain. The excessive gestational weight gain status group consisted of pregnant women whose gestational weight gain exceeded the maximum recommended gestational weight gain.

Table 15. Recommended gestational weight gain by prepregnancy weight status and month of pregnancy

Prepregnancy BMI (kg/m^2)	Month									
	1	2	3	4	5	6	7	8	9	10
Underweight (<18.5)										
Min (lbs)	0.4	1.2	2.2	5.0	9.0	13.0	17.0	20.0	24.0	28.0
Max (lbs)	1.2	3.6	6.6	10.0	15.0	20.0	25.0	30.0	35.0	40.0
Normal weight (18.5-24.9)										
Min (lbs)	0.4	1.2	2.2	5.0	8.0	11.0	15.0	18.0	22.0	25.0
Max (lbs)	1.2	3.6	6.6	10.0	14.0	18.0	22.0	27.0	31.0	35.0
Overweight (25.0-30)										
Min (lbs)	0.4	1.2	2.2	4.0	6.0	7.0	9.0	11.0	13.0	15.0
Max (lbs)	1.2	3.0	6.6	9.0	11.0	14.0	17.0	20.0	22.0	25.0
Obese (≥30)										
Min (lbs)	0.2	0.6	1.1	2.0	4.0	5.0	7.0	8.0	10.0	11.0
Max (lbs)	0.6	2.4	4.4	6.0	8.0	11.0	13.0	15.0	18.0	20.0

Source: N.C. Department of Health and Human Services; Women's and Children's Health Section. Prenatal weight gain chart. Adapted from: Institute of Medicine, 2009. Weight gain during pregnancy: reexamining the guidelines. Washington, DC. National Academies Press; Committee to Reexamine IOM Pregnancy Guidelines (Institute of Medicine, 2009)

5.3.4 Covariates

Analyses were adjusted for prepregnancy BMI, maternal age, race/ethnicity, family poverty income ratio, education, marital status, parity, and physical activity. Prepregnancy BMI (kg/m^2) was categorized into four groups (<18.5, 18.5-24.9, 25-29.9, ≥30). Maternal age was divided into three groups (≤24, 25-34, ≥35 years). The study group consists of Mexican-American or other Hispanic, non-Hispanic White, non-Hispanic Black, or other races. Family poverty income ratio was divided into three categories (≤1.85, 1.85-4, >4). Maternal education was grouped by the number of completed years of school (≤11^{th} grade, high school grade, above college). Marital status was divided into three groups (married, widowed/divorced/ separated/living with a partner, single). Parity was divided into three groups (none, 1-3, ≥4). Physical activity was divided into three groups (0 to <500, 500 to <1,000, ≥1,000 MET-min/week).

5.3.5 Statistical Analyses

To extract dietary patterns, data analysis was performed in two steps. In the first step, we reduced the number of food items in the FFQ from 216 individual items to 36 predefined food groups (Table 16), which are comparable with the grouping schemes reported in the Food Patterns Equivalents Database (FPED) (Bowman et al., 2014). In the second step, dietary pattern analysis was derived using factor analysis of 36 food groups (Expressed as a frequency of consumption per day). We conducted the analysis using the PROC FACTOR procedure in SAS software (version 9.3; SAS Institute, Cary, NC). Scree plots and the interpretability of each component were also used to determine the appropriate number of components to select. Varimax rotation was employed to aid the interpretation of components. Each component describes a dietary pattern and the linear combination allows the calculation of a component score for each pregnant woman; the higher the score, the more likely this pattern is present in an individual's diet. The patterns described by each component may be interpreted by its factor loadings, which are the correlations between the component and each input variable. Large positive or negative factor loadings indicate the foods that are important in that component; loadings with the magnitude of at least 0.2 were considered when describing dietary patterns. The proportion of variance explained by each dietary pattern was calculated by dividing the sum of the squares of the respective factor loadings by the number of food groups. All individuals received a factor score for each pattern calculated by summing the intakes of food groups weighted by their factor loadings.

For all dietary patterns, we calculated adjusted ORs for inadequate or excessive gestational weight gain across dietary pattern score tertiles, with the lowest tertile as the reference, using multivariable logistic regression, after controlling for covariates. To analyze the magnitude of collinearity among covariates, the variance inflation factor (VIF) was used to test with VIF <5 set as the acceptable level (O'Brien, 2007). We calculated *P*-value for trend by modeling the dietary pattern score as a continuous variable. We accounted for the stratified,

multi-stage probability design used in the NHANES 2003–2006. Appropriate sample weights were applied in all statistical analyses to produce estimates of means and percentiles that can be generalized to the healthy U.S. adult population. All analyses were carried out using SAS software (version 9.3; SAS Institute, Cary, NC). A *P*-value <0.05 was declared as statistically significant.

Table 16. Thirty-six pre-defined food groups to extract dietary patterns

#	Food Groups	Food Items
1	Added sugar	Maple syrup on pancakes/ etc, Sugars/honey/ not in coffee/tea, Sugars/honey/ all in coffee or tea, Artificial sweetener in coffee/tea
2	Beer	Beer
3	Butter	Butter/ regular on bread/pan/waffle, Butter/ reduced fat on bread/pan/waffle, Butter/ regular on pot/veg/grains, Butter/ reduced fat on pot/veg/grains
4	Cheese	Cottage/ricotta cheese Cheese/ regular, Cheese/ low fat, Cream cheese/ regular, Cream cheese/ low fat, Macaroni and cheese
5	Coffee	Coffee/ regular/ no cream/sugar, Coffee/ decaf/ no cream/sugar
6	Cold breakfast cereals	RTE cereal/<half whole grain, RTE cereal/> half whole grain
7	Cured Meat	Ham/ not luncheon, Sausage/ regular, Sausage/ turkey/low fat, Hot dogs/ regular, Hot dogs/ turkey/low fat, Short ribs/spareribs, Cold cuts/ regular, Cold cuts/ low fat, Cold cuts/ poultry, Ham/ cold cut/ lunch meat/ regular, Ham/ cold cut/ lunch meat/ low fat
8	Dairy products	Ice cream/ regular, Ice cream/ice milk/ low fat, Milk/ whole in cereal, Milk/ 2% in cereal, Milk/ 1% in cereal, Milk/ nonfat/skim in cereal, Milk/ rice/ in cereal, Milk/ whole to drink, Milk/ 2% to drink, Milk/ 1% to drink, Milk/ nonfat to drink, Milk/ rice/ to drink, Milk/ whole in coffee or tea, Milk/ 2% in coffee or tea, Milk/ 1% in coffee or tea, Milk/ nonfat/skim in coffee or tea, Milk/ evaporated/condensed in coffee or tea, Milk/ rice in coffee or tea, Meal replacement/ liquid, Milk, unpasteurized not in coffee/tea, Milk, unpasteurized in cereal, Milk, unpasteurized in coffee/tea, Milk/ other to drink, Milk/ other in cereal, Milk/ other in coffee/tea, Yogurt/ all, Frozen yogurt/ ices/ sorbet/ etc
9	Dark green vegetables	Raw spinach/greens, Cooked spinach/greens, no fat added, Broccoli, no fat added, Lettuce/ dark green
10	Eggs	Eggs/ regular, Eggs/ whites only, Eggs/ substitutes, Eggs/ salad
11	Fruit drinks	Fruit drinks/ regular, Fruit drinks/ diet, Orange/grapefruit juice/ all, Other juice, Tomato/veg juice/ all, Apple juice, Grape juice
12	Fruits	Oranges/ tangelo etc, Grapefruit, Apples, Applesauce/cooked apples, Pears, Peaches/nectarines/plums, Bananas, Melons, Strawberries, Grapes/ all, Dried fruit, Other fruits, Pineapple
13	High-energy drinks	Soft drinks/ regular/ caffeine, Soft drinks/ regular/ decaf
14	Legumes	Beans, Peas, no fat added
15	Liquor	Alcoholic beverage/ liquor
16	Low-energy drinks	Soft drinks/ diet/ caffeine, Soft drinks/ diet/ decaf
17	Margarine	Margarine/ regular on bread/pan/waffle, Margarine/ low-fat on bread/pan/waffle, Margarine/ regular on pot/veg/grains, Margarine/ diet on pot/veg/grains
18	Meat	Beef/ steaks/ regular, Beef/ steaks/ lean, Beef/ roast, Beef stews/pot pies/mixtures, Beef/ burgers/ lean, Beef/ burgers / regular, Beef/ gr/ meatballs/loaf/mixtures, Pork, Bacon/ regular, Bacon/ lean/Canadian Liver/ liverwurst, Roast beef in sandwich
19	Nuts and seeds	Nuts/seeds/ whole, Nuts/seeds/ butters
20	Oils	Oils/ olive, Oils/ corn, Oils/ canola, Oils/ other
21	Other vegetables	Sweet potatoes, no fat added, Corn, no fat added, Lettuce, not dark green, Chili, Pickled veg/fruit, String beans, no fat added, Cabbage/sauerkraut, Coleslaw, Cauliflower/Brussels Sprouts, no fat added, Peppers, no fat added, Onions, no fat added, Veg med, no fat added, Other vegetables, no fat added, Cucumbers, Squash, Carrots, no fat added

Table 16 (cont'd)

#	Food Groups	Food Items
22	Pizza	Lasagna/ rav/ shells/ etc, Pizza/ with meat, Pizza/ without meat
23	Potatoes	Potatoes/ white, no fat added, Potatoes/ fried, Potato salads
24	Poultry	Chicken/ fried/ light w/skin, Chicken/ fried/ light wo/skin, Chicken/ fried/ dark w/skin, Chicken fried/ dark wo/skin, Chicken/ light w/skin, Chicken/ light wo/skin, Chicken/ dark w/skin, Chicken/ dark wo/skin, Chicken/turkey ground, Chicken/ mixtures, Turkey
25	Refined grains	English muffin/bagel, Breads/rolls/ white, Stuffing/dumplings, Cornbread/muffins, Biscuits/ all, Donuts/ sweet rolls/ danish/ pop tarts, Muffins/dessert breads, Pancake/ waffle/ French toast, Rice/grains/ white, Pasta/ no fat added, Pasta/ fat added, Pasta/ meatless red sauce, Pasta/ meat/fish sauce, Bread/not white, Crackers, Pasta salad, Hot breakfast cereals/ (not oatmeal)
26	Salad dressings	Salad dressing/ all on salad or veg, Mayonnaise/ regular, Mayonnaise/ diet
27	Seafood	Fish/ smoked, Sushi/ raw fish, Sushi/ no raw fish, Tuna canned, Fish fried, Fish/ not fried, Fish/ oysters
28	Snacks	Popcorn, Pretzels, Tortillas/tacos/ corn, Tortillas/tacos/ wheat, Potato/other chips (not corn)/ regular, Potato/other chips (not corn)/ low-fat, Corn chips/ regular, Corn chips/ low-fat
29	Solid fats	Non-dairy cream/ powdered/ regular in coffee or tea, Non-dairy cream/ powdered/ diet in coffee or tea, Non-dairy cream/ liquid/ r regular in coffee or tea, Non-dairy cream/ liquid/ diet in coffee or tea, Cream/ regular or 1/2&1/2 in coffee or tea, Sour cream/ regular, Sour cream/ low-fat, Gravy
30	Soups	Soups/ broth w noodles/rice, Soups/ w veggies, Soups/ bean-type, Soups/ creamed
31	Soy products	Milk/ soy/ in cereal, Milk/ soy/ to drink, Milk/ soy in coffee or tea, Tofu/ soy meats
32	Sweets	Puddings/custards, Cookies/ brownies, Cakes, Pies/ fruit, Pies, cream/custard/other, Crisps/cobblers, Candy/ chocolate, Candy/ not chocolate, Jams/ jelly/ fruit butters
33	Tea	Tea/ regular / no cream/sugar, Tea/ decaf/ no cream/sugar
34	Tomatoes	Tomatoes/ raw, Tomato salsa, Tomato catsup
35	Whole grain	Granola bars, Oatmeal, Rice/grains/ whole grain
36	Wine	Wine

5.4 Results

The final study consisted of 391 pregnant women. Table 17 shows the maternal characteristics according to the adequacy of gestational weight gain. Women in the excessive gestational weight gain group were more likely to be non-Hispanic white and overweight before pregnancy. Women in the inadequate gestational weight gain group were more likely to be underweight prior to pregnancy. Multi-collinearity between age, race/ethnicity, family poverty income ratio, education, marital status, parity number, trimester of pregnancy, prepregnancy weight status, and physical activity did not exist. The VIF for the confounding variables ranged from 1.1 to 1.9. These findings suggest that collinearity between these confounding variables was not significant.

Three dietary patterns were identified among the pregnant women, and they were named according to food group factor loadings on them as ‘mixed’, ‘healthy’, and ‘western’. The 36 food groups with factor loading values on the dietary patterns are presented in Table 4. The ‘mixed’ pattern was characterized by a high loading of added sugar, butter, cheese, cold breakfast cereals, cured meat, dairy products, fruit drinks, fruits, high-energy drinks, legumes, nuts and seed, pizza, potatoes, poultry, refined and whole grains, salad dressings, seafood, and snacks. The ‘healthy’ pattern was characterized by the consumption of cheese, coffee, dairy products, dark green vegetables, eggs, fruits, legumes, nuts and seeds, oils, poultry, seafood, and tomatoes and a low consumption of high-energy drinks and alcohol. Lastly, the ‘western’ pattern was characterized by a high consumption of added sugar, beer, butter, cheese, cured meat, fruit drinks, liquor, margarine, meat, pizza, salad dressing, and solid fats (Table 18).

Women with a higher ‘mixed’ pattern score (Tertile 3) tended to have a history of 1-3 previous live births. Women with a higher ‘healthy’ pattern diet (Tertile 3) tended to be 26-35 years old and married and women with an ‘western’ pattern score tended to be non-Hispanic white, physically active, and have family poverty income ratio between 1.85 to 4, above college level education, and normal prepregnancy weight (Table 19).

In the unadjusted analysis, there was no significant association between dietary patterns and the adequacy of gestational weight gain. After adjustment for prepregnancy BMI, age, race/ethnicity, family poverty income ratio, education level, and marital status there was still no significant associations of dietary patterns with gestational weight gain. After adjusting for physical activity level, women in the highest tertile of 'mixed' pattern had significantly greater odds of inadequate gestational weight gain compared to those in the lowest tertile (adjusted odd ratios (AOR) 4.72; 95% CI 1.07-20.94). Women in the mid-tertile of 'mixed' pattern had significantly lower odds of excessive gestational weight gain compared to those in the lowest tertile (AOR 0.39; 95% CI 0.15-0.99). No significant associations were found for the other two dietary patterns, 'healthy' and 'western' patterns in relation to the adequacy of gestational weight gain (Table 20).

Table 17. Maternal characteristics by the adequacy of gestational weight gain groups (n=391)

	Adequacy of Gestational Weight Gain									
	Inadequate			Adequate			Excessive			
	n	Wt'd[1] % (Row)	Wt'd % (Col)	n	Wt'd % (Row)	Wt'd % (Col)	n	Wt'd % (Row)	Wt'd % (Col)	*P* value[2]
Age										
≤25	59	40.6	31.4	23	37.8	17.7	78	35.0	50.9	0.34
26-35	52	56.6	29.8	49	57.3	18.3	104	52.5	51.9	
≥35	4	2.9	9.8	4	4.9	10.2	18	12.4	80.0	
Race										
Mexican American or other Hispanic	42	29.2	42.2	30	23.6	20.7	54	13.7	37.1	0.01
Non-Hispanic white	41	43.8	20.3	36	66.5	18.7	114	70.1	61.0	
Non-Hispanic black	24	18.9	41.8	5	6.1	8.2	26	12.0	50.0	
Other including multi-racial	8	8.1	44.2	5	3.8	12.6	6	4.2	43.2	
Family Poverty Income Ratio										
≤1.85	72	53.4	44.9	30	25.6	13.0	87	26.7	42.1	0.007
1.85-4	21	29.7	25.6	15	31.2	16.3	59	35.9	58.1	
>4	22	16.9	14.9	31	43.2	23.1	54	37.5	62.0	
Education Level										
≤11th grade	60	42.8	46.4	29	32.3	21.2	59	15.9	32.3	0.003
High school grade	15	9.9	26.2	8	6.7	10.8	33	12.7	63.0	
Above college	40	47.3	21.7	39	61.0	16.9	108	71.5	61.4	
Marital Status										
Married	63	62.8	26.7	50	67.9	17.5	145	69.9	55.8	0.67
Widowed/divorced/ separated/ living with a partner	21	15.4	25.2	13	17.4	17.2	26	18.8	57.6	
Single	31	21.7	41.8	13	14.7	17.2	29	11.4	41.0	
Parity (n=264)										
None	4	3.8	9.6	7	23.8	30.4	8	13.7	60.1	0.23
1-3	64	89.2	32.7	40	69.5	13.0	127	84.1	54.3	
≥4	4	7.0	48.5	3	6.7	23.8	7	2.3	27.7	

Table 17 (cont'd)

	Adequacy of Gestational Weight Gain									
	Inadequate			Adequate			Excessive			
	n	Wt'd[1] % (Row)	Wt'd % (Col)	n	Wt'd % (Row)	Wt'd % (Col)	n	Wt'd % (Row)	Wt'd % (Col)	*P* value[2]
Trimester of Pregnancy										
1st trimester	31	42.8	43.8	15	26.8	16.6	24	20.6	39.6	0.19
2nd trimester	54	31.1	26.4	25	28.0	14.4	80	37.2	59.2	
3rd trimester	30	26.1	19.6	36	45.2	20.7	96	42.2	59.7	
Prepregnancy weight status										
Underweight	24	19.3	58.2	3	2.1	3.8	13	6.7	38.0	0.07
Normal	41	30.9	19.4	45	61.9	23.5	96	48.5	57.1	
Overweight	23	16.8	24.7	18	12.6	11.3	55	23.2	64.0	
Obese	27	33.0	37.6	10	23.4	16.2	36	21.6	46.2	
Physical activity (n=232)										
0 to <500 MET-min/week	33	42.2	23.2	20	39.0	12.9	67	47.7	63.9	0.58
500 to <1,000 MET-min/week	13	24.6	20.2	15	43.3	21.5	25	29.1	58.3	
≥1,000 MET-min/week	9	33.3	33.1	12	17.7	10.6	38	23.2	56.3	

[1] Wt'd %: Weighted %. Sample weights are created in NHANES to account for the complex survey design (including oversampling of some subgroups), survey non-responses, and post-stratification. When a sample is weighted in NHANES, it is representative of the U.S. civilian non-institutionalized Census population.
Weighted percentages may not sum up to 100 due to rounding.
[2] *P* obtained from Chi-square tests.

Table 18. Factor loading matrix for dietary patterns from food-frequency questionnaires completed by pregnant women

		Dietary Patterns		
#	Food Group	'Mixed'	'Healthy'	'Western'
1	Butter	**0.33**[1]	0.05	**0.58**
2	Cold breakfast cereals	**0.45**	0.13	-0.13
3	Cured Meat	**0.65**	0.11	0.17
4	Dairy products	**0.52**	**0.30**	-0.08
5	Fruit drinks	**0.50**	0.05	**0.20**
6	Fruits	**0.49**	**0.53**	-0.14
7	High-energy drinks	**0.47**	**-0.33**	0.15
8	Margarine	**0.38**	-0.01	**0.54**
9	Meat	**0.64**	**0.23**	0.17
10	Nuts and seeds	**0.31**	**0.49**	0.14
11	Pizza	**0.65**	-0.01	**0.20**
12	Potatoes	**0.58**	0.09	0.18
13	Refined grains	**0.62**	**0.39**	0.18
14	Salad dressings	**0.31**	**0.21**	**0.55**
15	Snacks	**0.43**	**0.22**	-0.19
16	Soups	**0.31**	**0.31**	0.08
17	Sweets	**0.70**	0.16	0.08
18	Tomatoes	**0.21**	**0.49**	-0.02
19	Whole grain	**0.22**	**0.51**	-0.07
20	Cheese	**0.27**	0.18	**0.33**
21	Other vegetables	**0.27**	**0.73**	0.09
22	Poultry	**0.26**	**0.39**	0.11
23	Dark green vegetables	-0.05	**0.68**	**0.28**
24	Eggs	0.01	**0.39**	**0.43**
25	Legumes	0.13	**0.56**	-0.13
26	Seafood	0.12	**0.45**	0.17
27	Oils	0.10	**0.36**	-0.05
28	Soy products	-0.14	**0.31**	0.05
29	Solid fats	-0.03	**0.22**	**0.30**
30	Coffee	-0.04	**0.26**	**0.28**
31	Added sugar	0.17	0.01	**0.38**
32	Beer	0.04	-0.09	**0.69**
33	Liquor	-0.05	-0.15	**0.43**
34	Wine	-0.08	-0.01	**0.47**
35	Tea	0.15	0.00	**0.56**
36	Low-energy drinks	0.01	0.06	**0.22**
	Variance Explained (%)	13.4	10.8	9.1

[1] Factor loadings represent the magnitude and direction of association with factors (dietary patterns) and can range from -1.0 to 1.0. Food groups with factor loading values ≥ |0.20| are indicated in bold.

Table 19. Maternal characteristics by tertiles of dietary pattern scores

	'Mixed' Dietary Pattern							'Healthy' Dietary Pattern							'Western' Dietary Pattern						
	Tertile 1		Tertile 2		Tertile 3			Tertile 1		Tertile 2		Tertile 3			Tertile 1		Tertile 2		Tertile 3		
	n	Wt'd[1] %	n	Wt'd %	n	Wt'd %	*P*[2]	n	Wt'd %	n	Wt'd %	n	Wt'd %	*P*	n	Wt'd %	n	Wt'd %	n	Wt'd %	*P*
Age																					
≤25	42	34.4	50	30.9	68	34.6	0.57	69	52.2	52	27.2	39	20.5	<0.0001	61	25.6	55	33.7	44	40.8	0.47
26-35	78	28.6	74	38.6	53	32.7		54	29.3	72	37.4	79	33.3		61	19.9	69	48.1	75	32.0	
≥35	10	36.4	7	14.6	9	49.0		7	13.0	7	12.3	12	74.7		8	19.6	7	27.0	11	53.4	
Race																					
Mexican American or other Hispanic	49	28.5	38	34.9	39	36.6	0.51	23	15.0	45	34.4	58	50.6	0.0013	72	48.5	34	33.9	20	17.6	<0.0001
Non-Hispanic white	59	32.0	74	33.6	58	34.4		72	38.1	70	34.9	49	27.0		38	11.6	70	42.8	83	45.6	
Non-Hispanic black	11	23.4	16	43.0	28	33.6		30	59.6	12	18.6	13	21.8		15	25.3	21	42.6	19	32.2	
Other including multi-racial	11	55.8	3	8.0	5	36.2		5	40.5	4	12.3	10	47.2		5	35.5	6	42.5	8	22.1	
Family Poverty Income Ratio																					
≤1.85	57	20.5	56	34.8	76	44.7	0.21	65	37.4	59	28.4	65	34.2	0.70	82	36.7	60	34.3	47	29.0	0.02
1.85-4	26	32.9	37	34.0	32	33.1		34	42.5	30	29.4	31	28.1		25	16.8	35	39.4	35	43.9	
>4	47	41.4	38	32.4	22	26.2		31	29.2	42	37.0	34	33.8		23	11.9	36	49.6	48	38.6	
Education Level																					
≤11th grade	39	27.2	47	28.7	62	44.1	0.38	54	46.6	46	22.4	48	31.1	0.30	72	37.6	50	36.9	26	25.5	0.0013
High school grade	22	43.9	15	27.2	19	29.0		20	32.7	22	42.7	14	24.6		18	33.2	13	22.1	25	44.7	
Above college	69	31.1	69	37.0	49	31.9		56	32.8	63	33.4	68	33.8		40	13.5	68	46.0	79	40.6	
Marital Status																					
Married	97	32.0	92	36.8	69	31.2	0.69	66	26.4	93	38.1	99	35.5	0.0007	83	19.8	88	43.7	87	36.4	0.51
Widowed/ divorced/ separated/living with a partner	19	31.5	18	26.7	23	41.7		22	55.0	20	15.3	18	29.7		22	18.8	17	41.1	21	40.1	
Single	14	28.8	21	28.3	38	42.9		42	60.1	18	20.9	13	19.0		25	35.4	26	28.2	22	36.3	
Parity (n=264)																					
None	11	56.9	2	3.0	6	40.1	0.08	6	45.4	4	9.1	9	45.4	0.26	3	9.1	8	42.0	8	48.9	0.64

Table 19 (cont'd)

	'Mixed' Dietary Pattern							'Healthy' Dietary Pattern							'Western' Dietary Pattern						
	Tertile 1		Tertile 2		Tertile 3			Tertile 1		Tertile 2		Tertile 3			Tertile 1		Tertile 2		Tertile 3		
	n	Wt'd[1] %	n	Wt'd %	n	Wt'd %	*P*[2]	n	Wt'd %	n	Wt'd %	n	Wt'd %	*P*	n	Wt'd %	n	Wt'd %	n	Wt'd %	*P*
1-3	80	28.2	74	34.9	77	36.9		70	33.3	82	33.0	79	33.7		83	23.7	73	40.9	75	35.4	
≥4	3	14.4	6	53.4	5	32.2		6	58.0	4	27.7	4	14.2		3	23.1	6	20.2	5	56.7	
Trimester of Pregnancy																					
1st trimester	28	34.9	22	32.3	20	32.7	0.50	32	40.6	22	34.3	16	25.1	0.82	20	15.2	29	45.4	21	39.4	0.81
2nd trimester	58	38.0	57	35.4	44	26.5		53	35.3	58	33.6	48	31.0		53	24.1	51	41.4	55	34.5	
3rd trimester	44	23.0	52	33.3	66	43.7		45	34.3	51	27.6	66	38.1		57	25.1	51	37.3	54	37.6	
Prepregnancy weight status																					
Underweight	9	10.8	16	47.9	15	41.3	0.08	10	20.2	12	21.1	18	58.7	0.20	14	21.9	19	62.1	7	16.0	0.23
Normal	68	35.9	56	26.8	58	37.3		65	40.7	55	25.3	62	34.0		53	22.1	57	38.3	72	39.6	
Overweight	34	44.4	34	32.1	28	23.4		28	39.0	38	37.3	30	23.7		35	23.6	32	49.6	29	26.7	
Obese	19	21.1	25	42.4	29	36.6		27	32.9	26	42.2	20	24.9		28	20.4	23	31.1	22	48.5	
Physical activity (n=232)																					
0 to <500 MET-min/week	37	31.5	44	29.6	39	38.8	0.44	36	35.0	44	24.3	40	40.7	0.54	33	21.2	44	41.0	43	37.8	0.12
500 to <1,000 MET- min/week	20	38.6	14	31.8	19	29.5		13	26.9	20	43.4	20	29.7		18	10.8	21	62.5	14	26.7	
≥1,000 MET-min/week	20	18.0	21	47.3	18	34.7		17	29.2	18	40.1	24	30.7		14	11.3	21	36.6	24	52.2	

[1] Wt'd %: Weighted %. Sample weights are created in NHANES to account for the complex survey design (including oversampling of some subgroups), survey non-responses, and post-stratification. When a sample is weighted in NHANES, it is representative of the U.S. civilian non-institutionalized Census population. Weighted percentages may not sum up to 100 due to rounding.
[2] *P* obtained from Chi-square tests.

Table 20. Crude and adjusted odds ratios for being in the excessive or inadequate gestational weight gain compared with the adequate (reference) gestational weight gain by tertiles of dietary pattern scores

	Excessive vs. Adequate Gestational Weight Gain (reference)			Inadequate vs. Adequate Gestational Weight Gain (reference)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Mixed Dietary Pattern Score						
Tertile 1	1.00	1.00	1.00	1.00	1.00	1.00
Tertile 2	0.59 (0.21-1.70)	0.50 (0.17-1.47)	0.39 (0.15-0.99)*	3.01 (0.89-10.20)	2.79 (0.87-8.95)	3.49 (0.79-15.41)
Tertile 3	0.98 (0.23-4.19)	1.08 (0.33-3.59)	1.82 (0.49-6.74)	2.49 (0.49-12.57)	2.84 (0.66-12.22)	4.72 (1.07-20.94)*
P-trend	0.99	0.83	0.31	0.40	0.25	0.10
Healthy Dietary Pattern Score						
Tertile 1	1.00	1.00	1.00	1.00	1.00	1.00
Tertile 2	0.74 (0.17-3.17)	0.87 (0.18-4.12)	1.41 (0.29-6.92)	0.80 (0.16-3.93)	0.94 (0.17-5.18)	2.05 (0.28-15.13)
Tertile 3	1.39 (0.47-4.17)	1.78 (0.54-5.89)	2.60 (0.49-13.83)	0.73 (0.24-2.22)	0.59 (0.16-2.23)	0.77 (0.10-5.62)
P-trend	0.58	0.33	0.25	0.59	0.50	0.86
Western Dietary Pattern Score						
Tertile 1	1.00	1.00	1.00	1.00	1.00	1.00
Tertile 2	2.23 (0.87-5.70)	2.04 (0.65-6.42)	1.07 (0.29-3.92)	2.30 (0.74-7.19)	3.57 (0.92-13.79)	2.01 (0.40-10.23)
Tertile 3	1.61 (0.45-5.75)	1.52 (0.43-5.42)	1.34 (0.28-6.44)	0.82 (0.23-2.96)	1.88 (0.55-6.42)	0.64 (0.12-3.43)
P-trend	0.63	0.68	0.64	0.66	0.55	0.39

Model 1: Crude association between dietary patterns and gestational weight gain (n=391)
Model 2: Adjusted for prepregnancy BMI, age, race/ethnicity, family poverty income ratio, education level, and marital status (n=391)
Model 3: Adjusted for model 2 + physical activity level (n=232)
*$P<0.05$

5.5 Discussion

In our study, we identified three dietary patterns during pregnancy, namely 'mixed', 'healthy', and 'western'. The first dietary pattern, the 'mixed' pattern was characterized by a high consumption of added sugar, butter, cheese, cold breakfast cereals, cured meat, dairy products, fruit drinks, fruits, legumes, meat, nuts and seeds, other vegetables, potatoes, seafood, snacks, sweets, tea, tomatoes, and whole grains. Overall, the 'mixed' dietary pattern during pregnancy was inversely associated with excessive gestational weight gain after controlling for maternal sociodemographic variables, prepregnancy BMI, and physical activity. In the Norwegian Mother and Child Cohort Study of 66,597 pregnant women, normal weight pregnant women of prepregnancy BMI <25.0 kg/m^2 who adhered to a New Nordic Diet had lower odds of excessive gestational weight gain (OR 0.93; 95% CI 0.87-0.99) (Hillesund et al., 2014). The New Nordic Diet score was characterized by a high consumption of fruits and vegetables, whole grains, potatoes, fish, milk and drinking water pregnancy. Although the 'mixed' dietary pattern contains unhealthy food groups such as added sugar or butter, both the 'mixed' dietary pattern and the New Nordic Diet include frequent intake of fruits and vegetables, whole grains, and dairy products. These overlapping food groups may play a role in reducing excessive gestational weight gain in our study. It is possible that pregnant women with inadequate gestational weight gain may consume both healthy and unhealthy diets if they recognize that their gestational weight gain is under control.

A retrospective study of 3,360 Finnish pregnant women (Uusitalo et al., 2009) examined dietary patterns during the eight month of pregnancy using principal component analysis in relation to weekly gestational weight gain rate (kg/week). Out of the seven dietary patterns identified, the 'healthy' dietary pattern, characterized by a high loading of fruits and vegetables, fish, roots, berries, poultry, low-fat dairy was not associated with gestational weight gain. Consistent with this finding, 'the healthy' dietary pattern was not associated with gestational weight gain in the present study. In the Finnish study, the 'fast food' pattern was significantly

positively associated with gestational weight gain rate per week (ß=0.010, standard error (SE)=0.003), whereas the 'alcohol and butter' pattern was significantly inversely associated with gestational weight gain rate per week (ß=-0.010, SE=0.003). The 'fast food' pattern was characterized by high loadings of fast foods, sweets and desserts, fried potatoes, soft drinks, fruit juices, white bread, and processed meats, while the 'alcohol and butter' pattern was characterized by high intake of alcoholic beverages, butter, salad drinks, soft drinks. Interestingly, the 'western' pattern characterized by high loadings of butter, alcoholic beverages, added sugars, fruit juices and solid fats in our study was similar to the combinations of both 'fast food' and 'alcohol and butter' patterns identified from the Finnish study. A positive relationship between the 'fast food' pattern and an inverse relationship with alcohol and butter consumption with gestational weight gain may eliminate the overall effect of 'western' pattern on gestational weight gain in this study.

The association between dietary patterns and sociodemographic and lifestyle behaviors indicate that healthy food choices are part of a larger pattern of health-related behaviors (Randall et al., 1991; Kerver et al., 2003). Our study has shown that pregnant women who adhered to 'healthy' dietary pattern are more likely to be older, Mexican American, and married, whereas pregnant women who adhered to the 'western' dietary pattern were more likely to be non-Hispanic white, and had mid-level income, and a high-school to college-level education. Advanced maternal age may possess a role for 'healthy' dietary pattern. This may be due to older women being more disciplined regarding lifestyle choices such as diet (Hillesund et al., 2014). Non-Hispanic whites generally adhered to the 'western' dietary pattern, which was found to be associated with poor diet quality (Reedy et al., 2010). Laraia et al. (Laraia et al., 2007) reported that black pregnant women had significantly better diet quality during pregnancy as assessed by Diet Quality Index for Pregnancy, compared to white pregnant women (55.5 ± 12.4 vs. 54.3 ± 11.1, respectively) in the prospective Pregnancy, Nutrition, and Infection study of

2,394 pregnant women. Rifas-Shiman et al. (Rifas-Shiman et al., 2009) reported that African-American pregnant women demonstrated similar Alternate HEI, modified for Pregnancy (AHEI-P) scores in comparison to white pregnant women (mean difference 1.6 points, 95% CI -3.1 to -0.1) in the U.S. prospective cohort study of 1,777 pregnant women. These inconsistent findings may be due to the different indices used to assess diet quality during pregnancy (DQI-P vs. AHEI-P) used in the study, different pregnancy time periods when the diet quality was assessed (26-28 weeks' gestation vs. the first trimester of pregnancy), and different categorization of race/ethnicity in each study.

There are several limitations that pertain to this study. Total gestational weight gain, which is the difference between weight before pregnancy and before delivery, was not available in this study. Instead, we used gestational weight gain obtained at each month of pregnancy. For future research, multiple aspects and observations of gestational weight gain need to be considered, including weekly, total, and patterns of weight gain from the first trimester to the third trimester. Due to the cross-sectional study design of the NHANES, a cause-effect relationship cannot be proven. Dietary pattern approach help capturing the complexity of diet (Hu, 2002), however, the complexity possess subjective interpretation or researchers' bias when labeling the name of dietary patterns.

After controlling for potential confounders including physical activity, dietary patterns were significant determinants for gestational weight gain. The significant inverse association between the 'mixed' dietary pattern during pregnancy and excessive gestational weight gain needs to be considered in public health nutrition policies and interventions. This finding may be important for the prevention of excessive gestational weight gain, postpartum weight retention in their later lives, and its subsequent adverse health effects for the offspring. The authors address the significance of developing consolidated education messages that address both the nutrition and gestational weight gain guidelines for reproductive aged women to gain the recommended gestational weight gain, while meeting the essential nutritional needs during pregnancy.

Chapter Six: Dietary patterns during pregnancy are determinants of GDM risk in association with an inflammatory marker.

6.1 Abstract

Maternal dietary patterns before and during pregnancy play important roles in the development of gestational diabetes mellitus (GDM). The prevalence of GDM has been steadily rising since the 1980s. We aimed to identify dietary patterns that are associated with GDM risks and if the association is through inflammation in U.S. pregnant women. From a 24-hour dietary recall of 253 pregnant women (16-41y) included in the National Health and Nutrition Examination Survey (NHANES) 2003-2012, food items were aggregated into 28 food groups based on Food Patterns Equivalents Database. Three dietary patterns were identified by reduced rank regression with response including prepregnancy BMI, dietary fiber, and ratio of poly- and monounsaturated fatty acids to saturated fatty acid: 'refined grains and solid fats', 'nuts, seeds and oils', and 'added sugar, low fruits and vegetable'. GDM was diagnosed using fasting plasma glucose levels ≥ 92 mg/dl for gestation <24 weeks. Multivariable logistic regression models were used to estimate adjusted odds ratio (AOR) and 95% CIs for GDM, after controlling for maternal age, race/ethnicity, education, family poverty income ratio, marital status, prepregnancy BMI, gestational weight gain, energy intake, physical activity and log-transformed C-reactive protein (CRP). All statistical analyses accounted for the survey design and sample weights of NHANES. Of 253 pregnant women, 35 pregnant women (13.8%) had GDM. Multivariable AOR (95% CIs) of GDM for comparisons between the highest vs. lowest tertiles were 4.14 (1.07-16.01) for 'refined grains and solid fats' pattern, 5.58 (1.50-20.72) for 'nut, seeds and oils' pattern, and 12.61 (4.08-38.97) for 'added sugar, low fruits and vegetable' after controlling for maternal sociodemographic variables, prepregnancy BMI, gestational weight gain, energy intake and log-transformed CRP. All three dietary patterns were associated with the risk of GDM. The observed association between a high consumption of added sugars and

low intake of fruits and vegetables during pregnancy with higher odds for GDM, are consistent with generally accepted health benefits of healthy diets, but warrants further research to understand underlying pathophysiology of GDM associated with dietary behaviors during pregnancy.

6.2 Introduction

Gestational diabetes mellitus (GDM) is indicated when any degree of glucose intolerance is recognized for the first time during pregnancy, regardless of whether the condition may have predated the pregnancy or persisted after the pregnancy (Expert Committee on the and Classification of Diabetes, 2003). In the U.S, in 2014, approximately 7% of all pregnancies have been reported to be complicated by GDM, which accounts more than 200,000 cases annually (American Diabetes Association, 2014).

Several studies reported how macro- or micro-nutrient intakes are related to GDM risk (Wang et al., 2000; Bo et al., 2001; Saldana et al., 2004; Radesky et al., 2008; Zhang et al., 2008; Zhang et al., 2004). In 171 nulliparous Chinese pregnant women (Wang et al., 2000), macronutrient intake estimated from a 24-hour recall at 24-28 weeks of gestation were associated with glucose tolerance in pregnancy. Chinese women with GDM had a significantly lower polyunsaturated fat intake (% total fat) compared to women without GDM (28.2% vs. 31.6% of total fat) (Wang et al., 2000). In a study of 504 Italian pregnant women, Bo et al. (Bo et al., 2001) found that every 10% increase in saturated fat (% total fat) at 24 to 28 weeks of gestation was associated with an increased risk for GDM, whereas every 10% increase of polyunsaturated fat (% total fat) was associated with a 15% reduction of GDM risk. In a prospective cohort study entitled, Pregnancy, Infection, and Nutrition (PIN) of 1,698 U.S. pregnant women, women with GDM consumed a lower percentage of energy from carbohydrates and a higher percentage of energy from fat in the second trimester than women with normal glucose tolerance did (Saldana et al., 2004). In another prospective cohort study of

3,158 U.S. pregnant women, Qiu et al. (Qiu et al., 2011) reported that dietary heme iron intake in the first trimester was positively associated with an increased risk for GDM. The current body of literature indicates that high in intake of high saturated fat, n-3 fatty acids, and dietary heme iron and low levels of plasma vitamin C and vitamin D were associated with increased risk for GDM, whereas polyunsaturated fat intake was associated with decreased risk for GDM. However, the studies we have reviewed vary widely for the stage of pregnancy, dietary assessment tools (24-hour recalls vs. FFQs), and diagnostic criteria for GDM (75g or 100g oral glucose).

C-reactive protein (CRP) is an acute-phase reactant, a biomarker for the inflammatory process. Elevated maternal CRP concentration in the first trimester of pregnancy has been reported to be positively associated with the risk for GDM in the third trimester (Qiu et al., 2004; Ozgu-Erdinc et al., 2014). Scholl et al. (Scholl et al., 2011) have suggested that diet during pregnancy is associated with circulating levels of CRP in pregnant women and aggravates the inflammatory process (Scholl et al., 2011). The authors noted that lean women (prepregnancy BMI<25 kg/m^2) with high CRP (range, 7.06-137.41 mg/L) at 28 weeks' gestation had a higher intake of protein and cholesterol with a lower intake carbohydrates compared to those who had low CRP (range, 0.03-2.25 mg/L). It is questionable whether the maternal diet influences the risk for GDM through inflammation. Limited studies are available as to the role of dietary factors during pregnancy in relation to GDM risk (Zhang and Ning, 2011; Zhang, 2010) in association with an inflammatory marker, CRP.

Analyses of overall food patterns account for any interactions or synergistic effects among individual foods or nutrients (Hu, 2002). In literatures on dietary patterns in pregnant population, factors analysis or principal component analysis ("foods group-driven") (Zhang et al., 2006b; Brantsaeter et al., 2009; Englund-Ogge et al., 2014; Rasmussen et al., 2014; Jacka et al., 2013) were used to derive dietary patterns and related to pregnancy complications or birth outcomes. Reduced rank regression methods ("biomarker or nutrient-driven") have been

introduced to assess better the diet-disease relations compared to using factor analysis and principal component analysis (Hoffmann et al., 2004a), but the method has been underutilized among pregnant women. The reduced rank regression method has only been reported in the studies that assessed dietary patterns during pregnancy in relation to spina bifida (Vujkovic et al., 2009) and congenital heart defect (Obermann-Borst et al., 2011) in the Netherlands. Dietary patterns derived using the reduced rank regression method is expected to explain the maximum variation of GDM-related maternal nutrients and biomarkers as response variables in women with GDM.

A dietary pattern approach considers foods and nutrients that are consumed in many combinations and that nutrients may have synergistic effects (Hu, 2002). A few studies have examined the association between dietary patterns during pregnancy and the risk of GDM in U.S. representative pregnant women in consideration of CRP, which was found to be associated GDM (Qiu et al., 2004; Ozgu-Erdinc et al., 2014). The role of dietary patterns during pregnancy in relation to GDM is still uncertain. We hypothesized that dietary patterns during pregnancy derived from reduced rank regression are associated with the risk of GDM in conjunction with an inflammatory marker, CRP.

6.3 Material and Methods

6.3.1 Study Population

We used public domain data from the continuous National Health and Nutrition Examination (NHANES) 2003-2004, 2005-2006, 2007-2008, 2009-2010, and 2011-2012 for this study. Data from the NHANES 2003-2012 were combined for this study with greater statistical reliability. The NHANES is a program of studies cross-sectionally designed to assess the health and nutritional status of the civilian, non-institutionalized population in the U.S. conducted by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention

(CDC). The NHANES used a stratified multistage probability sample that was based on the selection of counties, blocks, households, and finally persons within households. The NHANES survey is unique in that it combines interviews and physical examinations. The participants were interviewed for the information of age, race/ethnicity, education level, marital status, family poverty income ratio, and physical activity. Reproductive health interviews obtained information on the month of gestation at the time of the survey. Pregnancy status was based on a positive urine pregnancy test. Prepregnancy weight was self-reported during the weight history questionnaire interview. A complete description of data-collection procedures and analytic guidelines has been provided elsewhere (Centers for Disease Control and Prevention, 2013a; Centers for Disease Control and Prevention, 2013b).

The 2003-2012 NHANES dataset included 761 pregnant women. Subjects were excluded if they reported unreliable dietary data, as defined by the NCHS (n=24) and had missing data of gestational weeks (n=105), measured height, weight and self-reported prepregnancy weight (n=35), glucose and insulin levels (n=310), and CRP levels (n=1). Lastly, pregnant women who did not participate in the fasting subsample for glucose and insulin were excluded from the analysis (n=33). The final analytic sample size was 253 pregnant women.

6.3.2 Dietary Assessment

The What We Eat in America component of the NHANES 2003-2012 collected dietary information by using an interviewer-administered 24-hour recall that used automated multiple pass methodology developed by the U.S. Department of Agriculture (Moshfegh et al., 2008). A second dietary recall, 3-10 days after the first dietary recall, was obtained by using phone calls (Centers for Disease Control and Prevention and National Center for Health Statistics, 2014b). Given the study aim to examine dietary patterns derived by food groups in association with GDM, our analysis used the information collected in the first dietary recall.

Dietary pattern analysis was performed in two steps to identify dietary patterns as predictors of the responses to GDM. In the first step, food items were aggregated into 28 food groups, which are comparable with the grouping schemes reported in the Food Patterns Equivalents Database (FPED) 2011-2012 (Bowman et al., 2014) (as shown in Table 21). The USDA's food code from an individual's day 1 dietary recall of NHANES was matched to the USDA food code of FPED 2011-2012. Since the components of FPED 2011-2012 are presented per 100 grams of food and beverages, an individual's food intake in grams was divided by 100 grams and multiplied by the number of FPED equivalents in FPED 2011-2012 (U.S. Department of Agriculture, 2014). To derive optimal dietary patterns, total fruit, total vegetables, total red and orange vegetables, total starch vegetables, total grains, total protein foods, total meat, poultry, and seafood, and total dairy from the original FPED 2011-2012's subgroups were removed because a total subgroup is the summation of its subgroup components. For example, total dairy is the summation of milk, yogurt, and cheese. In the second step, dietary pattern analysis was performed with the reduced rank regression method. The reduced rank regression method extracts linear combinations from predicting variables while maximizing the variance explained within a set of response variables (Hoffmann et al., 2004a). We used PROC PLS with the reduced rank regression method option to drive dietary patterns using SAS software (version 9.3; SAS Institute, Cary, NC). The analysis began with the selection of the 28 food groups on the basis of the number of cup equivalents of fruit, vegetables, and dairy; ounce equivalents of grains and protein foods; teaspoon equivalents of added sugars; gram equivalents of solid fats and oils; and number of alcoholic drinks as independent or exposure variables. This was followed by the choice of the prepregnancy BMI, nutrient intake, and maternal biomarkers related to GDM as response measures following log transformation. The predicting variables are the food groups from a 24-hour recall, and the final set of response measures are prepregnancy BMI, dietary fiber, and poly- and monounsaturated fatty acids to saturated fatty acid. The final number of response variables indicating the greatest

explanation of the total variation in foods groups and biomarkers was obtained by sensitivity analysis (Table 23).

The relationship between the 28 food groups and the identified dietary patterns was indicated by factor loadings, which represent the correlation coefficients between the food groups and the dietary patterns. The dietary patterns were labeled on the basis of food groups that loaded highest and/or lowest in the respective dietary pattern. Each pregnant woman was assigned a score of the derived dietary patterns, calculated as the product of the food group value and its factor loading and summed across the food groups.

6.3.3 Maternal Biomarkers

All the blood measurements used in this study were drawn and performed as part of the NHANES 2003-2012 surveys. A fasting blood glucose test was performed on eligible participants who were examined in the morning session after a 9 hour fast (Centers for Disease Control and Prevention and National Center for Health Statistics, 2008b). Plasma glucose was measured using an enzyme hexokinase method (Centers for Disease Control and Prevention and National Center for Health Statistics, 2008b). For NHANES 2003-2004, glucose and insulin measurements were performed by Diabetes Diagnostic Laboratory at University of Missouri (Columbia, MO) (Centers for Disease Control and Prevention and National Center for Health Statistics, 2006b), and for NHANES 2005-2012, glucose and insulin measurements were performed by the Fairview Medical Center Laboratory at the University of Minnesota (Minneapolis, MN) (Centers for Disease Control and Prevention and National Center for Health Statistics, 2008b). Insulin was measured using Tosoh AIA-PACK IRI immunoenzymometric assay in NHANES 2003-2004 (Centers for Disease Control and Prevention and National Center for Health Statistics, 2006b), and the Merocodia Insulin ELISA Immunoassay in NHANES 2005-2012 (Centers for Disease Control and Prevention and National Center for Health Statistics, 2008b). Insulin resistance was estimated using the homeostatic model assessment for insulin

resistance (HOMA-IR) by the following formula: fasting insulin (μU/mL) X fasting glucose (mmol/L)/22.5 (Matthews et al., 1985). HbA1C was measured using a Tosoh A1C 2.2 Plus Glycohemoglobin Analyzer or a Tosoh G7 Automated HPLC Analyzer (Centers for Disease Control and Prevention and National Center for Health Statistics, 2008a). CRP (mg/dL) was measured by latex-enhanced nephelometry (Centers for Disease Control and Prevention and National Center for Health Statistics, 2007). Vitamin C level in serum was measured using isocratic high performance liquid chromatography (HPLC) with electrochemical detection at 650 mV1 (Centers for Disease Control and Prevention and National Center for Health Statistics, 2009a). Lastly, vitamin D (ng/mL) concentration was measured by using the Diasorin 25-OH-Vitamin D assay (Centers for Disease Control and Prevention and National Center for Health Statistics, 2008c).

6.3.4 Outcome Variable

In this cross-sectional study, the average gestational age of study participants was 20 weeks, and four women reported that they were diagnosed with GDM at the time of the interview. GDM was diagnosed according to the 2010 International Association of Diabetes and Pregnancy Study Groups (IADPSG) Consensus Panel (International Association of Diabetes and Pregnancy Study Groups Consensus Panel, 2010) if the following criteria were met: fasting plasma glucose level ≥5.1 mmol/L (92 mg/dl) before 24 weeks of gestation.

6.3.5 Covariates

Analyses were adjusted for maternal age, race/ethnicity, family poverty income ratio, education, marital status, and physical activity level. Maternal age was divided into three groups: ≤24, 25-34 and ≥35 years. The study group consisted of Mexican-American or other Hispanic, non-Hispanic White, non-Hispanic Black and other race. Family poverty income ratio was divided into three categories: ≤1.85, 1.85-4 and >4. Maternal education was grouped by the

number of completed years of school: less than high school, high school diploma and more than high school. Marital status was divided into three groups: married, widowed /divorced separated/living with a partner, single. Physical activity level was divided into four groups: no activity, 0-500 MET-minutes/week, 500-1000 MET-minutes/week, ≥1,000 MET-minutes/week.

6.3.6 Statistical Analyses

Maternal characteristics were expressed as numbers (weighted percentages) by the status of GDM. The Chi-square test was performed to test the association between maternal characteristics and the status of GDM. The risk for GDM was categorized as yes or no, and Multivariable logistic regression models were applied to estimate odds ratios (ORs) (95% CI) of the risk for GDM across tertiles of dietary pattern scores. *P* for trend across dietary pattern was computed using dietary pattern scores as continuous variables. We first ran models testing crude associations, then models were adjusted in three ways: (1) maternal age, race/ethnicity, education, family poverty income ratio and marital status; (2) model 1 + prepregnancy BMI + gestational weight gain + energy intake; (3) model 2 + log-transformed CRP concentrations.

To analyze the magnitude of collinearity, the variance inflation factor (VIF) was used to test with VIF <5 set as the acceptable level (O'Brien, 2007). NAHENS uses a complex sample survey design including a multistage cluster sample and weighting methodology that oversamples certain groups of individuals to ensure adequate statistical power. All analyses were carried out using SAS software (version 9.3; SAS Institute, Cary, NC), which incorporates appropriate sampling weights to adjust for the complex sampling weights. Sampling weights associated with the smallest subsample (fasting subsample) were used as recommended by the NHANES (Centers for Disease Control and Prevention and National Center for Health Statistics, 2013b).

6.4 Results

Pregnant women's characteristics according to the status of GDM are shown in Table 22. Pregnant women with GDM generally had a family poverty income ratio ≤1.85 and excessive gestational weight gain. Pregnant women with GDM were less likely to be involved in physical activity compared to women without GDM. Multi-collinearity between age, race/ethnicity, family poverty income ratio, education, marital status, and physical activity did not exist. The VIF for all confounding variables was less than 2. These findings suggest that collinearity between these confounding variables was not significant.

Dietary patterns were derived using the reduced rank regression method. The reduced rank regression method derives dietary patterns from predictors to maximize the explained variation of a pre-defined set of responses chosen. Responses chosen for reduced rank regression were prepregnancy BMI and nutrients that have bene consistently associated with GDM in the literature such as dietary fiber and ratio of poly- and monounsaturated fatty acids to saturated fatty acids (Zhang et al., 2006a; Saldana et al., 2004; Bo et al., 2001). Sensitivity analysis using different numbers of response variables (different sets for prepregnancy BMI and GDM-related nutrients including or excluding GDM-related biomarkers) indicated that the best compilation of the total variation in foods and in responses was obtained using prepregnancy BMI, dietary fiber, and ratio of poly- and monounsaturated fatty acids to saturated fatty acids (Table 23). Three factors were extracted with reduced rank regression, explaining the 45.9% of the total variation in the response variables and the 15.0% variation in food groups (Table 24). Three dietary patterns were derived using reduced rank regression. Loading values for each of the 28 food groups for the reduced rank regression obtained dietary patterns are presented in Table 5. The 'refined grains and solid fats' pattern was characterized by high loadings of refined grains, solid fats, oils, and fruit juice. The 'nuts, seeds and oils' pattern was characterized by high loadings of nuts and seeds, solid fats, soybean products and low loadings of milk and cheese. The 'added sugar, low fruits and vegetable' pattern was represented by high loadings of

added sugars and organ meats and low loadings of fruits and vegetables and seafood (Table 25).

Maternal characteristics according to the tertiles of three dietary patterns' scores are presented in Table 26. Total energy intake, fat intake as percentages of energy and dietary fiber intake differed significantly by tertiles of the 'refined grains and solid fats' pattern score. Total energy intake, carbohydrate and fat intake as percentages of energy, dietary fiber, ratio of poly- and monounsaturated fatty acids to saturated fatty acid, serum vitamin D, and CRP levels significantly differed by the tertiles of 'nuts, seeds and oils' dietary pattern score. Prepregnancy BMI, carbohydrate and protein intake as percentages of energy, and HOMA-IR significantly differed by the tertiles of 'added sugar, low fruits and vegetable' dietary pattern score (Table 26).

Covariate-adjusted multivariable logistic regression analyses showed that all three dietary patterns were significantly and positively associated with a higher GDM risk (Table 27). In the fully adjusted multivariable model 4, comparing pregnant women in the highest tertile with those in the lowest reference tertile of 'refined grains and solid fats' pattern, pregnant women had higher odds of developing GDM (OR 4.14; 95% CI 1.07-16.01). Pregnant women in the highest tertile of the 'nuts, seeds and oils' pattern had higher odds of developing GDM (OR 5.58; 95% CI 1.50-20.72) than those in the lowest tertile (model 4). Pregnant women in the highest tertile of the 'added sugar, low fruits and vegetables' pattern had higher odds of developing GDM (OR 12.28; 95% CI 4.27-35.35) than those in the lowest tertile (model 3). The relationship between the 'added sugar, low fruits and vegetables' diet and GDM was even stronger after controlling for log-transformed CRP (OR 12.61; 95% CI 4.08-38.97) (model 4).

Table 21. Food patterns equivalents database (FPED) 2011-2012 food groups and modified groups used in the present study.

FPED[1] 2011-2012 Food Groups	Original FPED 2011-2012 subgroups	Modified FPED 2011-2012 subgroups
Fruit	1. Total fruit	*Removed*
	2. Citrus, melons, and berries	1. Citrus, melons, and berries
	3. Other fruits	2. Other fruits
	4. Fruit juice	3. Fruit juice
Vegetables	5. Total vegetables	*Removed*
	6. Dark green vegetables	4. Dark green vegetables
	7. Total red and orange vegetables	*Removed*
	8. Tomatoes	5. Tomatoes
	9. Other red and orange vegetables (excludes, tomatoes)	6. Other red and orange vegetables (excludes, tomatoes)
	10. Total starchy vegetables	*Removed*
	11. Potatoes (white potatoes)	7. Potatoes (white potatoes)
	12. Other starchy vegetables (excludes white potatoes)	8. Other starchy vegetables (excludes white potatoes)
	13. Other vegetables	9. Other vegetables
	14. Beans and peas computed as vegetables	10. Beans and peas computed as vegetables
Grains	15. Total grains	*Removed*
	16. Whole grains	11. Whole grains
	17. Refined grains	12. Refined grains
Protein Foods	18. Total protein foods	*Removed*
	19. Total meat, poultry, and seafood	*Removed*
	20. Meat (beef, veal, pork, lamb, game)	13. Meat (beef, veal, pork, lamb, game)
	21. Cured meat (frankfurters, sausage, corned beef, cured ham and luncheon meat made from beef, pork, poultry)	14. Cured meat (frankfurters, sausage, corned beef, cured ham and luncheon meat made from beef, pork, poultry)
	22. Organ meat (from beef, veal, pork, lamb, game, poultry)	15. Organ meat (from beef, veal, pork, lamb, game, poultry)
	23. Poultry (chicken, turkey, other fowl)	16. Poultry (chicken, turkey, other fowl)
	24. Seafood high in n-3 fatty acids	17. Seafood high in n-3 fatty acids
	25. Seafood low in n-3 fatty acids	18. Seafood low in n-3 fatty acids
	26. Eggs	19. Eggs
	27. Soybean products (excludes calcium fortified soy milk and mature soybeans)	20. Soybean products (excludes calcium fortified soy milk and mature soybeans)
	28. Nuts and seeds	21. Nuts and seeds
	29. Beans and peas computed as protein foods	*Removed*

Table 21 (cont'd)

FPED[1] 2011-2012 Food Groups	Original FPED 2011-2012 subgroups	Modified FPED 2011-2012 subgroups
Dairy	30. Total dairy (milk, yogurt, cheese, whey)	*Removed*
	31. Milk (includes calcium fortified soy milk)	22. Milk (includes calcium fortified soy milk)
	32. Yogurt	23. Yogurt
	33. Cheese	24. Cheese
Oils	34. Oils	25. Oils
Solid Fats	35. Solid fats	26. Solid fats
Added Sugars	36. Added sugars	27. Added sugars
Alcoholic Drinks	37. Alcoholic drinks	28. Alcoholic drinks

USDA's Food Patterns Equivalents Database 2011-12 (FPED 2011-12) converts foods and beverages in the Food and Nutrient Database for Dietary Studies (FNDDS) 2011-12 to 37 Food Patterns (FP) components (U.S. Department of Agriculture, 2014).

[1]The FPED provides a unique research tool to evaluate food and beverage intakes of Americans compared to recommendations of the 2010 Dietary Guidelines for Americans.

Table 22. Maternal characteristics in relation to risk of gestational diabetes mellitus (GDM)

	GDM			No GDM			
	n	Wt'd[1] % (Col)	Wt'd % (Row)	n	Wt'd % (Col)	Wt'd % (Row)	*P* value[2]
Age							
≤25	17	53.5	26.0	95	36.4	74.0	0.29
26-35	14	36.1	13.1	112	57.0	86.9	
≥35	4	10.4	27.5	11	6.5	72.5	
Race							
Mexican American or other Hispanic	10	19.5	17.3	76	19.5	82.7	0.99
Non-Hispanic white	18	58.6	20.3	97	58.6	79.7	
Non-Hispanic black	4	13.4	18.9	32	13.4	81.1	
Other including multi-racial	3	8.5	18.2	13	8.5	81.8	
Family Poverty Income Ratio							
≤1.85	21	65.1	28.9	110	38.2	71.1	0.01
1.85-4	5	5.5	3.5	61	36.8	96.5	
>4	9	29.4	21.9	47	25.0	78.1	
Education Level							
≤11th grade	12	35.2	26.2	77	23.7	73.8	0.41
High school grade	5	7.6	8.8	38	18.9	91.2	
Above college	18	57.2	19.2	103	57.4	80.8	
Marital Status							
Married	22	64.5	17.8	138	71.1	82.2	0.81
Widowed/divorced/ separated/living with a partner	8	20.3	21.6	43	17.5	78.4	
Single	22	15.3	17.8	138	11.4	82.2	
Parity (n=182)							
None	1	12.7	31.0	12	6.4	69.0	0.51
1	14	51.7	19.3	81	48.9	80.7	
2	10	34.6	19.4	39	32.4	80.6	
≥3	1	1.1	2.0	24	12.3	98.0	
Trimester of Pregnancy							
1st trimester	12	47.4	28.1	40	29.0	71.9	0.21
2nd trimester	13	31.8	17.4	88	36.0	82.6	
3rd trimester	10	20.8	12.4	90	34.9	87.6	
Prepregnancy weight status							
BMI <25kg/m^2	9	34.2	12.0	134	60.1	88.0	0.11
BMI ≥25kg/m^2	26	65.8	28.3	84	39.9	71.7	
Gestational Weight Gain							
Inadequate	8	13.9	10.1	60	29.6	89.9	0.08
Adequate	4	18.0	16.0	49	22.5	84.0	
Excessive	23	68.1	25.3	109	48.0	74.7	
Physical activity (n=158)							
None	6	26.7	33.7	10	14.0	66.3	0.16

Table 22 (cont'd)

	GDM			No GDM			
	n	Wt'd[1] % (Col)	Wt'd % (Row)	n	Wt'd % (Col)	Wt'd % (Row)	*P* value[2]
0 to <500 MET-min/week	11	49.4	22.3	66	46.0	77.7	
500 to <1,000 MET-min/week	5	19.9	25.8	24	15.3	74.2	
≥1,000 MET-min/week	3	4.0	4.2	33	24.7	95.8	
C-reactive protein							
>0.3 mg/dl	29	76.5	19.7	167	74.6	80.3	0.86
≤0.3 mg/dl	6	23.5	18.1	51	25.4	81.9	

[1] Wt'd %: Weighted %. Sample weights are created in NHANES to account for the complex survey design (including oversampling of some subgroups), survey non-responses, and post-stratification. When a sample is weighted in NHANES, it is representative of the U.S. civilian non-institutionalized Census population. Weighted percentages may not sum up to 100 due to rounding.

[2] *P* value obtained from Chi-square tests.

Table 23. Selection process of response variables to derive dietary patterns using reduced rank regression

Response Variables		
1st Set	2nd Set	3rd Set
Prepregnancy BMI	Prepregnancy BMI	Prepregnancy BMI
Fatty acids[1]	Fatty acids	Fatty acids
Dietary fiber	Dietary fiber	Dietary fiber
Glycohemoglobin	Glycohemoglobin	
HOMA-IR	HOMA-IR	
Glucose	Glucose	
Vitamin C		
Vitamin D		
CRP		
Food Groups: 15.6%[1]	Food Groups: 15.0%	Food Groups: 15.0%
Responses: 18.6%	Responses: 25.4%	Responses: 45.9%

[1] Ratio of poly- and monounsaturated fatty acids to saturated fatty acids
[2] Explained variation

Table 24. Explained variations of response variables and food groups by extracted dietary patterns

	'Refined Grains and Solid Fats' Dietary Pattern	'Nuts, Seeds and Oils' Dietary Pattern	'Added Sugars, Low Fruits and Vegetables' Dietary Pattern	Total explained variation
Explained variation				
Food groups	6.7%	4.8%	3.5%	15.0%
Responses	28.5%	14.9%	2.5%	45.9%

Dietary patterns obtained with reduced rank regression using pregnancy BMI, ratio of poly- and monounsaturated fatty acids to saturated fatty acids, and dietary fiber as response variables in the procedure.

Table 25. Loadings of food groups in dietary pattern scores in pregnant women

#	Food Group	'Refined Grains and Solid Fats' Pattern	'Nuts, Seeds and Oils' Pattern	'Added Sugars, Low Fruits and Vegetables' Pattern
1	Other starchy vegetables (excludes white potatoes)	**0.14**	-0.03	-0.01
2	Refined grains	**0.30**	**-0.14**	0.03
3	Whole grains	**0.26**	-0.01	0.03
4	Milk (includes calcium fortified soy milk)	**0.12**	**-0.33**	-0.02
5	Other fruits	**0.26**	**-0.21**	-0.06
6	Tomatoes	**0.26**	**-0.13**	-0.01
7	Soybean products (excludes calcium fortified soy milk and mature soybeans)	**0.17**	**0.41**	**-0.24**
8	Other vegetables	**0.24**	**0.17**	**-0.28**
9	Beans and peas	**0.36**	**-0.19**	**0.25**
10	Nuts and seeds	**0.26**	**0.24**	**0.17**
11	Citrus, melons, and berries	**0.20**	**-0.13**	**-0.21**
12	Cheese	**0.17**	**-0.25**	**-0.10**
13	Oils	**0.23**	**0.44**	**0.15**
14	Solid fats	**0.14**	**-0.40**	**-0.19**
15	Fruit juice	**0.14**	0.08	**-0.17**
16	Other red and orange vegetables (excludes, tomatoes)	**0.23**	0.05	**-0.17**
17	Potatoes (white potatoes)	**0.17**	0.09	**-0.25**
18	Meat (beef, veal, pork, lamb, game)	0.03	**-0.15**	**-0.38**
19	Dark green vegetables	0.09	0.00	**0.15**
20	Added sugars	-0.04	0.01	**0.28**
21	Alcoholic drinks	-0.03	0.01	**-0.12**
22	Organ meat (from beef, veal, pork, lamb, game, poultry)	0.03	-0.01	**0.12**
23	Cured meat (frankfurters, sausage, corned beef, cured ham and luncheon meat made from beef, pork, poultry)	-0.06	-0.02	**-0.11**
24	Seafood low in n-3 fatty acids	-0.01	0.05	**-0.11**
25	Eggs	0.03	-0.05	**-0.40**
26	Poultry (chicken, turkey, other fowl)	0.04	0.09	-0.03
27	Seafood high in n-3 fatty acids	0.03	0.06	0.02
28	Yogurt	0.06	-0.06	-0.06

[1] Factor loadings represent the magnitude and direction of association with factors (dietary patterns) and can range from -1.0 to 1.0. Food groups with factor loading values ≥ |0.10| are indicated in bold.

Table 26. Maternal characteristics by tertiles of dietary pattern scores

	'Refined Grains and Solid Fats' Pattern				'Nuts, Seeds and Oils' Pattern				'Added Sugars, Low Fruits and Vegetables' Pattern			
	T1 (n=84)	T2 (n=85)	T3 (n=84)	*P* trend	T1 (n=84)	T2 (n=85)	T3 (n=84)	*P* trend	T1 (n=84)	T2 (n=85)	T3 (n=84)	*P* trend
Age (y)	26.4±0.8[1]	28.2±0.8	27.5±0.7	0.40	29±0.9	26.7±0.7	26.4±0.7	0.06	29.2±1	26.6±0.6	26.8±0.8	0.05
Prepregnancy BMI (kg/m^2)	26.1±1.5	27.8±0.9	25.3±0.7	0.06	25.9±1.2	25.8±0.9	27.9±1.5	0.43	24.9±1.1	24.6±0.8	29±1.3	0.009
Total energy (kcal/d)	1942.7±131.2	2529.4±138.9	2783.6±149.4	0.0004	2842.7±114.2	2097.3±115.9	2248.6±145.6	<0.0001	2606.8±126.4	2230.9±197.1	2390.2±113.7	0.17
Carbohydrate (% of energy/d)	51.8±2.3	53±1.1	54.3±1.6	0.67	52.6±1.8	55.7±1.4	49.9±1.7	0.03	48.9±1.3	51.6±1.2	56.4±1.9	0.005
Protein (% of energy/d)	16.4±0.7	13.9±0.4	14.1±0.5	0.01	14.8±0.6	15.0±0.7	14.8±0.6	0.97	16.7±0.9	15.5±0.9	13.2±0.6	0.001
Total fat (% of energy/d)	32.4±1.8	34.4±1.2	33.7±1.2	0.66	33.7±1.6	30.7±1.3	36.5±1.3	0.01	35.5±1.0	33.8±1.6	32.0±1.3	0.10
MUFA (% of energy/d)	12.1±0.8	12.6±0.5	12.1±0.5	0.81	12.1±0.7	11.5±0.5	13.3±0.6	0.08	12.9±0.4	12.7±0.7	11.6±0.5	0.07
SFA (% of energy/d)	11.1±0.7	11.5±0.6	11±0.6	0.82	12.4±0.6	10.5±0.7	10.8±0.6	0.08	12.2±0.5	10.9±0.8	10.8±0.5	0.19
Dietary fiber (g/d)	10.8±1	16.5±0.6	26.0±1.3	<0.0001	20.5±1.3	15.7±1.4	15.2±0.9	0.005	19.3±1.3	14.8±1.3	17.8±1.3	0.07
Fatty acids ratio[2]	1.6±0.1	1.6±0.1	1.8±0.1	0.52	1.3±0.1	1.6±0.1	2.1±0.1	<0.0001	1.6±0.1	1.8±0.1	1.6±0.1	0.60
Glycohemoglobin (%)	5.0±0.1	5.0±0.0	5.0±0.0	0.50	4.9±0.1	5.0±0.0	5.1±0.1	0.32	5.0±0.1	4.9±0.0	5.0±0.1	0.35
HOMA-IR	2.4±0.3	2.5±0.3	2.4±0.3	0.98	2.3±0.3	2.1±0.2	3.0±0.4	0.14	2.4±0.2	1.8±0.2	3.0±0.3	0.01
Fasting glucose (mg/dL)	84.9±1.5	83.5±1.2	86.2±1.1	0.22	84.1±1.7	85.6±1.2	84.5±1.5	0.71	84.6±1.4	82.9±1.1	86.5±1.6	0.18
Serum Vitamin C (mg/dL)	1.1±0.1	1.0±0.1	1.2±0.1	0.15	1.1±0.1	1.2±0.1	1.1±0.1	0.78	1.1±0.0	1.3±0.1	1.0±0.1	0.11
Serum Vitamin D (mg/dL)	26.2±1.9	31±3.2	28.3±2.4	0.36	29.1±1.6	31.3±3.3	24.5±1.7	0.04	28.1±1.5	30.7±3.4	27.0±2.2	0.62
C-reactive protein (mg/dL)	0.8±0.2	0.7±0.1	0.6±0.1	0.69	0.5±0.1	0.7±0.1	1.0±0.2	0.04	0.7±0.1	0.6±0.1	0.9±0.2	0.16

[1] Mean ± SE (all such values)
[2] Ratio of poly- and monounsaturated fatty acids to saturated fatty acid

Table 27. Odds ratios (and 95% CIs) for risk of gestational diabetes mellitus (GDM) according to tertiles of dietary pattern scores derived from reduced rank regression (n=253)

	Tertile 1	Tertile 2	Tertile 3	*P* trend
'Refined Grains and Solid Fats' Pattern				
GDM/pregnancies	9/84	11/85	15/84	
Model 1	1.00	0.90 (0.27-2.99)	2.88 (0.71-11.65)	0.16
Model 2	1.00	1.37 (0.40-4.68)	5.14 (1.14-23.25)*	0.38
Model 3	1.00	0.95 (0.31-2.93)	4.41 (1.04-18.67)*	0.02
Model 4	1.00	0.99 (0.31-3.20)	4.14 (1.07-16.01)*	0.02
'Nuts, Seeds and Oils' Pattern				
GDM/pregnancies	10/84	11/85	14/84	
Model 1	1.00	2.71 (0.78-9.43)	2.85 (0.85-9.58)	0.09
Model 2	1.00	2.96 (0.89-9.85)	3.82 (1.17-12.49)*	0.02
Model 3	1.00	4.76 (2.11-10.72)*	6.39 (1.64-24.95)*	0.01
Model 4	1.00	4.33 (1.86-10.07)*	5.58 (1.50-20.72)*	0.02
'Added Sugar, Low Fruits and Vegetables' Pattern				
GDM/pregnancies	6/84	8/85	21/84	
Model 1	1.00	0.69 (0.13-3.65)	5.74 (1.39-23.63)*	0.02
Model 2	1.00	0.99 (0.23-4.34)	10.06 (3.02-33.52)*	0.0003
Model 3	1.00	1.37 (0.55-3.44)	12.28 (4.27-35.35)*	<0.0001
Model 4	1.00	1.53 (0.58-4.00)	12.61 (4.08-38.97)*	<0.0001

Model 1: Crude association between dietary patterns and gestational diabetes mellitus

Model 2: Adjusted for age, race/ethnicity, family poverty income ratio, education level, and marital status

Model 3: Adjusted for model 2 + energy intake, prepregnancy BMI, and gestational weight gain

Model 4: Adjusted for model 3 + log-transformed CRP

*$P<0.05$

6.5 Discussion

In this cross-sectional study, three dietary patterns during pregnancy were identified with the choice of response variables including prepregnancy BMI, ratio of poly- and monounsaturated fatty acids to saturated fatty acids and dietary fiber: 'refined grains and solid fats' pattern, 'nuts, seeds and oils' pattern, and 'added sugars, low fruits and vegetable' patterns. Despite small differences, all three dietary patterns were associated with increased risks for GDM. Among three dietary patterns, the strongest connection to GDM risk was found for the 'added sugars, low fruits and vegetables' pattern. The positive association of the 'added sugars, low fruits and vegetables' pattern with GDM was largely explained by the high consumption of added sugars and low consumption of fruits and vegetables. Sugar-sweetened beverages are one of the leading sources of added sugars in the American diet (Bray et al., 2004). In the Nurses' Health Study II, intake of sugar-sweetened coke before pregnancy was positively associated with the risk of GDM (Chen et al., 2009a). Compared to women who consumed 1 serving/month, those women who consumed ≥5 servings/week of sugar-sweetened coke had a 22% greater risk for GDM (relative risk (RR) 1.22; 95% CI 1.01-1.47). Epidemiologic studies demonstrate that the high consumption of sugar-sweetened beverages was associated with increased risks for type 2 diabetes among the general adult populations (Montonen et al., 2007; Palmer et al., 2008; Malik et al., 2010). The high levels of rapidly absorbable carbohydrates in the form of added sugars of sugar-sweetened beverages (Malik et al., 2010) may increase the levels of fasting blood glucose levels and insulin resistance. In our study, low intake of the "fruits and vegetables" pattern was associated with an increased risk for GDM. Although the biological mechanisms for the inverse associations of fruits and vegetable intake and GDM risk are not clear, Bazzano et al. (Bazzano et al., 2002) explained that the consumption of fruits and green leafy vegetables may contribute to a decreased incidence of type 2 diabetes through their low energy density, low glycemic load, and high fiber. This mechanism may partially explain the association of low intake of fruits and vegetables in relation to the decreased risk for GDM. Our

findings are further supported by the findings from the Nurses' Health Study II (Zhang et al., 2006b). Women in the lowest quintile of the prudent pattern characterized by a high intake of fruit, vegetables, and green leafy vegetables (lowest adherence) were associated with increased risks for GDM compared to those women in the highest quintile (highest adherence) (RR 1.39; 95% CI 1.08-1.80). In the same prospective cohort of Nurses' Health Study II, intake of whole fruits and green leafy green vegetables was inversely associated with incidence of type 2 diabetes in the middle-aged U.S. women (Bazzano et al., 2008).

The association with 'refined grains and solid fats' pattern was largely explained by high intakes of refined grains and solid fats. Our findings are in accordance with the evidence of positive associations of the 'Western' dietary pattern, characterized by a high intake of refined grains and solid fats with GDM in pregnant women (Zhang et al., 2006b). In the Nurses' Health Study II (Zhang et al., 2006b), the 'Western' dietary pattern before pregnancy characterized by high intake of red meat, processed meat, refined grain products, and sweets were associated with the risk of GDM. In contrast, the 'Western' dietary pattern in the first month of pregnancy, which included red and processed meats, sugar-sweetened beverages, and refined grains, was not associated with the risk of GDM in the prospective cohort study of Project Viva (Radesky et al., 2008). The authors explained that once insulin resistance has been established from years of following the 'Western' dietary pattern, what women eat in the first few months of pregnancy may not have additional effect on the risk of GDM.

The positive association of the 'nuts, seeds and oils' pattern with GDM was largely explained by a low intake of fruits, tomatoes, and beans and peas. Low intake of fruits may partially explain the positive association between 'nut, seeds and oil' pattern and the risk for GDM. Low consumption of fruits, lack of phytonutrients, including carotenoids and vitamins such as vitamin C (Craig, 1997), found to have preventive effect on GDM (Zhang et al., 2004) may explain the association.

There are inconsistent findings regarding the relationship between elevated CRP and the risk for GDM. Elevated maternal CRP concentration in the first trimester of pregnancy has been reported to be positively associated with the risk for GDM in the third trimester (Qiu et al., 2004; Wolf et al., 2003). In contrast, maternal serum levels of CRP were not associated with the risk for GDM but significantly correlated with prepregnancy obesity in a cross-sectional study (Retnakaran et al., 2003). In our study, CRP levels (≤0.3 mg/dl vs. >0.3 mg/dl) did not significantly differed by the presence of GDM. For this reason, after adjustment for CRP level, a significant relationship between dietary patterns and the risk for GDM persisted.

The strengths of this study are that first, the reduced rank regression method allowed for a hypothesis regarding pathways (by the response variables) between diet and disease (GDM) to be evaluated (Hoffmann et al., 2004b). Although traditional principal component analysis has been useful in the past studies, the pattern solely focused on inter-correlations among food groups, which may not represent diet qualities relevant to specific disease etiology (Hoffmann et al., 2004b). Reduced rank regression is useful for etiological investigation explaining how a certain dietary pattern is associated with the health outcome of interest (Nettleton et al., 2007). In our study, a great number of potential confounders such as physical activity, prepregnancy BMI and gestational weight gain were controlled in the analysis. We also confirmed no multi-collinearity among covariates. Lastly, our study is unique in that we studied the U.S. representative diverse pregnant women with a reliable dietary intake recall.

The study has several limitations. Due to the use of cross-sectional study design of NHANES, we cannot provide evidence of a causal relationship between dietary patterns during pregnancy and the risk for GDM. Particularly, this could be the result of reverse causality in which subjects may change or adapt to different styles of diet after the diagnosis for GDM. Another limitation is that a history of family type 2 diabetes was not controlled for in our analysis. Due to the relative sample size of pregnant women, low statistical power may cause the wide confidence intervals in our analysis. The relationship between diet and GDM may be mediated

through pathways by other undefined biomarkers. It is possible that women with GDM are consuming foods high in added sugars and solid fats without recognizing that they are diagnosed with GDM. Among 35 pregnant women with GDM, we could obtain data from 10 pregnant women with self-reported information on whether or not they were told by a doctor or other health professionals that they had GDM during pregnancy. This information was available during the NHANES 2007-2012, not for the NHANES 2003-2006, which oversampled pregnant women. Surprisingly, only 4 out of 35 pregnant women with GDM reported that they were diagnosed with GDM during pregnancy. A high proportion of unawareness of GDM may partially contribute to unrestricted dietary behaviors of pregnant women in this study. Lastly, FFQ would have been better to capture dietary patterns than 24-hour recalls.

In conclusion, a dietary pattern during pregnancy characterized by a high consumption of added sugars, solid fats and refined grains and low intakes of fruits and vegetables were associated with increased risks for GDM independent of an inflammatory marker, CRP. The high consumption (tertile 3) of all three dietary patterns were all significantly associated with increased risk for GDM. Prospective and cohort studies are needed to further evaluate and monitor changes in dietary patterns before and during pregnancy and its effect on the risk for GDM in consideration of GDM-related lifestyle factors such as physical activity and prepregnancy weight status.

Chapter Seven: Conclusion

7.1 Conclusion

We found three independent modifiable determinants for GDM after controlling for maternal sociodemographic characteristics and physical activity. Those are prepregnancy overweight and obesity, inadequate gestational weight gain and three dietary patterns during pregnancy. These findings are hoped to provide scientific bases to establish recommendations on diet, weight or weight gain during pregnancy in efforts to reduce the risk for GDM.

7.2 Implications

Pregnant women and women who are planning to have children are highly motivated to follow advice to improve the birth outcomes of their offspring (Zhang, 2010). Pregnancy is also a unique opportunity to learn to monitor weight, weight gains and adopting healthy dietary practices. The findings of this study indicate that GDM risks may be reduced with successful preconception and prenatal counseling that includes prepregnancy weight status, gestational weight gain, and dietary patterns during pregnancy. The specific dietary patterns identified from the study in relation to GDM risk support the use of dietary pattern approach in establishing public health recommendations for dietary prevention of GDM risk. Evidence from this study recommends increasing fruit and vegetable intake and decreasing added sugar intake during pregnancy as a means to reduce the risk for GDM.

Interestingly, we found that HEI-2010 scores of diet during pregnancy decreased with increasing prepregnancy BMI after controlling for maternal sociodemographic characteristics and physical activity during pregnancy. This indicates that prepregnancy weight status is associated with diet quality during pregnancy, and thus gestational weight gain (Institute of Medicine, 2009) and pregnancy complications and birth outcomes such as preterm labor and small- and large-for-gestational-age infants (Shin and Song, 2015). Women of prepregnancy

overweight or obesity should receive nutrition education to improve overall diet quality during pregnancy while emphasizing intake of whole fruit, whole grains, seafood and plant proteins.

The IOM Pregnancy Weight Guidelines (Institute of Medicine, 2009) are for the welfare of the infant and health of the mother. The Dietary Reference Intakes (DRIs) for pregnancy set by the Food and Nutrition Board of the IOM (Institute of Medicine, 2005) emphasize the diet quality and nutritional adequacy during each trimester of pregnancy to bring the favorable birth outcomes. Both gestational weight gain guidelines and DRIs for pregnant women aim to optimize birth outcomes and minimize pregnancy complications. This study hoped to merge these two public guidelines for pregnancy into one. In the present study, excessive gestational weight gain was inversely associated with consumption of the 'mixed' dietary pattern that was characterized by high in fruits, vegetables, meat, and dairy products.

Our findings underscore the close and independent linkage between the risk of GDM and each of modifiable determinants including prepregnancy weight status, gestational weight gain, and dietary patterns during pregnancy. Additionally, our findings show that diet during pregnancy measured by HEI-2010 and derived by factor analysis explains the relationship between prepregnancy weight status and gestational weight gain. Overall, identifying an independent role of each of modifiable determinants for GDM would help to establish systematic intervention studies in efforts to reduce GDM and its associated multigenerational health consequences in women as well as in their offspring.

7.3 Recommendations for Future Research

Continued research and efforts to reduce GDM is important for the rapid increase in the prevalence of GDM in the U.S. pregnant women (Correa et al., 2015) and the potential adverse health impact of GDM on the mother and their offspring (Langer et al., 2005; Hapo Study Cooperative Research Group et al., 2008; Vohr and Boney, 2008; Xiang et al., 2015). Through the present cross-sectional study, we uncovered the associations among prepregnancy weight

and diet quality during pregnancy as risks for GDM. These findings need to be investigated as causal–effect relations through systematic intervention studies. Further variables to be included in such intervention studies are prepregnancy weight status, gestational weight gain, diet during pregnancy and physical activity. Before initiating these intervention studies, adequately powered dose-response studies are required to evaluate the efficiency of these interventions and to define the optimal combinations of interventions (Zhang, 2010). The effectiveness of these interventions also needs to be examined in relation to both the mother and offspring's short- and long-term health consequences.

In the present study, we could not substantiate if the pregnant women received advice on gestational weight gain recommendations in relation to prepregnancy weight status, nor the level of knowledge and healthy nutrition practices during pregnancy. It is significant to identify what percentages of pregnant women receive advice from their health professionals if prenatal care included nutrition counseling or what other sources are available for them to assist for a healthy pregnancy in future research.

In a cohort of U.S. men in the Health Professionals Follow-Up Study (Mekary et al., 2012), those men who reported consuming evening snacks after dinner had higher risk for type 2 diabetes during the follow-up years compared to those who did not have evening snacks (RR 1.18; 95% CI 1.08-1.30). Snacking pattern seems to play an important role in the development of type 2 diabetes. However, little is known about the independent role of snacking patterns in relation to the risk of GDM among pregnant women. A few studies have examined the role of snacking as a component of total dietary intake or as an independent indicator in relation to the risk of GDM. Dietary pattern including both meals and snacks cannot explain the independent role of snack patterns in the development of GDM. Since snacking is significant component of the overall dietary pattern (Shin et al., 2015), differentiating dietary patterns into snack patterns can more clearly address the role of snacking behaviors in relation to GDM risk in future research.

Although we controlled for various confounding variables in the present study, we may not have included unidentified and unknown confounders. One of the potential confounders that we did not include in this study was psychological factors that are reported to influence dietary patterns during pregnancy (Hurley et al., 2005). Pregnant women with fatigue, stress, and anxiety are reported to have a higher caloric intake in general (Hurley et al., 2005). Postpartum depression is a serious mental health condition affecting 12-20% of the U.S. mothers after childbirth (Centers for Disease Control and Prevention, 2008), and women with GDM are prone to have postpartum depression after childbirth (Mautner et al., 2009). Women with depression tend to have a higher number of comorbid conditions including type 2 diabetes, thyroid problems and metabolic syndrome (Kim et al., 2015). This addresses the importance of women's psychological mental health in studying the association of dietary patterns during pregnancy with GDM risk.

A pregnancy complication, GDM was included as an outcome in the present study. For future research, not only the pregnancy complication itself, but also birth outcomes in offspring need to be considered. Recently, the presence of a male fetus has been reported to be associated with an increased risk for GDM in the mother (Retnakaran et al., 2015). In the study, pregnant women carrying a male fetus had poorer ß-cell function and thus increased risk for GDM compared to those carrying a female fetus. Hocher et al. (Hocher et al., 2011) demonstrated that fetal sex may influence on maternal total glycated hemoglobin at delivery depending on the maternal angiotensin converting enzyme polymorphism. Research on determinants of GDM, such as prepregnancy weight status, gestational weight gain and dietary patterns during pregnancy stratified by fetal sex needs to be further investigated.

In the present study, CRP levels did not differ by the presence of GDM. The relation between dietary patterns during pregnancy and GDM remained after controlling for CRP concentrations measured at pregnancy, energy intake, prepregnancy BMI, gestational weight gain, and maternal sociodemographic factors. Controlled for other inflammatory markers such

as adiponectin, interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha) before pregnancy may uncover different relations between dietary patterns during pregnancy and GDM mediated by inflammation. Hedderson et al. (Hedderson et al., 2013) reported that adiponectin measured seven years before pregnancy was significantly lower among women who developed GDM compared to those who did not. Inflammatory markers such as adiponectin, IL-6 and TNF-alpha before pregnancy may be useful in uncovering the relationship between dietary patterns during pregnancy and the risk of GDM medicated by inflammation.

This study focused on modifiable determinants for GDM while controlling for maternal age, race/ethnicity, income, education and marital status. Emerging findings suggest that serum microRNAs (miR) including miR-29a, miR-222 and miR-132 (Zhao et al., 2011) and maternal genetic factors (Tarquini et al., 2015) are associated with the risk of GDM. Many biological pathways are of importance along with modifiable determinants in the development of GDM.

In an effort to reduce the burden of GDM in the U.S., surveillance and prevention programs are important to focus on lifestyle modification before and during pregnancy for reproductive aged women and pregnant women, particularly those with high-risk factors, such as prepregnancy overweight and obesity, inadequate or excessive gestational weight gain, and unhealthy dietary patterns during pregnancy.

Much is still unknown of the determinants and their inter-relationships with regard to GDM and its subsequent short- and long-term health outcomes for the mother and offspring. Future research needs to consider both well-known and potential determinants and their relationship in the development of GDM while investigating its long-term health consequences for both the mother and offspring over the life course of women.

APPENDIX

Table A.1. Intake of added sugars in pregnant women by the status of gestational diabetes mellitus (GDM)

	GDM	No GDM	*P* value[1]
Added sugars (g)	102.4 (10.0)	88.3 (8.0)	0.27
Added sugars (% of energy)	16.7 (1.3)	14.9 (1.2)	0.33

Data are presented as mean (SEM).

[1]Based on t-test

Table A.2. Lists of foods included in the food groups of food patterns equivalent database (FPED) 2011-12 (U.S. Department of Agriculture, 2014)

#	Food Group	Food Items
1	Other starchy vegetables (excludes white potatoes)	Breadfruit, Burdock Cassava (Yuca blanca), Corn, sweet (raw), Dasheen, Green bananas, Hominy, Jicama (Yam beans), Lima beans, immature, Lotus root, Parsnips, Immature peas (e.g., immature cowpeas, blackeye peas, green peas, pigeon, peas), Plantains, Salsify, Tannier, Tapioca, Taro, Water chestnuts, Yams
2	Refined grains	Barley, pearled, Barley, pearled, flour, Barley malt flour, Bran (all grains), Corn flour or meal (degermed), Corn grits, Cream of wheat, Couscous, Farina, Masa, Oat flour (debranned), Rice (milled, not whole grain), Rice, milled, flour, Rye flour (light and medium), Semolina, Wheat flour (milled, not whole grain), Wheat germ
3	Whole grains	Amaranth, Barley, whole, Barley flour (from whole barley) Barley meal, Brown rice, Brown rice flour, Buckwheat groats, Bulgur, Corn, whole grain, Corn meal or flour (whole grain), Millett, Oats, Oat flour, Oatmeal, Popcorn, Quinoa, Rye, whole grain, Rye flour (dark), Triticale, Wheat, Whole wheat flour, Wild rice
4	Milk (includes calcium fortified soy milk)	Buttermilk, Evaporated milk, Filled milk, Milk, dry, Milk, evaporated, Milk, fluid, Goat milk, fluid, Soy milk (soymilk), calcium added
5	Other fruits	Apples, Apricots, Bananas, Cherries, Currants, Dates, Figs, Grapes, Guava, Lychees, Mangoes, Nectarines, Papayas, Passion fruits, Peaches, Pears, Persimmons, Pineapple, Plums (Ciruelas), Pomegranates, Prunes, Raisins, Rhubarb, Soursop (Guanabana), Starfruit (Carambola), Tamarind
6	Tomatoes	Tomatoes (canned, cooked, raw, stewed), Tomatoes, dried Tomato juice, Tomato paste, Tomato puree, Tomato sauce
7	Soybean products (excludes calcium fortified soy milk and mature soybeans)	Miso, Natto, Soybean curd or tofu, Soybean flour, Soybean meal, Soybean protein, isolate and concentrate, Soy milk (soymilk), not calcium fortified, Soy nuts
8	Other vegetables	Alfalfa sprouts, Artichoke, Asparagus, Avocado, Bamboo shoots, Beans (green, yellow, snap, string), Bean sprouts, Beets, Bitter melon (bitter gourd, balsam pear), Broccoflower, Brussels sprouts, Cabbage, Cactus (Nopales), Capers, Cauliflower, Celeriac, Celery, Chayote (Christophine), Chinese cabbage (Pei-tsai), Chinese okra (Luffa), Chives, Cucumber, Eggplant, Fennel bulb, Flowers, edible, Garlic, Ginger root, Horseradish pods, Jute Kohlrabi, Leeks, Lettuce (varieties not in dark green category), Mushrooms, Okra, Olives, Onions, Palm hearts, Peas, podded Peppers, bell and non-bell peppers (not red or orange in color), Pokeberry shoots, Radicchio, Radish, Rutabaga, Scallions, Seaweed, Snow peas, Sprouted beans (e.g. mung, soybean), Squash (green, sequin, spaghetti, yellow, zucchini, most summer varieties), Tomatillos, Tomatoes, green, Turnips, Winter melon

Table A.2. (cont'd)

#	Food Group	Food Items
9	Beans and peas	Black beans, Blackeye peas, Brown beans, Bayo beans, Calico beans, Carob, Chickpeas (Garbanzo beans), Cowpeas, Fava beans, Kidney beans, Lentils, Mature lima beans, Mung beans, Navy beans, Pink beans, Pinto beans, Red Mexican beans, Soybeans (mature), Split peas, White beans
10	Nuts and seeds	Almonds, Almond butter, Almond paste, Brazil nuts, Cashew, Cashew butter, Chestnuts, Flax seeds, Hazelnuts, Macadamia nuts, Peanuts, Peanut butter, Peanut flour, Pecans, Pine nuts, Pistachios, Pumpkin seeds, Squash seeds, Sesame butter (tahini), Sesame seeds, Sesame paste, Sunflower seeds, Walnuts
11	Citrus, melons, and berries	Blackberries, Blueberries, Boysenberries, Calamondin, Cantaloupe, Casaba, Cranberries, Dewberries, Grapefruit, Honeydew, Huckleberries, Juneberries, Kiwi fruit, Kumquats, Lemons, Limes, Loganberries, Mandarins, Mulberries, Oranges, Raspberries, Strawberries, Tangelos, Tangerines, Watermelon, Youngberries
12	Cheese	American cheese, Blue cheese, Brick cheese, Brie cheese, Camembert cheese, Cheddar cheese, Colby cheese, Colby Jack cheese, Cottage cheese, Cream cheese, fat free, Edam cheese, Feta cheese, Fontina cheese, Goat cheese, Gouda cheese, Gruyere cheese, Limburger cheese, Mexican cheese blend, Monterey cheese, Mozzarella cheese, Muenster cheese, Parmesan cheese, Pasteurized cheese, Port de salut cheese, Provolone cheese, Ricotta cheese, Romano cheese, Roquefort cheese, Swiss cheese, Queso anejo, Queso asadero, Queso chihuahua, Queso del pais blanco, Queso fresco
13	Oils	Almond oil, Canola oil, Corn oil, Cottonseed oil, Fish oil, Flaxseed oil, Olive oil, Peanut oil, Rapeseed oil, Safflower oil, Sesame oil, Spreads, Soybean oil, Sunflower oil, Vegetable oil, Walnut oil, Wheat germ oil
14	Solid fats	Butter, Cocoa butter, Cocoa fat, Coconut oil, Cream, Cream substitute, Cream Cheese, regular and low-fat, Fully or partially hydrogenated oils, Ghee, Lard, Palm oil, Tallow, Shortening (animal and vegetable), Sour cream
15	Fruit juice	Citrus and non-citrus fruit juices
16	Other red and orange vegetables (excludes, tomatoes)	Calabaza (Spanish pumpkin), Carrots, Carrot juice, Red colored bell, and nonball peppers, Pimiento, Pumpkin, Squash (most winter varieties), Sweet potatoes
17	Potatoes (white potatoes)	White potatoes, White potato flour, White potato flakes
18	Meat (beef, veal, pork, lamb, game)	Armadillo, Bacon (not cured), Bear, Beaver, Beef, Bison, Caribou, Game meat (other), Goat, Ground hog, Ham (not cured), Lamb, Moose, Opossum, Oxtail, Pork, Rabbit, Raccoon, Squirrel, Veal, Venison, Wild pig

Table A.2. (cont'd)

#	Food Group	Food Items
19	Dark green vegetables	Arugula, Basil, Beet greens, Bitter melon leaves, Broccoli, Broccoli raab, Chinese Cabbage (Pak-choi), Chrysanthemum garland, Chard, Chicory leaves, Cilantro (Coriander), Collards, Cress, Dandelion greens, Endive, Escarole, Greens, Horseradish leaves, Kale, Lambsquarters, Leaves of grapes pumpkin, squash, sweet potato, swamp cabbage, taro, and thistle, Lettuce (Boston, butterhead, green or red leaf, cos or romaine), Mustard cabbage, Mustard greens, Parsley, Poke greens, Spinach, Turnip greens, Watercress
20	Added sugars	Brown Sugar, Cane syrup, Confectioners' sugar, Corn Syrups, Corn syrup solids, Dextrose, Fructose, Fruit juice concentrates, Fruit syrups, Granulated sugar, Honey, Maple syrup, Molasses, Pancake syrups, Powdered sugar, Raw sugar, Sorghum syrups, White sugar (cane and beet)
21	Alcoholic drinks	Beer, Wine, Distilled spirits, Alcohol (ethanol) present in cocktails and other alcoholic beverages, Alcohol (ethanol) added to foods after cooking
22	Organ meat (from beef, veal, pork, lamb, game, poultry)	Brain, Chitterlings, Giblets, Gizzard, Heart, Kidney, Liver, Stomach, Sweetbreads, Thymus, Tongue, Tripe
23	Cured meat (frankfurters, sausage, corned beef, cured ham and luncheon meat made from beef, pork, poultry)	Bacon, Beef sausage, Beef luncheon meat, Blood sausage, Bockwurst, Bologna, Bratwurst, Braunschweiger, Capicola, Cervelat, Chicken sticks, Chicken luncheon meat, Chicken or turkey loaf, Chorizo, Cold cut deli meat, Corned beef, Chipped beef, Dutch brand loaf, Frankfurters, Ham (cured, smoked, deli, deviled, loaf, luncheon meat, minced), Head cheese, Honey loaf, Hotdogs, Italian sausage, Jerky (all meat types), Kielbasa, Knockwurst, Liverwurst, Meat spreads, Meat sticks, Mettwurst, Mortadella, Pastrami, Pepperoni, Pepper loaf, Polish sausage, Pork luncheon meat, Pork sausage, Potted meats, Salami, Sandwich loaf, Souse, Thuringer, Turkey luncheon meat, Turkey sausage, Turkey, smoked, Turkey sticks, Veal loaf, Vienna sausage
24	Seafood low in n-3 fatty acids	Abalone, Carp, Catfish, Clams, Cod, Crab, Crayfish, Croaker, Eel, Flounder, Frog legs, Haddock, Halibut, Lobster, Mullet, Mussels, Ocean perch, Octopus, Oyster, Perch, Pike, Pollock, Porgy, Scallop, Scup, Shrimp, Snail, Snapper, Sole, Squid, Sturgeon, Tilapia, Tuna (excludes albacore & bluefin), Turtle, Whitefish, Whiting
25	Eggs	Eggs, whole (chicken, duck, goose, quail, and other birds), Egg white, Egg yolk, Egg substitute, Egg, dried
26	Poultry (chicken, turkey, other fowl)	Chicken, Cornish game hen, Dove, Duck, Goose, Ostrich, Pheasant, Quail, Turkey
27	Seafood high in n-3 fatty acids	Anchovy, Barracuda, Caviar (Roe), Cisco, Herring, Mackerel, Pompano, Ray, Salmon, Sardine, Sea bass, Shad, Shark, Swordfish, Trout, Tuna (albacore & bluefin)
28	Yogurt	Includes yogurt of all fat-types and yogurt present in flavored and frozen yogurt

Table A.3. The Healthy Eating Index (HEI)-2010 scores by gestational weight gain groups (n=640)

HEI-2010 and its components	Adequacy of Gestational Weight Gain				
	Max. Points	Inadequate (n=187)	Adequate (n=134)	Excessive (n=319)	*P* trend
Overall HEI-2010	100	47.9 ± 2.0	55.0 ± 3.3	50.8 ± 1.4	0.479
Total Vegetables	5	3.1 ± 0.2	3.4 ± 0.2	2.9 ± 0.1	0.271
Greens and Beans	5	1.5 ± 0.3	1.2 ± 0.3	1.7 ± 0.3	0.453
Total Fruit	5	2.7 ± 0.3	2.9 ± 0.3	3.0 ± 0.2	0.401
Whole Fruit	5	2.2 ± 0.3	2.7 ± 0.3	2.7 ± 0.2	0.185
Whole Grains	10	1.5 ± 0.3[a]	2.9 ± 0.7[ab]	2.5 ± 0.3[bc]	0.068
Dairy	10	6.3 ± 0.5	5.7 ± 0.6	6.7 ± 0.3	0.410
Total Protein Foods	5	3.9 ± 0.2	4.3 ± 0.2	3.9 ± 0.1	0.675
Seafood and Plant Proteins	5	1.5 ± 0.2	2.2 ± 0.4	1.7 ± 0.2	0.797
Fatty Acids	10	3.4 ± 0.4	5.2 ± 0.7	3.3 ± 0.4	0.410
Sodium	10	5.1 ± 0.4	4.8 ± 0.7	5.6 ± 0.3	0.276
Refined Grains	10	5.8 ± 0.4	5.8 ± 0.5	5.7 ± 0.3	0.930
Empty Calories	20	11.0 ± 0.7[ab]	13.9 ± 0.9[b]	11.1 ± 0.6[a]	0.616

[1] Values are weighted mean ± SEM. Labeled means in a row without a common letter differ, *P*<0.0167 (Bonferroni-adjusted P < 0.0125).

Table A.4. Odds ratios for gaining inadequate or excessive gestational weight gain by diet quality measured by the Healthy Eating Index (HEI)-2010 during pregnancy

	Excessive vs. Adequate Gestational Weight Gain (reference)			Inadequate vs. Adequate Gestational Weight Gain (reference)		
HEI-2010	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Tertile 1	1.00	1.00	1.00	1.00	1.00	1.00
Tertile 2	0.89 (0.22-3.60)	1.07 (0.32-3.58)	2.19 (0.45-10.78)	0.45 (0.14-1.48)	0.53 (0.17-1.67)	1.40 (0.26-7.70)
Tertile 3	0.73 (0.20-2.72)	0.81 (0.19-3.50)	0.78 (0.13-4.75)	0.99 (0.26-3.82)	1.07 (0.25-4.58)	1.41 (0.23-8.71)

Model 1: Crude association between HEI-2010 and gestational weight gain

Model 2: Adjusted for age, race/ethnicity, family poverty income ratio, education level, and marital status

Model 3: Adjusted for model 2 + physical activity level

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