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Gestational Weight Gain, Pregnancy Outcomes, and Use of Perinatal Health Services

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DEDICATION

To my dear Dad and Mom, my husband, Shuqun, and all my friends.

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ABSTRACT

This dissertation consists of three studies that were undertaken to better understand 1) the role of gestational weight gain (GWG) during early pregnancy on subsequent blood pressure changes and the risk of pregnancy-induced hypertension (PIH), 2) the causal effect of GWG in both early and mid-late pregnancy on the subtypes of preterm births, and 3) the impact of personal capital on the use of perinatal health services (i.e., prenatal care use and preconception care counseling). The first two studies were based on the data from the 1988 National Maternal and Infant Health Survey and the third study employed the data from the 2007 and 2010 Los Angeles Mommy and Baby Survey. In the first study, the latent class growth model revealed four trajectories of GWG in early pregnancy. Then using linear mix model as well as generalized equation method, we found women with high growth trajectory of GWG during early pregnancy had higher blood pressure and in higher risk of PIH . In the second study, using marginal structure models we found that among women who were in normal body mass index before pregnancy, both inadequate and excessive GWGs in mid-late pregnancy were associated the increased odds of spontaneous preterm births, while excessive GWG in mid-late pregnancy increased the odds of medically indicated preterm births. Among women who were overweight or obese before pregnancy, those with inadequate weight gain in early pregnancy were protected from medically indicated preterm births. In the third study, using multilevel analysis, we found that higher personal capital was associated with higher odds of receiving preconception counseling among Whites and

Asians and was negatively associated with late prenatal care initiation among Hispanics, Blacks and Asians. Sub-components such as internal resources, partner support, social support and neighborhood supported were associated differently with the utilization of perinatal health services among racial groups. In conclusion, appropriate weight gain in pregnancy holds promise to reduce the risks of PIH and preterm births and to increase personal capital can be an effective strategy to improve women's use of perinatal health services.

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CHAPTER 1

INTRODUCTION

This dissertation focused on pregnancy health and health service delivery for pregnant women. It consisted of three studies. Studies 1 and 2 examined the impacts of gestational weight gain (GWG) on the development of hypertensive disorders and the delivery of preterm infants (< 37 weeks of gestation), respectively. Study 3 investigated the roles of personal capital on the receipt of perinatal health services (i.e., preconception counseling and prenatal care).

There are six chapters in this dissertation. Chapter 1 gave a brief introduction of problems to be addressed in this dissertation and discussed the overall significance for the dissertation. Chapter 2 summarized the literature in related areas in details and illustrated the research gaps in existed studies. Chapter 3 laid out specific aims and research questions. Chapter 4 further outlined study methodology, including a description of study population, data sources, key measurements, and statistical analysis plans for each of the three studies. Chapters 5 through 7 presented results for Studies 1-3 in manuscript format. That is, each chapter included the sections of each study such as background, methods, results, discussions, and conclusions. Finally, Chapter 8 summarized key findings from three studies, their implications and limitations, areas for future studies, and concluding statements for the dissertation.

Statement of the problem

Improving maternal and child health is one of the eight Millennium Development Goals. (Hogan et al. 2010) *Healthy People 2020* also listed thirty three objectives, aiming to reduce women, infant and child mortality and morbidity and improve their health and health care services in the United States (U.S.). (US Department of Health Human Services 2011) However, to date, there are still nearly one third of pregnancies being affected by some types of perinatal complications such as pregnancy-induced hypertension (PIH), and preterm delivery. (Berg et al. 2010) Those pregnancy or delivery complications resulted in about 650 women died each year (Berg et al. 2010) and over 40% of neonatal deaths (Heron 2012; Martin et al. 2013).

Hypertensive disorders and preterm delivery are major adverse pregnancy outcomes. Hypertensive disorders, as the most frequent cardiovascular events during pregnancy, occurred in about 10% of all pregnancies. (Steegers et al. 2010; Hutcheon et al. 2012) PIH, the most frequent type of hypertensive disorders during pregnancy, has increased 1.8 times from 1987 to 2004. (Wallis et al. 2008) It has become a leading cause of maternal and fetal mortality affecting about 5% to 7% of all pregnancies. (Lindheirmer et al. 2009) Preterm birth is another major cause of neonatal morbidity and mortality, and has long-term adverse consequences on the health of survived infants. (Lawn et al. 2005; Kaempf et al. 2006; Morgan et al. 2008; Saigal and Doyle 2008) Reports showed that about one out of every eight infants in the U.S. was delivered preterm, and caring for those preterm births incurs enormous health care expenditures. (Martin JA et al. 2012; American College of Obstetricians and Gynecologists 2013; Martin et al. 2013) Thus, effective strategies are needed to prevent those adverse pregnancy outcomes.

Racial disparities in maternal and child health have become another serious public health concerns. In all, minorities suffer disproportionately by the burden of diseases and experience higher rates of mortality(Centers for Disease Control 2007). Approximately 83,000 preventable deaths occur each year as a result of racial disparities, including high infant mortality rates. (Suthers 2008) The infant mortality rate for Blacks is 2.4 times the rate of non-Hispanic White women. The leading cause of infant mortality is low birth weight, which Black women have a 3-4 times higher risk than Whites. (Mathews and MacDorman 2011) Although racial disparities in infant mortality and low birth weight are evident, their root causes are complex and varies among different communities. In addition to the disparities in infants, minority women were also reported to experience worse health outcomes and poorer quality of health care compared to non-Hispanic White women.(Derose and Baker 2000; Nelson 2002; Cohen and Christakis 2006) For example, Black community faced higher rates of maternal mortality and maternal depression, (Johnson and Theberge 2007) and were more likely to have gestational diabetes and hypertension, however, they were found with high rate of smoking cessation during pregnancy. Regarding health care, according to a 2007 study by the Kaiser Family Foundation, about 23% of all minority women receive late or no prenatal care services, compared to 11% of White women. (The Henry J. Kaiser Family Foundation 2009) Lastly, health disparities brought severe economic consequences for society and the healthcare system. A 2009 study found that $229.4 billion in direct medical costs and another $1.24 trillion in indirect costs such as loss of wages and work productivity between 2003 and 2006 were associated with health inequalities.(LaVeist et al. 2009) An estimated 30 percent of direct medical care expenditures for African-American, Asians, and Hispanic were excess costs due to health inequalities. Thus, effective strategies are urgently needed to eliminate racial disparities in health and to reduce medical care costs associated with racial disparities.

This dissertation had two major themes: 1) to examine the association of GWG, a modifiable predictor, on those adverse pregnancy outcomes, which can be useful in designing effective interventions to improve pregnant outcomes, and 2) to investigate the role of personal capital, a group of social determinants, in perinatal health services use, which can be used to deliver better health care to all women in need. The new knowledge in these areas is important as they can be used to improve the health of women, infants and children and to reduce racial disparities in maternal and child health outcomes.

Significance of the dissertation

Study #1

The current literature has shown the high prevalence of PIH. (Lindheirmer et al. 2009; Steegers et al. 2010; Hutcheon et al. 2012) However, there is no effective treatment for it, thus preventing the risk of PIH is essential. Managing weight in proper range is an important strategy to control blood pressure. (Abrams and Selvin 1995; Thadhani et al. 1999; Thorsdottir et al. 2002; Brennand et al. 2005; Duckitt and Harrington 2005; Jensen et al. 2005; DeVader et al. 2007; Crane et al. 2009; Poon et al. 2009; Beyerlein et al. 2011; Gaillard et al. 2011; Heude et al. 2012; Thangaratinam et al. 2012; Gaillard et al. 2013; Li et al. 2013; Macdonald-Wallis et al. 2013) Pregnancy provides a “teachable moment” for weight management intervention,(Phelan 2010) as women are more care about their health condition during pregnancy. Early pregnancy (i.e., before 20 weeks gestation) is a potential window for preventing PIH, because substantial blood pressure rise occurs after 20 weeks' gestation. This study was the first to investigate the GWG trajectory during early pregnancy and associate it with subsequent blood pressure changes and risk of PIH. Results will provide scientific evidence to design weight management intervention.

Study #2

This study shed a light for dealing with time-dependent exposure and managing intermediators in perinatal studies. Results provided accurate estimation of the casual effect of GWG in both early and mid-late pregnancy on subtypes of preterm births, explaining the inconsistent findings in previous studies and suggesting that weight management during pregnancy hold promise to reduce preterm births. By applying causal inference via Marginal Structure Models to estimate the causal effect, it helped to reduce the costs and ethical concerns usually seen in randomized clinical trials, which may become useful strategy in future epidemiological studies.

Study #3

Approximately one million women did not enter into prenatal care in the first trimester of pregnancy (U.S. Department of Health and Human Services et al. 2013) and very low prevalence of preconception counseling were received by a small proportion of women in child-bearing ages (Williams et al. 2012). Meanwhile, racial disparities existed in the use of those perinatal health services. Personal capital is a composite structure, which evaluates one's internal and external resources. It was hypothesized to be associated with multiple birth outcomes. Our study was the first to associate the racial-specific personal capital with perinatal health services use. Results were useful in understanding the role of personal and social resources on promoting health care utilization, and being suggestive for improving public health intervention strategies, which will finally contribute to improving maternal and child health outcomes.

CHAPTER 2

LITERATURE REVIEW

Gestational weight gain (GWG)

Recommendations for GWG

The amount of weight gained during pregnancy, which is attributed by the expansion of maternal tissues, fetal and placental growth and amniotic fluid accumulation (Neufeld et al. 2004), can largely affect the immediate and future health of a woman and her infant.

Since the 1950s, recommendations for pregnancy weight gain have been highly controversial in the U.S. During the first half of the last century, American obstetricians restricted weight gain during pregnancy to prevent toxemia, difficult births, and maternal obesity. (Eastman N and Helloman L 1966; Schoendorf et al. 1992; Beck et al. 2002) The recommendation was challenged in the 1960s, when experts began to recognize that the relatively high rates of infant mortality, disability, and mental retardation seen in the U.S. were a function of low birth weight.(Abrams et al. 2000) In the 1970s, with scientificevidence supporting that the usual practice of restricting maternal weigh gain was associated with increased risk of low birth weight, the recommended amount of weight gain was lifted again.(Eastman N and Helloman L 1966) As the result, in the following years, there was an average increase of three kilograms and 150 grams on pregnancy weight gain and infant birth weight, respectively.(Abrams 1994)

Those significant increases and its related impact on various maternal and fetal outcomes attracted attention from researchers, leading to the new guidelines of GWG published by the Institute of Medicine (IOM) in 1990. Specifically, a gain of 12.5-18 kg, 11.5-16 kg, and 7.0-11.5 kg is recommended for pregnant women who have a low prepregnancy BMI (i.e., <19.8), normal prepregnancy BMI (i.e., 19.8-26.0), and high prepregnancy BMI (i.e., >26.0-29.0), respectively.(National Research Council 1970) The appropriateness of this recommendation was supported by many studies in the almost 10 years since it was published, such as women who gained weight within this IOM's recommendations experienced better birth outcomes than women who did not.(Carmichael et al. 1997) However, with lifestyle changed in the past 20 years, obesity has become a public health crisis in the U.S. For instance, In 1995 over 50% of the U.S. adult population were overweight or obese. Now the prevalence of excessive weight (i.e. BMI$\geq$25 kg/m^2) has risen to approximate 70%.(Institute of Medicine (Subcommittees on Nutritional Status and Weight Gain During Pregnancy and Dietary Intake and Nutrient Supplements During Pregnancy 1990) Accompanying with the obesity epidemic, more than half of women gained excessive weight during pregnancy.(Abrams et al. 2000; Davis et al. 2012) As the result, women become more at risk for developing pregnancy complications and led to increased morbidity in the year after childbearing life events.(Institute of Medicine(IOM) and National Research Council(NRC) 2009) Thus, in 2009, the IOM released new guidelines for weight gain during pregnancy. (Table 2.1) The new recommendation changed in two ways from 1990's recommendation. First, the cutoff points for the BMI categories were set based on World Health Organization (WHO)'s cut off points (i.e., underweight [<18.5], normal weight [18.5–24.9], overweight [25.0–29.9], and obese

[≥30]). Second, upper limit was added for obese women. In terms of the trajectory, weight gain follows a sigmoidal growth with low rate in first trimester and increased rate in second and third trimester. (Yaktine and Rasmussen 2009) The 2009 committees established this recommendation refer to a large body of literatures; however, the appropriateness of this recommendation was still controversial. Specifically, the growth trajectories of GWG and its correlates were unclear and the associations with pregnancy outcomes needed more studies to evaluate and establish.

Table 2.1 New recommendations for total and rate of weight gain during pregnancy, by prepregnancy BMI

	Total Weight Gain		Rates of Weight Gain† 2nd and 3rd Trimester	
Prepregnancy BMI	Range in kg	Range in lbs	Mean (range) in kg/week	Mean (range) in lbs/week
Underweight (< 18.5 kg/m^2)	12.5–18.0	28.0–40.0	0.5 (0.4–0.6)	1.0 (1.0–1.3)
Normal weight (18.5–24.9 kg/m^2)	11.5–16.0	25.0–35.0	0.4 (0.4–0.5)	1.0 (0.8–1.0)
Overweight (25.0–29.9 kg/m^2)	7.0–11.5	15.0–25.0	0.3 (0.2–0.3)	0.6 (0.5–0.7)
Obese (≥ 30.0 kg/m^2)	5.0–9.0	11.0–20.0	0.2 (0.2–0.3)	0.5 (0.4–0.6)

†Calculations assume a 0.5–2 kg (1.1–4.4 lbs) weight gain in the first trimester
Source: *Weight Gain During Pregnancy: Reexamining the Guidelines*, K.M. Rasmussen and A.L. Yaktine, Editors. 2009: Washington (DC).

GWG measurements

Three ways were frequently used to measure the GWG, that are total weight gain at delivery, rate of weight gain, and adequacy ratio of weight gain that related to IOM guidelines.(Hutcheon et al. 2012) Those traditional methods have its intrinsic limitations that may bias results. Total weight gain at delivery is clearly correlated with GA at delivery because women who deliver at earlier gestation do not have as much time to gain weight as women who deliver at later GA. The measure of average rate of weight gain would be appropriate if the rate of weight gain was constant throughout gestation. However, GWG follows a pattern of minimal weight gain in the first trimester and linear growth in the second and third trimesters. (Figure 2.1) This means that the measure of average rate of GWG becomes positively correlated with GA at delivery. For example, a woman on a steady, healthy weight gain trajectory will have a lower average rate of GWG if she delivers at 28 weeks than if she continues along the same trajectory but delivers at 40 weeks. The third commonly used method, IOM GWG adequacy ratio does not rely on the assumption that weight gain is linear throughout pregnancy, but it limited in its own assumption that of healthy pregnancy BMI gain 2kg in the first trimester. However, if the average weight gain in the first trimester is higher than this amount, the adequacy ratio will become negatively associated with GA, with the weight above 2kg averaged over a shorter period of time for women delivering at younger GAs. Also, as estimates of the average weight gain in the first trimester are all based on data of weight gain patters from the mid-late 1980(Siega-Riz et al. 1994; Carmichael et al. 1997; Fraser et al. 2010), the validity of this assumption in contemporary cohorts of pregnant women may be questionable. (Hutcheon et al. 2012)

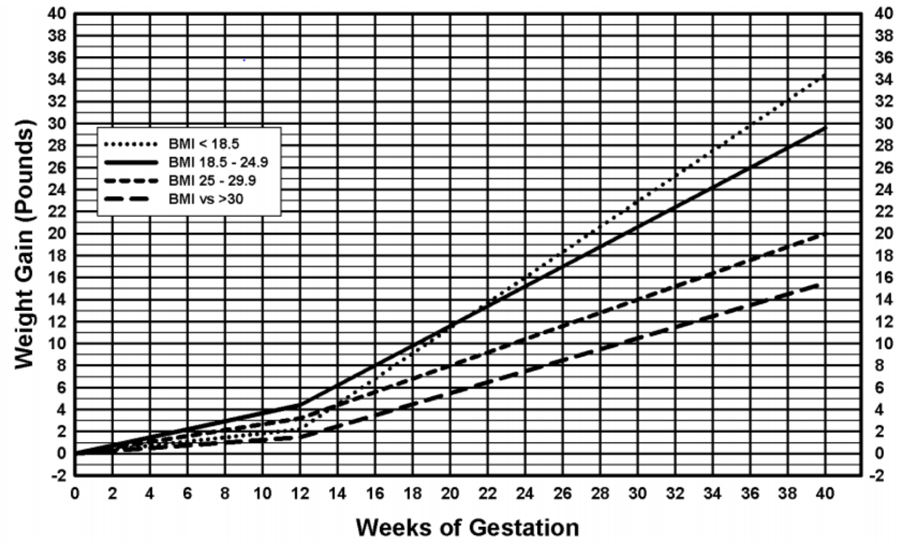

Figure 2.1 Recommended weight gain by week of pregnancy by prepregnacy BMI status. Sources: *Weight Gain During Pregnancy: Reexamining the Guidelines*, K.M. Rasmussen and A.L. Yaktine, Editors. 2009: Washington (DC); Diabetes-pregnancy.ca website http://diabetes-pregnancy.ca/weight-gain/

Trajectory of GWG

The trajectory of GWG depicts a dynamic weight changes during pregnancy. It is well-accepted that the best way to describe this process was to collect series weight gain data by weighing all pregnant women in a representative community at frequent intervals from their conception till delivery.(American College of Obstetricians and Gynecologists and Pediatrics 2002) With statistical analyzed approaches developing in the last decades, the result was available from relatively small samples with less data. Dawes et al in 1991(Dawes and Grudzinskas 1991) and Abrams et al in 1995 and 1996 (Abrams et al. 1995; Abrams and Selvin 1995) generated weight did not increase linearly and reported a wide variation of GWG was seen in women with different characteristics. Carmichael et al in 1997 (Carmichael et al. 1997) describes the pattern of GWG in women with good pregnancy outcomes and found trimester rats of gain varied by BMI category and exceeded IOM guidelines in all groups. Although these earlier studies often named their measurement of GWG as pattern, most of them described trimesters' changes. Then, in the following years, studies started to use repeated measurements in regression models to predict the mean changes of weight gain during pregnancy,(Macdonald-Wallis et al. 2013) which illustrated a true growth trajectory of GWG. In 2013, Hutcheon et al proposed a z-score chart for assessing GWG in pregnancy.(Hutcheon et al. 2013) This method, on one hand, accounted for the nonlinear shape of growth trajectories throughout gestation, and on the other hand, by using z-score and percentiles rather than ratio, it made less prone to bias and solved difficulties in interpretations due to nonlinearity, because their statistical characteristic. (Allison et al. 1995) In conclusion, to date, GWG was generated as a sigmoidal growth with relatively low rate at first trimester and fast rate at second and third trimester.(Institute of Medicine(IOM) and National Research Council(NRC) 2009)

GWG trajectory and health outcomes

As pointed in 2009 IOM guidelines, both excessive and inadequate GWG were responsible for complications during pregnancy and adverse birth outcomes, such as gestational induced-hypertension, gestational diabetes (GDM), preterm delivery and perinatal mortality.(Abrams et al. 1989; Crane et al. 2009; Gaillard et al. 2011) However, the specific results were inconsistent as to that reported in each outcome. (Abrams and Selvin 1995; Thorsdottir et al. 2002; Brennand et al. 2005; Jensen et al. 2005; DeVader et al. 2007; Crane et al. 2009; Beyerlein et al. 2011; Gaillard et al. 2011; Heude et al. 2012; Thangaratinam et al. 2012; Gaillard et al. 2013; Li et al. 2013; Macdonald-Wallis et al. 2013) As discussed above, traditional measures of GWG may be inappropriate to examine certain associations.(Hutcheon et al. 2012) The trajectory of GWG, which is advanced in depicting the instant rate of weight gain during pregnancy, was recommended by researchers in such topics. However, due to the data and statistical restriction, few studies have indeed related this accurate measurement with pregnancy outcomes. Studies were limited in depicting the rough picture of average weight gain in trimesters, (Hediger et al. 1989; Hickey et al. 1996; Carmichael et al. 1997) or investigating the correlates of GWG patterns and its association with pregnancy outcomes in particular sampled women. (Hood et al. 2007; Hutcheon et al. 2013) These trajectories with arbitrary criteria might be problematic as the selection on such women introduces distortion of results, and therefore cause an inaccurate estimation of the effect between GWG and health outcomes and misunderstood of correlates as well.

Correlates of the trajectories of GWG

Maternal age, and race, parity and prepregnancy BMI status were important predictors for predicting cumulative weight gain during pregnancy.(Abrams et al. 1995; Hickey et al. 1996; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Nohr et al. 2009) In the Abrams et al (Abrams et al. 1995) study, older women were reported to gained more weight during the first trimester and less during the second and third. Hispanic gained faster during the second trimester than other racial groups. In the Hicker et al (Hickey et al. 1996) study, they reported a higher increase in the first trimester and lower increase in the second trimester among non-Hispanic Black Americans. This finding was also reflected in the Misar et al (Maryland Department of Health and Mental Hygiene Center for Maternal and Child Health and Vital Statistics

Adminstration 2013) study, that African-Americans have higher rate of weight gain from preconception period to 16-20weeks gestation than Non-African-Americans. In second and third trimester, nulliparous mother were more likely to gain excessive weight than multiparous mothers, while cigarette smokers gained less than non-smokers.(Billewicz and Thomson 1957; Abrams et al. 1995) Although a large body of literature suggested that GWG varied by maternal characteristics, a recent published article by Lisa et al (Bodnar et al. 2011) revealed a useless of tailoring GWG guidelines by those characteristics. They examined the role of GWG with different maternal characteristics on pregnancy outcomes and identified no differences. The uncertain effects of maternal characteristics on GWG were also mentioned in 2009 IOM guidelines, that the committees suggested calling for more studies to fulfill the research gap in detailing the interacted effects between maternal characteristics and the trajectory of GWG on health outcomes.(Institute of Medicine(IOM) and National Research Council(NRC) 2009)

Pregnancy complications

So far the literatures on the health impacts of GWG have mainly focused on gestational diabetes, birth weight, and its linkage with childhood obesity.(Abrams et al. 1989; Hediger et al. 1989; Abrams et al. 1995; Viswanathan et al. 2008; Magriples et al. 2013) Limited studies have investigated the relationship between GWG and maternal blood pressure changes during pregnancy and preterm delivery. However, as PIH is the most common medical complication of pregnancy and preterm delivery is the leading cause of perinatal morbidity and mortality (Peters and Flack 2004; Steegers et al. 2010; Luton et al. 2014), it is critical to understand the role of GWG on those health outcomes.

Specifically, studies needed to answer the questions “What is the most appropriate trajectory of GWG?”, “How is the trajectory of GWG impact PIH and preterm birth”, “Is there any preventive periods during pregnancy can help to lower the risk of PIH and preterm birth?”, “Does early abnormal GWG predict subsequent PIH and preterm birth?” and “Is GWG associated with blood pressure change and duration of gestation?” and so on.(Martin JA et al. 2012)

Normal blood pressure change during pregnancy

Blood pressure (BP), is summarized by two measurements, systolic and diastolic, which depend on whether the heart muscle is contracting (systolic) or relaxed between beats (diastolic). Normal blood pressure at rest is within the range of 100-140mmHg systolic and 60-90mmHg diastolic. During pregnancy, blood pressure falls during first trimester and second trimester, and be at its lowest in mid-pregnancy and starts to rise gradually again from 24 weeks pregnant. Finally, if all is well, the blood pressure will return to its pre-pregnancy levels in the last few weeks before your baby is born. (National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy 2000; James et al. 2014)

Hypertensive disorders

In 2000, the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy defined four categories of hypertension in pregnancy: Chronic hypertension, PIH, preeclampsia, and preeclampsia superimposed on chronic hypertension.(Page and Christianson 1976; American College of Obstetricians and Gynecologists 2013) Chronic hypertension is defined as a blood pressure measurement elevated to or above 140/90 mmHg on two occasions before 20 weeks of gestation or persisting beyond 12 weeks postpartum. PIH is defined when a pregnant women develop hypertension (same definition as chronic hypertension) without proteinuria after 20 weeks of gestation. Originally, this hypertension during pregnancy was considered as a temporal blood pressure elevation. However, this disorder is now believed to associate with essential hypertension in the later lives of these women.(Rahman et al. 2008) It may represent an early phase of pre-eclampsia, in which proteinuria has not yet appeared. One study showed that around 50% of women diagnosed with PIH between 24 and 35 weeks develop preeclampsia.(Barton et al. 2001)

Preeclampsia is a multi-organ disease process of unknown etiology, which is characterized by the development of hypertension (same definition as chronic hypertension) and proteinuria after 20 weeks of gestation. Severe preeclampsia increases the risk of developing eclamptic seizure, which may appear also unexpectedly in patient with minimally elevated blood pressure and no proteinuria.

Epidemiology of hypertensive disorders

Hypertensive disorders are the most frequent cardiovascular events during pregnancy, occurring in about 10% of all pregnancies.(Peters and Flack 2004; Steegers et al. 2010) Each type of hypertensive disorders carries risks for both women and their babies, resulting in substantial maternal morbidity and perinatal mortality.(Nochy et al. 1980; Barton et al. 2001; Rahman et al. 2008; Ye et al. 2010; Adane et al. 2014) PIH increased significantly from 1987-2004 (by 185%).(Lindheirmer et al. 2009) To date, it has becoming a leading cause of maternal fetal mortality, threatening about 5% to 7% of all pregnancies.(Wallis et al. 2008) PIH was also reported to associate with adverse birth outcomes such as stillbirth, low birth weight baby, and preterm birth, due to insufficient blood supply to placenta.(Nochy et al. 1980; Ye et al. 2010; Adane et al. 2014)

Association between GWG and pregnancy induced-hypertension

Although it is possible that aforementioned fast increases in the prevalence of PIH was due to the revision of clinical guidelines published in 1990s, which reduced diagnostic of preeclampsia, many studies have demonstrated that this tremendous increase was attributed by the increased maternal obesity and abnormal GWG. High prepregnancy BMI has been well-established to associate with increased risk for PIH during pregnancy.(Thadhani et al. 1999; Duckitt and Harrington 2005; Poon et al. 2009) It is reported that nearly two thirds of reproductive-aged women in U.S. are currently over-weighted or obese, and these women are in high risk of developing hypertensive disorders.(Thadhani et al. 1999; Poon et al. 2009; Flegal et al. 2010; Shaikh et al. 2010) GWG is another potentially modifiable risk factor of PIH during pregnancy. Yet existing studies are inconclusive about the association between GWG and PIH.(Abrams and Selvin 1995; Thorsdottir et al. 2002; Brennand et al. 2005; Jensen et al. 2005; DeVader et al. 2007; Crane et al. 2009; Beyerlein et al. 2011; Gaillard et al. 2011; Heude et al. 2012; Thangaratinam et al. 2012; Gaillard et al. 2013; Li et al. 2013; Macdonald-Wallis et al. 2013) A retrospective cohort study reported that gestational weight loss was associated with the decreased risk of PIH,(Parks et al. 2013) while excessive total weight gain and high rate of weight gain during pregnancy were positively correlated to increased risk of PIH.(Thomson et al. 1967; Gaillard et al. 2011; Heude et al. 2012) It is worth noting that, although these studies indicate GWG is an important predictor, their methodology may be issued. Specifically, women who develop hypertension during pregnancy are more likely to experience edema during late pregnancy than those who remain in normotension. As the result, the hypertensive women may gain much more GWG.(Cnattingius et al. 2013) Therefore, analysis on total weight gain or weight gain in late weeks during pregnancy may exaggerate the association. Two European studies overcame the limitations (Martin JA et al. 2012; Gaillard et al. 2013), particularly in Macdonald-Wallis et al. study, which examined repeated antenatal clinic measurements of weight and blood pressure. They suggested that GWG at early pregnancy affected subsequent blood pressure changes and GWG at any pregnant period were positively associated with concurrent blood pressure change.(Martin JA et al. 2012) However, they did not account for the potential non-linear increasing trend during early stage of pregnancy and did not consider the effect of GWG during late pregnancy when examined the effect of GWG during early pregnancy.(Institute of Medicine(IOM) and National Research Council(NRC) 2009) Also, both studies were conducted in European countries, therefore the results may not be generalizable to the U.S. population, due to different racial composition and different trends and prevalence in prepregnancy obesity, PIH, and excessive GWG.

Defining preterm birth

Preterm birth is the birth of a baby less than 37 weeks GA. It can be further categorized into: extremely preterm birth (22-27 weeks of gestation), very preterm birth (28-31 weeks of gestation), and moderately (32-36 weeks of gestation). Preterm birth can be the result of three obstetrical circumstances: 1) preterm labor with intact membranes;

2) preterm pre-labor rupture of membranes; and 3) medically indicated preterm birth, which occurs when maternal or fetal indications require delivery before 37 weeks of gestation. The first and second subtypes often combined named as spontaneous preterm birth.(Institute of Medicine (IOM) 2007)

Epidemiology of preterm birth

Preterm birth is a major cause of neonatal morbidity and mortality and has long-term adverse consequences on the health of survived infants.(Lawn et al. 2005; Kaempf et al. 2006; Morgan et al. 2008; Saigal and Doyle 2008) The prevalence of preterm birth increased during the past 20 years (20% since 1990 and nine percent since 2000), and reports showed that about one out of every nine infants in the U.S. was delivered preterm and caring for those preterm births incurs large health care expenditures.(Martin JA et al. 2012; American College of Obstetricians and Gynecologists 2013; Martin et al. 2013) The increase of preterm birth can be partly explained by the increased rate of cesarean deliveries, as majority of increase occurred in the moderate preterm births.(Caughey et al. 2014) However, the medical intervention cannot cover all aspects. Further studies are needed to investigate the reasons for the persistent high rate of preterm births.

Association between GWG and preterm birth

Both prepregnancy BMI and GWG are potential modifiable risk factors for preterm births. The overall opinion was prepregancy BMI and excessive GWG interactively impacted on preterm birth.(American Academy of Pediatrics and The American college of Obstetricians and Gynecologists 2002) Studies showed a U-shaped association, which meant for those women who were underweight with low GWG and those overweight/obese with high GWG, their risks of preterm birth were higher.(Berkowitz and Papiernik 1993; Savitz et al. 2011; Masho et al. 2013) Yet, the association between GWG and preterm births was not very clear. One of the underlying reasons was the unspecified subtypes of preterm births in previous studies, which occurred under different pathophysiological mechanisms.(Savitz 2008) Existed findings showed prepregnancy BMI (i.e., underweight, overweight and obese) was a risk factor for all types of preterm births,(American Academy of Pediatrics and The American college of Obstetricians and Gynecologists 2002) and illustrated a strong association between excessive GWG and an increased risk of medically indicated preterm births via cesarean delivery.(Berkowitz et al. 1998; Rudra et al. 2008; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Wise et al. 2010; Gawade et al. 2011) However, effects of inadequate GWG on both spontaneous and medically indicated preterm births were unclear.(Hickey et al. 1995; Carnero et al. 2012; Gaillard et al. 2013; Macdonald-Wallis et al. 2013; Masho et al. 2013; Fujiwara et al. 2014; Park et al. 2014) Next, it is uncertain about how GWG impacted preterm births. As weight gain changes while pregnancy processes, it is interesting to know which period has the strongest effect, which become a potential period for health interventions. Few previous studies used rate of weight gain considered the trimesters' effects, which showed excessive GWG in the second and third trimester has a stronger effect than the first trimester on preterm births. (Hickey et al. 1995; Rudra et al. 2008; Wise et al. 2010) However, these studies may in a risk of generating spurious associations, because as weight changed during pregnancy, potential confounders might change as well. Those confounders are likely to become confounder and intermediators, simultaneously. For example, hypertensive disorders played the role on the GWG and preterm pathway.(Hickey et al. 1995; Thangaratinam et al. 2012; Drehmer et al. 2013; Gaillard et al. 2013; Masho et al. 2013; Xinxo et al. 2013; Fujiwara et al. 2014) Studies usually treated those variables such as hypertensive disorders as similarly as confouder (Hickey et al. 1995; Siega-Riz et al. 1996; Rudra et al. 2008) or excluded those women with certain annoyance from analyses.(Schieve et al. 1999) However, first, statistical study showed that the traditional adjustement approach was not suitbale for those pathways included mediators, as backdoors were likely to occur via unknown factors and this mediator and caused the estimations in bias.(Robins et al. 2000) Then, exclusions limited the application of study's results for those exlucded women, who might be the person in most need of advice and interventions. For example, many women who delivered preterm were complicated by PIH,(Buchbinder et al. 2002; Li et al. 2013; Macdonald-Wallis et al. 2013) they were acturally in double risk and therefore needed more care. However, due to the difficulties in statistical analysis, few evidence were avaible for those high risk women to design their own interventions. Lastly, as discussed above, there is a potential interactive effect between hypertensive disorders and GWG on preterm birth. Hypertensive disorders occurred after 20 weeks of gestation and can directly induce preterm births.(Li et al. 2013; Macdonald-Wallis et al. 2013) It can be caused by excessive GWG during early pregnancy (Crane et al. 2009; Gaillard et al. 2013; Macdonald-Wallis et al. 2013) and may further lead to extra weight gain in late pregnancy due to its sequel such as edema.(Abrams et al. 1995; Abrams and Selvin 1995; Thorsdottir et al. 2002; Jensen et al. 2005; Khalil et al. 2009) However, none of the studies has accounted for this interaction. In all, regarding the association between GWG and preterm birth, the 2009 IOM committee concluded that more evidence for detailing the associations between subtypes of preterm births and GWG were needed.(Institute of Medicine(IOM) and National Research Council(NRC) 2009)

Perinatal health services

In this dissertation, perinatal health services included both prenatal care and preconception counseling.

Prenatal care

Prenatal care is the health care that women have received while they are pregnant. Adequacy of prenatal care was characterized in two dimensions, which are "the adequacy of initiation of prenatal care" and "the adequacy of received services". (Kotelchuck 1994) For the timing of prenatal care, the earlier prenatal care begins the better. American College of Obstetricians and Gynecologists (ACOG) recommends prenatal care begin in the first months of pregnancy; the IOM encourages preconception care (six month before pregnancy). For the number of prenatal care, it is based on ACOG standards (one visit per month through 28 weeks, one visit every 2 weeks through 36 weeks, and one visit per week thereafter, adjusted for data of initiation of PNC). (Kotelchuck 1994) Health researchers further came ups measures to define inadequacy of prenatal care as prenatal care begun after the 4^{th} month or under 50% of expected visits were received. Intermediate care is defined as prenatal care begun by month 4 and between 50-79% of expected visits were received. Adequate care is defined as prenatal care begun by month 4 and of 80-109% of expected visits were received. Adequate plus care is defined as prenatal care begun by month4 and 110% or more of expected visits were received.

Epidemiology of prenatal care use

In 2011, among the 36 states and District of Columbia, 73.7% of women giving birth received early prenatal care in the first trimester, while 36.3% of women began prenatal care in the third trimester or did not receive any prenatal care. Rates of first trimester prenatal care increased with greater educational attainment (58.0 % of mothers with less than a high school diploma to 86.3% of mothers with a bachelor's degree or higher). First trimester prenatal care initiation was highest among non-Hispanic White and non-Hispanic Asian women (78.8% and 77.8%, respectively), followed by Hispanic (68.3%) and non-Hispanic Black women (63.4%), while non-Hispanic American Indian/Alaska Native and non-Hispanic Native Hawaiian/Other Pacific Islander women had the lowest rates of early prenatal care (59.0% and 55.7%, respectively). (U.S. Department of Health and Human Services et al. 2013)

Preconception counseling

Preconception care is usually defined as the care of a woman received six month before she gets pregnant. It was proposed as the increasing concerns that even early prenatal care is too late for interventions to prevent maternal and infant adverse health outcomes, and prenatal care may not be sufficient to explain the persistent racial-ethnic health disparities in mothers, infants and children, such as higher prevalence of preterm birth and low birth weight in Blacks than Whites. (March of Dimes Birth Defects Foundation 2002; Atrash et al. 2006; Lu et al. 2006) Also, many researchers concerned the impact of prenatal care on birth outcomes might have plateaued; (Kogan et al. 1998; Lu et al. 2003; Hamilton et al. 2013) they suggested that the paradigm for women's primary health care has to shift to a longer reproductive period.(Lu and Halfon 2003; Lu et al. 2006; Lu et al. 2010) Preconception care was therefore developed, included as a part of women's clinical preventive services recommended by the Institute of Medicine (IOM) to all women in reproductive ages.(Institute of Medicine 2011) It provided an opportunity to identify existing health risks before pregnancy, which has become important public health strategies to improve women's health and to decrease infant morbidity and mortality in the U.S. and around the world.(Atrash et al. 2006; Johnson et al. 2006; US Department of Health and Human Services 2010; World Health Organization 2012; World Health Organization 2012)

Epidemiology of preconception counseling

To date, only two published studies and a few online reports have estimated the prevalence of using preconception care in the U.S.(Williams et al. 2012; Robbins et al. 2014) A recent MMWR report using data from Pregnancy Risk Assessment Monitoring System (PRAMS) in four states (i.e., Maryland, Michigan, New Jersey, and Ohio) showed that only 18.4% of women received preconception care counselling from a health care provider before pregnancy in 2009.(Robbins et al. 2014) Another earlier study also used the PRAMS data from four states (New Jersey, Utah, Vermont, and Maine) found that 32.4% of women reported preconception care counseling in the period of 2004-2008.(Williams et al. 2012) One online report found that preconception care counseling was 13.5% among Oklahoma women in 2004-5.(Oklahoma State Department of Health 2008) These data revealed that the use of preconception counseling is low and varies by geographical area and time. In all, our knowledge on the reasons for women to decide to use or not use preconception counseling, and whether using preconception care is associated with better health behaviors before pregnancy was very limited.

Personal capital

In the context of pregnancy, many factors can influence health care utilization from different perspective. Relevant individual-level factors includes medial, genetic, behavioral, stress and emotion and etc.(Grimm 1967) Relationship-level factors include social network, social support, partner relationship, family, and intergenerational influences. Sociocultural-level factors include race/ethnicity, nativity, acculturation, social-economic-status, and cultural norms and values. Community-level factors include the physical environment, characteristics of neighborhoods, health-care access and quality and related geographical factors. Each of these has received attention in past research on pregnancy, with a stronger emphasis historically on medical and behavioral risk. Recently, more attention has been paid on ecological environment (sociocultural and community factors), because findings showed that pregnancy for many women today is an experience characterized by a lack of adequate resources, both socioeconomic and psychosocial, and the presence of many stressors such as work and family responsibilities. (Dunkel Schetter 2011)

Bronfenbrenner's ecological model

The Bronfenbrenner's ecological model defined the ecological environment as a nested arrangement of structures, each contained within the next, including microsystem, mesosystem, exosystem and macrosystem. Microsystem refers to the complex relations between the developing person and environment in an immediate setting containing that person (e.g., home, school, work place, etc.). A setting is defined as a place with particular physical features in which the participants engage in particular activities in particular roles (e.g., daughter, parent, teacher, employee, etc.) for particular periods of time. The factors of place, time, physical features, activity, participants, and role constitute the elements of setting. A mesosystem comprises the interrelations among major setting containing the developing person at a particular point of his or her life. An exoxytem is an extension of the mesosystem embrace in another specific social structures, both formal and informal, that do not themselves contain the developing persons but impinge upon or encompass the immediate settings in which that person is found, and thereby influence, delimit, or even determine what goes on there. A macroystems refers to the overarching institutional patterns of the culture or subculture, such as the economic, social, educational, legal, and political systems, of which micro-, meso, and exosystems are the concrete manifestations. Those systems are further weighted on the basis of the impact on individuals. Microsystem has the larger and more direct impact than mesosystem and exosystem.

Defining Personal capital

Personal capital is defined as the internal or external resources that impacts people exposed to different psychological and behavioral factors.(Dunkel Schetter 2011) Those resources may exist in every ecological system as mentioned above. Thus, previous studies have applied Bronfenbrenner’s ecological model to conceptualize personal capitals, particular in perinatal studies.(Bronfenbrenner 1977; Bronfenbrenner 2009;

Wakeel et al. 2013; Wakeel et al. 2013) Typically, it was still defined on three levels, which included individual level (microsystem) of internal resources (self-esteem and mastery), interpersonal level (mesosystem) of social resources (partner support and social support), and community level (exosystem) of neighborhood support (social cohesion and reciprocal exchange). As the weighting scheme, internal resources, partner support, social network support, and neighborhood support comprised 32.5, 27.5, 22.5, 17.5%, respectively, of the overall personal capital. (Figure 2.2) (Wakeel et al. 2013) As those psychological and behavioral factors may further impact health outcomes, personal capital were believed to associate with health outcomes.(Wakeel et al. 2013)

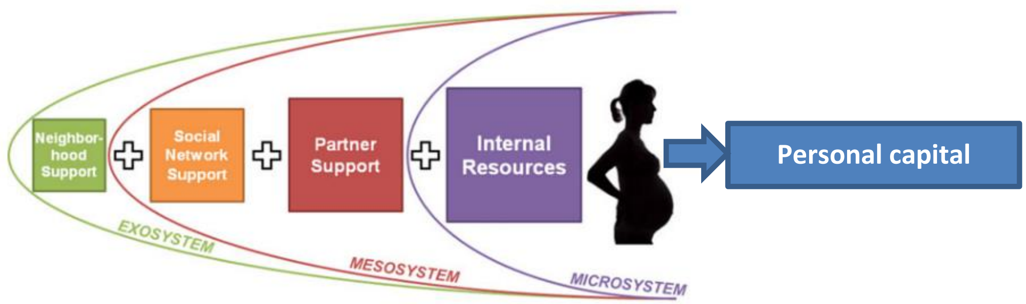

Figure 2.2 Construction of personal capital.
Wakeel, F., et al., *Racial and Ethnic Disparities in Personal Capital During Pregnancy: Findings from the 2007 Los Angeles Mommy and Baby (LAMB) Study*. Maternal and Child Health Journal, 2013.

Association between personal capital and health outcomes

Although as an overall index, personal capital has been under-explored in the literature, the individual personal capital has been broadly tied to obstetric outcomes. Self-esteem and mastery have been associated with higher infant birth weight and decreased risk of intrauterine growth retardation. (Goldenberg RL et al. 1991; Rini et al. 1999) Partner support and social network support have been linked to increased fetal growth, better labor progress, higher birth weight, and higher infant APGAR scores.(Collins et al. 1993; Feldman et al. 2000) Neighborhood support played an indirect role in lowering women's risk of adverse obstetric outcomes. (Bell et al. 2006) In addition, two studies have used this composite construct in perinatal studies and found it was differed by racial-ethnic groups and associated with adverse obstetric outcomes either. They also considered that this composite structure has more implications for public health programs, because it provided more opportunities for health interventions.(Wakeel et al. 2013; Wakeel et al. 2013)

Racial disparities in personal capital

Same as racial disparities existed in health services use; disparities were also reported in personal capital. Regarding internal resources, previous studies indicated that compared to other racial-ethnic groups, Blacks have reported higher levels of self-esteem, whereas Asians have reported the lowest levels. (Twenge and Crocker 2002; Wakeel et al. 2013) Regarding social resources, Hispanic women have reported relatively high partner and social network support.(Norbeck and Anderson 1989; West et al. 1998; Diaz et al. 2007) Furthermore, those racial disparities displayed distinctively by regions/areas.(Chandra and Skinner 2003) Wakeel et al (Wakeel et al. 2013) studied 2007

LAMB survey, revealing contradict findings in LA county, that Hispanic women reported the lowest social support. Over half of the Hispanic participants in LAMB survey were immigrants, who may be in a transitional phase, such that they have left behind valuable social networks in their native countries and are currently unable to garner viable social ties in the U.S. due to economic, lingual, and racial barriers. (Keefe 1987; Sundquist and Winkleby 1999) They also showed Asians with significantly lower neighborhood support, which contradicted to the theory that Asian immigrants have stronger social networks in same ethnic enclaves.(Walton 2009) This contradiction may be attributed to the relatively high SES of Asians in LA county. It is realized that when immigrants become socioeconomically secure, they will move to high-SES neighborhoods (predominantly White residents), which induced less support benefits than when they lived in predominantly Asian neighborhoods.(Iceland and Nelson 2010) However, despite the inconsistent findings in previous studies, they all highlighted an importance of accounting racial -specific personal capital effect in future studies.

Literature gaps

Study #1 and Study#2

First, many risk factors such as maternal age, race, parity, prepregnancy body mass index (BMI), and GWG are reported to be related with PIH and preterm births. Among those potential risk factors, prepregnancy BMI and GWG are considered as modifiable risk factors that can be intervened in clinical practice and public health intervention programs. High prepregnancy BMI is a well-known risk factor for both PIH and preterm births. (Thadhani et al. 1999; Duckitt and Harrington 2005; Poon et al. 2009)

However, the clinical practice based lifestyle interventions were found ineffective in eliciting behavior changes.(Ashenden et al. 1997) GWG, as another potential modifiable risk factor has attracted a lot attention from researchers because pregnancy provides a "teachable moment" that women care more about their health conditions during pregnancy and therefore they might be more compliant to weight management interventions.(Phelan 2010) Thus, evidence on whether GWG is related pregnancy outcomes is needed. The results would be useful for both health practitioners to provide individualized preconception and prenatal care to high risk women, and for public health decision-makers to design more effective programs to promote maternal and child health.

Next, to date, existing studies on aforementioned effects of GWG on pregnancy outcomes are inconsistent, largely due to methodological limitations. First, traditional measures of GWG such as total GWG at delivery (Thorsdottir et al. 2002; Brennand et al. 2005; Jensen et al. 2005; DeVader et al. 2007; Crane et al. 2009; Beyerlein et al. 2011; Gaillard et al. 2011), weekly rate of GWG (Gaillard et al. 2013), and adequacy ratio of GWG based on the 2009 Institute of Medicine (IOM) guidelines (Bodnar et al. 2004; Bodnar et al. 2010), are challenged in reflecting the sigmoidal growth of GWG and can be impacted by confounders such as the duration of the pregnancy (i.e, gestational age (GA) at delivery).(Hutcheon et al. 2012) Those issues may derive spurious associations when assessing GA-related health outcomes. Second, because the rate of weight gain changes by the stage of pregnancy, a one-time measure of total GWG is not accurate to examine the potential dynamic effects of GWG on health outcomes. (Hickey et al. 1995; Rudra et al. 2008; Wise et al. 2010) Third, similar to the issue in measuring GWG, as pregnancy progresses, confounders can become confounders and intermediators simultaneously. Thus, traditional methods of adjusting confounders and intermediators concurrently are criticized for neglecting the possible interactions between exposure and mediators and other unknown confounding factors.(Robins et al. 2000; Richiardi et al. 2013) Thus, new approaches of measuring GWG and analyzing time-varying exposure and intermediators are warranted to illustrate an accurate association and further provide scientific evidence for better health interventions.(Hutcheon et al. 2012; Hutcheon et al. 2013)

Study #3

Regarding prenatal care, it is a well-accepted health care during pregnancy.(Higgins et al. 1994; Ta and Hayes 2010; Leal et al. 2011) Many studies have been conducted to explore strategies to improve early prenatal care initiation, however, to date, around one million of women limited prenatal care after 1st trimester and the proportion of the late initiation of prenatal care was higher among African Americans and Hispanics.(Kramer et al. 2000; Lu and Halfon 2003) Extra strategies are needed. Previous studies have shown social support has become a significant role in prenatal care utilization in nowadays. (St Clair et al. 1989; Leal Mdo et al. 2011) However, empirical evidence is needed to examine the race-specific associations between those social resources and perinatal health services use. Regarding preconception care, it is a novel concept; (Abrams et al. 1995; Lu and Halfon 2003; Atrash et al. 2006; Moore LK et al. 2008; Macdonald-Wallis et al. 2013) studies are needed to explore the strategies to disseminate the concept and improve the utilization.

Personal capital was created on a multidimensional scale (Dunkel Schetter 2011), have been associated with maternal and child health outcomes by researchers in recent studies(Goldenberg RL et al. 1991; Collins et al. 1993; Rini et al. 1999; Feldman et al. 2000; Bell et al. 2006; Wakeel et al. 2013; Wakeel et al. 2014). However, to our knowledge no studies have used a multidimensional measure of personal capital to assess its overall impact on prenatal care and on preconception counseling. Furthermore, no studies have explained whether the associations varied by racial groups. However, better knowledge on whether personal capital might be a protective factor for perinatal health service utilization and how its impact might vary by racial groups will be useful to the design of programs aiming at improving perinatal health care use and narrowing racial disparities in maternal and child health outcomes.

CHAPTER 3

RESEARCH AIMS

To address the research gaps in literature in the areas related to pregnancy health and better health service utilization among women of reproductive ages, the specific aims and research questions for this dissertation were as follows:

Specific Aims and Research Questions

Aim 1: To describe the natural growth trajectory of GWG during early pregnancy (8-20 weeks gestation) and its correlates and to examine the independent association of the trajectories of GWG during early pregnancy on the subsequent development of PIH and blood pressure change.

*Research Question 1.1.*What is the natural growth trajectory of GWG during early pregnancy?

Research Question 1.2. Does GWG during early pregnancy impact subsequent blood pressure change among normotensive women? What are the risky trajectories?

Research Question 1.3. Does GWG during early pregnancy impact the development of PIH? What are the risky trajectories?

Aim 2: To describe GWG pattern in early pregnancy (≤20 weeks' gestation) and mid-late pregnancy (> 20 weeks' gestation) and explore the correlates of those patterns, and to estimate the causal effect of GWG during pregnancy, a time-varying exposure, on the odds of preterm births.

Research Question 2.1. How weight gain during early pregnancy and mid-late pregnancy?

Research Question 2.2. What are the correlates for GWG during those two periods?

Research Question 2.3. Does the time-varying exposure, GWG have an effect on inducing preterm births?

Aim 3: To examine the association between personal capital and perinatal health services use and explore the role roles of each component in personal capital on perinatal health services use.

Research Question 3.1. Does personal capital impact the receipt of preconception counseling and prenatal care? How this differentiated by racial groups?

Research Question 3.2. What components of personal capital contribute to perinatal health services use? How these differentiated by racial groups?

CHAPTER 4

METHODS

This dissertation analyzed data from two surveys. The analyses for the first two aims used the data from the 1988 National Maternal and Infant Health Survey (NMIHS). The third aim was based on data from the 2007 and 2010 Los Angeles Mommy and Baby Survey (LAMBS).

National Maternal and Infant Health Survey (NMIHS) (Studies 1 and 2)

The NMIHS was conducted by the National Center for Health Statistics, aiming to study the factors related to poor pregnancy outcomes, such as inadequacy of prenatal care; inadequate and excessive weight gain during pregnancy; maternal smoking, drinking, and drug use; and pregnancy and delivery complications. It is a nationally representative sample, of which the data was collected from mothers who delivered a baby in 1988 and were residents of United States at the time. The survey contains three parts, including 1988 vital records, mothers' questionnaire, and prenatal care provider and hospital questionnaire. Vital records included the information on demographic characteristics of the parents, pregnancy history, characteristics of the new born, and etc. Mother's questionnaires were administrated postpartum with a mean interval of 17 months between delivery time and interview. It asked their health providers' name, delivery hospitals, and supplemented the vital records with social and demographic characteristics of the parents, and timing and content of prenatal care.

In the questionnaires sent to prenatal care providers and hospital, additional information on labor and delivery, health of the mother and infant, and prenatal care were included. The data from the two questionnaires were unduplicated and combined to form a single medical-source record. Finally, the three parts (vital record, mothers' questionnaire, provider/hospital questionnaire) were merged together. In total, 13,417 live birth, 4,772 fetal deaths and 8,166 infant deaths were randomly drawn from vital records from 48 states, the District of Columbia, and New York City. Black infants and low birth weight infants were oversampled in the live-birth components. Therefore, to assure a representative sample, the live birth records were stratified by race (black, nonblack) and birth weight (<1500 gram, 1500-2499 gram, 2500+ gram). The overall response rate for the national file was 71%. Previous reports showed that mothers were more likely to respond if they were over 30 years old, white, married, and had at least high school education. Figure 4.1 showed the general sample flow for study1 and study2. Previous study has described the study design and response rate in detail.(Sanderson and Gonzalez 1998) Major assessments included in the three data source are presented in Table 4.1. The details of how each variable was chosen from different sources for analysis are described below. To reflect national counts, data from the NMIHS were weighted based on the probability of selection, other sampling adjusting (i.e., multiple births and some known sampling inconsistencies, plus adjustments for the probability of selection), nonresponse (given a weight of zero), and post-stratification adjustment (i.e., the number of events divided by the sum of weights). Each record was then assigned a final weight to reduce the variability of the estimates. (Sanderson and Gonzalez 1998)

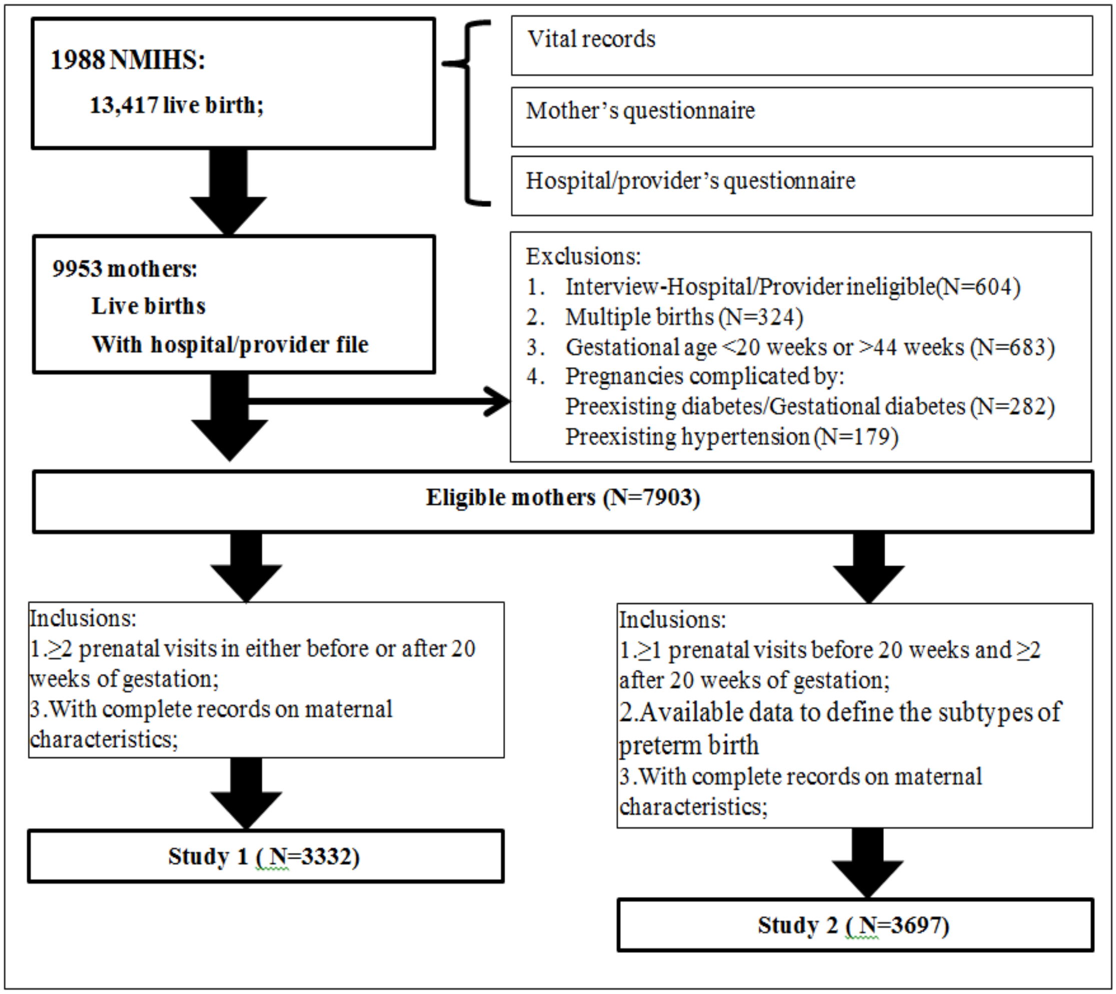

Figure 4.1 Sample flow for Study 1 and Study 2.
Source: Sanderson, M. and J.F. Gonzalez, *1988 National Maternal and Infant Health Survey: methods and response characteristics.* Vital Health Stat 2, 1998(125): p.

Table 4.1 Data available on NMIHS

	Vital records	Mothers' questionnaire	Hospital/Prenatal Care Provider Questionnaire
Demographics			
Age	x	x	x
Sex	x	x	x
Race	x	x	x
Education	x	x	x
Income	x	x	x
Marital status	x	x	x
Insurance	x	x	x
Parity status	x	x	x
Singleton	x	x	x
Medical History record			
Historical hypertension	x	x	x
Historical diabetes	x	x	x
Weight history	x	x	x
Prenatal care visit		x	
Date of last menstrual period	x	x	x
Gestational duration	x	x	x
Date of delivery		x	x
Gestational duration at delivery		x	x
Maternal prepregnancy weight	x	x	x
Maternal prepregnancy length	x	x	x
Prepregnancy BMI	x	x	x
Weight at each prenatal visit			x
Weight at delivery room		x	x
Gestational Diabetes Mellitus	x	x	x
Blood pressure at each prenatal visit			x
Gestation induced hypertension	x	x	x
Urine protein at each prenatal visit			
Pre-eclampsia	x	x	x
Health Behaviors			

Smoking during pregnancy	x	x
Physical activity during pregnancy	x	x
Multivitamin intake	x	x

Source: Sanderson, M. and J.F. Gonzalez, *1988 National Maternal and Infant Health Survey: methods and response characteristics.* Vital Health Stat 2, 1998(125): p. 1-39.

Study 1: GWG and blood pressure

Purpose

Aim 1: 1) to describe the natural growth trajectory of GWG during early pregnancy (8-20 weeks gestation) and its correlates and 2) to examine the independent association of the trajectories of GWG during early pregnancy on the subsequent development of PIH and blood pressure change.

Study Design

A prospective cohort design using secondary data

Study Population

In this study (Figure 2.1), We included 9953 participants who gave live births and had a complete hospital/provider form.(Schieve et al. 2000) We further restricted to 7903 women who delivered a singleton birth between 20-44 weeks and were free of preexisting medical conditions such as diabetes and hypertension, and gestational diabetes in this pregnancy. These women were excluded because those preexisting conditions and related medical interventions might modify weight gain during pregnancy. To examine longitudinal change of GWG in early pregnancy and to relate it with PIH in mid-to-late pregnancy, we restricted the participants who had at least twice prenatal care visits in either early pregnancy (8 to 20 weeks) or mid-to-late gestation (after 20 weeks' gestation). The above inclusion and exclusion criteria resulted in 3,332 women remaining in the final analyses.

Gestational duration and gestational weight gain

Data elements such as gestational age (GA) at each prenatal visit, mothers' prepregnancy weight and weight gain at each prenatal visit were used to produce the trajectories of GWG in early pregnancy from 8 to 20 week's gestation. Records before 8 weeks were not used because very few women had data at that early period and maternal weights do not change much before 8 weeks of gestation.(Hutcheon et al. 2013; Macdonald-Wallis et al. 2013) GA at each prenatal visit was computed as the number of weeks between the last menstrual period (LMP) and the date of prenatal visits.(Schieve et al. 2000) Data on mother's prepregnancy weight were primarily obtained from the prenatal care provider/hospital forms (87.6%), then supplemented by records in birth certificates (12.4%).(World Health Organization 2012) Maternal weight at each prenatal visit and delivery was abstracted from the hospital/provider forms (Schieve et al. 2000) and was used to compute maternal weight gain at each prenatal visit by subtracting mother's prepregnancy weight. We calculated total weight gain in early gestation by mother's weight at delivery room less the last record of mother's weight before 20 week's gestation (average of 18 week, interquartile range [IQR]:16-19 week), and total weight gain in mid-to-late gestation (after 20 weeks' gestation) by mother's weight at delivery room less her total weight gain during early gestation. We incorporated the last measurement prior to 20 weeks to calculate the rate of weight gain during mid-to-late gestation (i.e., weight gain after early gestation divided by weeks after early gestation).(Khalil et al. 2009) Furthermore, total GWG during the entire pregnancy were categorized into inadequate, adequate and excessive GWG, based on 2009 Institute of Medicine's recommendation.(Bodnar et al. 2004; Bodnar et al. 2010) This will help to understand the transition of GWG from early gestation to delivery. In addition, to minimize effects of data entry or recording errors, implausible GWG values at certain prenatal visits (weight gain >80 lbs or < -30 lbs) were recoded as missing values.(Hutcheon et al. 2013)

Antenatal blood pressure measurements and PIH and Pre-eclampsia

Provider/hospital records in NMIHS included data on serial systolic and diastolic blood pressure measurements and urine protein test results.(Gunderson et al. 2000) PIH was defined as having at least two occasions of systolic blood pressure (SBP) equal or greater than 140 mmHg or diastolic blood pressure (DBP) equal or greater than 90 mmHg, and without proteinuria after the 20th week of gestation.(Leeman and Fontaine 2008) Preeclampsia was further defined as the development of PIH and proteinuria after the 20th week of gestation. Due to lack of data, our definition of preeclampsia could not take into account organ function, as recently suggested by the American Congress of Obstetricians and Gynecologists (ACOG).(American College of Obstetricians and Gynecologists 2013) Hypertensive disorders in this study were defined as women with either PIH or preeclampsia.

Covariates

Many covariates were considered in our analyses. Data on mother's age, race/ethnicity, education attainment, marital status, smoking status before pregnancy, and parity came from birth certificates. Data on family income and physical activity during pregnancy were taken from mother's questionnaire. Women were defined as 'none exerciser' if they responded "no" to the question "Did you exercise or play sports at least three times a week after you found out you were pregnant?" Among women who reported exercising during the pregnancy, they were further classified as exercising <5 months or ≥5 months' gestation based on reported duration of exercise during pregnancy. Women's BMI was calculated by prepregnancy weight in kilograms divided by the square of measured height in meters, and further categorized as underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), and obese (≥30).(Druzin et al. 2008) To assess the independent effects of GWG in early pregnancy on blood pressure or PIH after 20 weeks gestation, last blood pressure records (i.e., SBP, DBP) before 20 weeks gestation and rate of GWG after 20 weeks gestation were also included as covariates.

Statistical Analysis

All analyses were done using SAS software (version 9.3, SAS Institute, Cary, NC) and were weighted; p-values were two-tailed and values that less than 0.05 were considered as a statistical significance.

The definitive analysis began with an exploratory analysis using basic descriptive statistics such as frequencies, means and percentages. The appropriate tests for any group differences were assessed by chi-square or t-tests where appropriate. The first table was used to present the characteristics of participants and compare the differences between included and excluded participants.

Trajectory of GWG during early pregnancy. Latent Class Growth Modeling (LCGM) was used to define the longitudinal gestational age-associated changes in GWG up to 20 weeks' gestation. The LCGM procedure further grouped all women regarding their instant rates of GWG.(Llabre et al. 2004; Andruff H et al. 2009; Martin JA et al.

2012) LCGM is a semi-parametric statistical technique, which has been broadly used to identify distinct subgroups of individuals following a similar pattern of change over time on a variable of interest (e.g., gestational age). This means it can assume the data follows a pattern of change in which both the strength and the direction of the relationship between the independent and dependent variables differ across cases. In this analysis, we set four latent groups for all the participants, because there is a broad agreement of the trajectory of GWG varied by pre-pregnancy BMI categories (i.e., underweight, normal weight, overweight and obesity). The quadratic term of gestation age was used to describe the sigmoidal growth of weight gain.(Institute of Medicine(IOM) and National Research Council(NRC) 2009) In addition to these priori knowledge concerning the number and the shape of trajectories, the Bayesian Information Criterion (BIC) value could be obtained from each model tested ,which is a fit index used to compare competing models that include different numbers of trajectories or trajectories of various shapes (e.g., linear versus quadratic).(Heather Andruff et al. 2009) Weight gain was log-transformed in order to satisfy the assumption of normal distribution. A constant of 15 was added to all values to shift the minimum values of the distribution to 1(i.e., to ensure nonnegative observations).(Hutcheon et al. 2013) We used PROC TRAJ in SAS software (SAS Institute Inc. 2003) to produce the trajectory.

Association between GWG trajectories in early pregnancy and blood pressure change after 20 weeks of gestation. This analysis was restricted to normotensive women during the entire pregnancy (n=3069), because pregnant women in hypertension were mandatory to take medicines to keep blood pressure normal. Linear mixed models (LMM) was used to describe the longitudinal blood pressure measurements (SBP and

DBP) as a function of the trajectories of GWG in early pregnancy, respectively; these models can accommodate unbalanced, unequally spaced observations over time. Mother's gestational age (>20 weeks) was included as a measure of time. Random effects were specified for the model intercept and gestational age, with a component symmetric covariance structure. Because the interaction term between gestational age (continuous) and rate of weight gain in mid-to-late pregnancy (>20 weeks) was statistically significant ($p<0.001$), we stratified our analyses into two groups based on delivery dates (≥ 37 and <37 weeks of gestation). We first examined the crude association between GWG in early pregnancy and blood pressure change. The second model additionally included maternal characteristics and behavioral factors.

Association between GWG trajectories in early pregnancy and the development of PIH and preeclampsia. Generalized estimating equations (GEE) method with a Poisson distribution and log link was used to model the development of PIH and preeclampsia while taking into account the repeated measurements and the approximate Poisson distribution for PIH and preeclampsia outcomes.(Sagiv et al. 2005) The independent working correlation matrix was chosen by Quasi-Akaike Information Criterion (QIC) values. We first built a crude model and then added the rate of GWG after 20 weeks and all covariates to the adjusted model.

Study 2: GWG and preterm birth

Propose

Aim 2: 1) to describe GWG pattern in early pregnancy (≤20 weeks' gestation) and mid-late pregnancy (> 20 weeks' gestation) and explore the correlates of GWG, and 2) to estimate the causal effect of GWG during pregnancy, a time-varying exposure, on the odds of preterm births.

Study Design

A prospective cohort design using secondary data (NMIHS).

Study Population

Similary as Study #1, we included 9953 participants who gave live births and had a complete hospital/provider form.(Schieve et al. 2000) We further restricted to 7106 women who delivered a singleton birth between 20-44 weeks, were free of chronic diabetes, chronic hypertension, gestational diabetes in this pregnancy, and with prepregnancy BMI above 18.5 kg/m^2. Women with preexisting medical conditions were excluded because related medical interventions might modify weight gain during pregnancy. We focus on normal and overweight or obese women and provided provisional data for underweight women, due to the small sample size of underweight women (N=328) and only nine of them developed hypertensive disorders. To examine the changing rate of GWG during pregnancy and its associations with hypertensive disorders and preterm births, participants were required to 1) have at least one prenatal care visits between 8 to 20 weeks' gestation and at least two prenatal care visits after 20 weeks' gestation (excluding records on delivery day) (N=3433), and 2) have available data (i.e., records of labor and rupture of membranes) to define the subtypes of preterm birth. The above inclusion and exclusion criteria resulted in 3320 women remaining in the final analyses.

Preterm birth

Continuous variable of gestational week was used to determine the gestational duration at delivery. It was further categorized to extremely preterm (<28 weeks gestation), very preterm (28 to <32 weeks' gestation) and moderate to late preterm (32 to <37 weeks' gestation). In addition, based on the circumstances surrounding the delivery, preterm birth will be further classified into spontaneuous preterm birth or inducted preterm birth. This information will be obtained from both providers and hospitals' questionnaires. Specifically, women who had spontaneous rupture of membranes at least one hour before labor were defined as preterm premature rupture of membranes (PPROM). This was reported as pregnancy complicated with PROM in vital record. Furthermore, women whose labor began spontaneously (not medical induction) were identified as having preterm labor. Those two scenarios were grouped together as spontaneous preterm births, because these women were spontaneously labored. Then, women who had either artificial rupture of membranes to induce labor, drugs used to induce labor in the absence of ruptured membranes, or a cesarean section performed in the absence of either spontaneous preterm labor or preterm premature rupture of membranes were coded as medically indicated preterm births. All these deliveries were grouped as a result of medical intervention. (Carmichael et al. 1997)

Gestational weight gain

Except to the description of GWG in Study #1, as we also considered the dynamic effect of GWG on preterm birth, and hypertensive disorder is an intermediator on the pathway from GWG to preterm births, GWG were calculated for two periods, that is, early pregnancy (≤20 weeks) and mid-late (>20 weeks) pregnancy. GWG in early pregnancy was computed by the last record of mother's weight before 20 week's gestation (average of 18 week, interquartile range [IQR]:17-19 week) less mother's prepregnancy weight. Women's GWG in mid-late pregnancy was calculated as mother's weight at delivery room less the last record of mother's weight before 20 week's gestation. Adequacy ratio of GWG was adopted to categorized GWG in each period as: inadequate, adequate and excessive gain. Specifically, according to the 2009 Institutes of Medicine (IOM) guidelines, it assumes normal weight (18.5–24.9 kg/m^2) women typically gain 4.4 lbs during the first 12 weeks of pregnancy, while overweight (25.0–29.9 kg/m^2) women gained 2.2 lbs and obese (≥30.0 kg/m^2) women gained 1.1 lbs.(Institute of Medicine(IOM) and National Research Council(NRC) 2009) These assumptions as well as the weight gain in second and third trimester were used to obtain the adequacy of GWG in relation to 2009 IOM guidelines. (Bodnar et al. 2004; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Bodnar et al. 2010) We considered this measurement is independent with gestational age, which reduces the misclassification of GWG as the results of inconsistent cut off points between two pregnancy periods among women.

Mediator and covariates

Hypertensive disorders included pregnancy-induced hypertension and preeclampsia was considered as intermediators on the pathway from GWG to preterm births. Definition of mediators (i.e., PIH and hypertensive disorders) and covariates were similar to that reported in Study #1.

Statistical analysis plan

Motivation of using MSMs. We aimed at studying the total causal effect of maternal GWG on preterm births via both direct and indirect pathways through hypertensive disorders (Figure 1). As the causal effect are defined as the contrast in an individual with two potential outcomes (preterm vs not preterm births). Thus, in order to predict the outcomes, all covariates are required to equally distributed between exposed cohort and unexposed cohort as designed in randomized clinical trials. This objective is more clearly achieved by MSMs, as it creates pseudo population that balances covariates' distribution in the cohort.(Robins et al. 2000; Bodnar et al. 2004) More details were introduced below.

Effect of GWG on preterm birth. MSMs were accomplished in a three-stage process. In stage I, baseline exposure (GWG_1 in Figure 1) was modeled as an outcome. After adjusting all covariates mentioned above (L_1), a probability of associated with certain category of GWG_1 would be estimated. Then, based on those probabilities, each woman was assigned with a stabilized inverse-probability-of GWG category weights (IPW_1) (1). The lower the IPW_1 of a woman assigned, the higher the probability of the woman was in the certain category of GWG and vice-versa. The purpose of allocating IPW_1 to each woman was to weight covariates distribution for women in different GWG categories. In the other words, this process created a pseudo population in which GWG category and the covariates are no longer associated with each other. In stage 2, similar procedure is applied by modeling the secondary exposure effect (GWG_2 in Figure 1) as an outcome. All baseline covariates, GWG_1 category (i.e., inadequate, adequate and excessive GWG during early pregnancy), PIH were incorporate in the regression model to derive secondary probability of each woman. Correspondingly, each woman will receive stabilized inverse-probability of GWG categories weights at mid-late pregnancy (IPW_2) (2). To estimate the causal association of two exposures (i.e., GWG before and after 20 weeks' gestation) through MSMs, we recomputed final inverse probabilities weight (IPW) by multiplying IPW_1 and IPW_2. The details have been described in previous studies.(Robins et al. 2000; Bodnar et al. 2004)

$$IPW_1=P(GWG_1=gwg_{1i})/P(GWG_1=gwg_{1i}|L_1=l_{1i}) \quad (1)$$

$$IPW_2=P(GWG_2=gwg_{2i}|GWG_1=gwg_{1i})/P(GWG_1=gwg_{0i}|GWG_0=gwg_{0i},L_1=l_{1i},PIH=pih_{2i}) \quad (2)$$

At stage 3, we employed a marginal model with weighted function of the stabilized IPW and two exposures (GWG_1 and GWG_2) on the outcome of PRETERM BIRTHS in this final pseudo population to obtain the causal parameters. Under the stabilized IPW, all the covariates and potential mediator were no longer associated with GWG. We then performed interaction test between PIH and GWG_1 and GWG_2, respectively (P-values >0.05).

Analysis plans. Analyses were done using SAS software (version 9.3, SAS Institute, Cary, NC). PROC GENMOD was applied to model the marginal effects. Because PROC GENMOD is often used for binary outcomes, all above stages were conducted in different sample size. For example, to examine the effect of GWG on spontaneous preterm births, we excluded women with medically indicated preterm births from analysis (N=143) and verse-vasa. We tested the interaction between prepregnancy BMI and GWG, but it was insignificant in any of the preterm birth subtypes. Nevertheless, we stratified all models by prepregnancy BMI, based on previous reports of diagnosing the interaction(Spinillo et al. 1998; Schieve et al. 2000; Dietz et al. 2006; Smith et al. 2007) and the theoretical plausibility of such effect modification, as well as the importance of the maternal prepregnancy BMI on previous reports and recommendations.(Institute of Medicine(IOM) and National Research Council(NRC) 2009) We focused the pathway through hypertensive disorders of PIH and preeclampsia, but also provide analysis on the pathway through PIH. Finally, we tested interaction between hypertensive disorders and GWG, but it was insignificant and results remained unchange when we stratified by hypertensive disorders' status. All P-values were two-tailed, and values that less than 0.05 were considered to indicate statistical significance.

Study 3 personal capital and perinatal care services

Purpose

Aim 3: To examined the association between personal capital and perinatal health services use and explore the role roles of each component in personal capital on perinatal health services use

Research Question 3.1. Does personal capital impact the receipt of preconception counseling and prenatal care? How this differentiated by racial groups?

Research Question 3.2. What components of personal capital contribute to perinatal health services use? How these differentiated by racial groups?

Study Design

This is a cross-sectional, population-based study conducted in Los Angeles County.

Study population

Data came from the 2007 and 2010 Los Angeles Mommy and Baby (LAMB) study, a cross-sectional, population-based mail or telephone survey of women who had recently delivered a live birth in Los Angeles (LA) county in 2007 and 2010. The survey focused on preconception, prenatal, and postpartum correlates of adverse maternal and child health outcomes. The 2007 LAMB Study was collaboration between the University of California, Los Angeles (UCLA) and the Maternal, Child, and Adolescent Health Program (MCAH) of LA County's Department of Public Health. The 2010 LAMB survey was administered and sponsored by LA County's Department of Public Health.

The 2007 LAMB study employed multi-stage and clustered design in which all census tracts in LA County were divided into two strata that corresponded to high and low perinatal health risk. MCAH had identified 150 high-risk zip codes within the county using six perinatal indicators including the number and proportion of women of reproductive age living on incomes below 200% of poverty, births to mothers receiving Medi-Cal, births to mothers age 18 and under, low birth weight births, and percent of late onset or no prenatal care, and infant mortality rate. All census tracts within these high-risk zip codes were categorized as high-risk tracts and the remaining tracts in LA County were low-risk tracts. Women giving birth to low birthweight (<2500 grams) and preterm (<37 completed weeks' gestation) babies were oversampled. The response rates in 2007 were 56%.(Los Angeles Maternal) The 2010 LAMB study a population-based survey that utilizes a stratified random sampling method, by Service Planning Area, race and age. It oversampled African American and teenage mothers to ensure an adequate sample for subgroup analysis. The response rate in 2010 was 57%.(Los Angeles County Department of Public Health et al. 2012)

The data we used for analysis is the combined 2007 and 2010. It identified 14 Best Start communities as the high need areas of LA County by assessing the risk indicators such as low-birth weight, low-performing schools and poverty, and evaluating the strengths and capacity of each community including its leadership infrastructure and its potential for partnership. To get a representative picture of the mothers who gave birth in LA County in 2007 and 2010, a weight was created by post-stratifying on selected maternal and infant characteristics to minimize selection and response bias due to different sampling frames in 2007 and 2010. (Los Angeles County Department of Public Health and Maternal) Specific factors selected in post-stratification included community level (14 communities and other), mother's race/ethnicity, mother's age, mother's education and infant's birth outcome status (low birth weight). The designation of survey respondents to each of the 14 communities were based on census tract correspondence tables (2000 census tract for 2007 data and 2010 for 2010 data). (Los Angeles County Department of Public Health and Maternal) The LAMB survey collected detailed information regarding preconception counseling and women's health behaviors prior to the pregnancy or in early pregnancy, which provided a unique opportunity to examine the proposed questions.

Exposure and Outcomes

Prenatal care and preconception counseling

The LAMB survey asked women to report whether she talked to a doctor, nurse, or other health care worker during the six months before she got pregnant with the new baby. This was used to create the binary exposure of preconception counseling. LAMB survey also asked pregnant women about the time when they had their first prenatal care visit. Information was used to classify early prenatal care initiation (within 13 weeks of gestation) or late prenatal care initiation (after 13 weeks of gestation). (Los Angeles Maternal)

Personal capital

Personal capital was measured by four components based on Bronfenbrenner's ecological model.(Bronfenbrenner 1977; Bronfenbrenner 2009; Wakeel et al. 2013; Wakeel et al. 2013) (Table 7.1, Appendix 1) LAMB survey used 28 questions to assess women internal resources (7 items) of self-esteem (3 items) and mastery ability (4 items), partner support (6 items), social supports(7 items), neighborhood support (10 items) of social cohesion (5 items) and social reciprocal exchange (5 items). Specifically, self-esteem was defined based an overall evaluation of an individual's value.(Jesse et al. 2006) Mastery evaluated the ability of one's control over her life.(Rini et al. 1999) Partner and social supports considered physical and emotional support from the baby's father or her kin and close friends, respectively.(Smart 1977; Fragile Families and CHild Wellbeing Study 2003) Neighborhood support included neighborhood social cohesion and reciprocal exchange and concerned a mutual assistance and support among neighbors.(Buka et al. 2003) This definition summarized an individual's total personal capital at three levels: 1) internal resources at individual level, 2) partner support and social network support at interpersonal, and 3) neighborhood support at community level. According to Bronfenbrenner's conceptual model, internal resources had the largest and most direct impact on individual, followed by partner support, social network support and neighborhood support sequentially. Therefore, after those item-specific scores (with different range) were summed up to form component scores, they were first weighted to reflect the different impacts of each component on individuals and then summed to calculate the total personal capital score (with higher scores reflecting greater levels). As applied in previous study (Wakeel et al. 2013; Wakeel et al. 2014), internal resources, partner support, social network support, and neighborhood support were weighted to represent 32.5, 27.5, 22.5, and 17.5% of the overall score, respectively. Finally, the weighted personal capital score was standardized to range from 1 to 100, with a mean of 50 and a standard deviation of 10. Cronbach's tests were used to identify the internal consistency of all items included in each component.

Covariates

Same-ethnic density effect. Same-ethnic density was defined as the proportion of one ethnic group living in each census tract of an individual woman. Because cultural influence would vary in neighborhoods depending on same-ethnic density level, which may further result in different personal capital and different health outcomes.(Faris and Dunham 1939; Pickett et al. 2005; Shaw et al. 2010; Bécares et al. 2012) Thus, in our analyses, we considered the same-ethnic density as a potential confounder or effect modifier in the relationship between personal capital and perinatal health services use. In our study, it was measured by the percentage of Whites, Hispanics, Blacks, Asians living in each census tract based on 2010 U.S. Census and initially categorized into five levels as 0%-0.99%, 1%-4.99%, 5%-14.99%, 15%-49.99%, and ≥50%. (Pickett et al. 2009) Because small cell sizes in some categories, we further categorized three levels as 0%-14.99%, 15%-49.99%, and ≥50% for Hispanic density.

Socio-demographic factors. We considered mother's age, race/ethnicity, parity, marital status, education, health insurance, nativity, and pregnancy intendedness.

Medical and adverse obstetric history. LAMB survey asked all participants to report whether they had the following conditions in the 6 months before the pregnancy: depression, anxiety, high blood pressure (hypertension), high blood sugar (diabetes), anemia (poor blood, low iron), heart problems, problems with gums or teeth, and asthma. We examined grouped these medical problems into 0, 1, and ≥ 2 conditions. Regarding adverse obstetric history before last pregnancy, LAMB survey asked women whether they have one or more obstetric problems, including preterm birth, delivering low birth weight infant, miscarriage, stillbirth, abortion, and infant death and defects. This was further grouped into: 1) preterm birth and/or low birth weight infant, 2) miscarriage and /or still birth, 3) abortion, and 4) infant death and/or defects. In our analysis, we also created a dichotomous variable for adverse obstetric history (yes versus no).

Statistical Analysis

All analyses were conducted using SAS 9.3 (SAS Institute Inc., Cary, NC) and were weighted to account for the complex survey design and non-responses. One-way

ANOVA tests compared the mean scores for overall personal capital and components for covariates. Chi-square tests of independence were used to examine differences in maternal characteristics among Whites, Hispanics, Blacks and Asians. Statistical significance was set at $p<0.05$. Next, late prenatal care initiation (adverse event) and the receipt of preconception counseling (good event) were chosen as the outcome of interest. We chose to model late prenatal care initiation because 73% of U.S. women initiated prenatal care within the 13 weeks of gestation (Higgins et al. 1994; Ta and Hayes 2010; Leal et al. 2011) and thus, to identify the risk factor for the late initiation of prenatal care is more straightforward for public health interventions. On the other hand, the receipt of preconception counselling has a low prevalence, thus targeting potential risk factors to improve its utilization are more relevant. Multilevel logistic regression models were used for each outcome while considering the confounding by same-ethnic density, maternal demographics, health behaviors and individual medical and adverse obstetric history factors. We additionally adjusted preconception counseling when used late prenatal care initiation as outcome. Furthermore, to better understand the role of each component of personal capital on perinatal health services and provided potential intervention strategies, we ran separate models by including the four components of personal capital in different weights one at a time. Lastly, to examine whether those effects would vary by racial groups, we conducted stratified regression analyses for two outcomes.

CHAPTER 5 ~ CHAPTER7

RESULTS

The results from studies one, two and three are presented in manuscript format. The first manuscript, entitled "Early gestational weight gain is associated with pregnancy-induced hypertension" addressed aim one. The second manuscript, entitled "Associations of gestational weight gain and subtypes of preterm deliveries estimated with marginal structural models" addressed aim two. The third manuscript, entitled "Influence of personal capital on improving perinatal health service uses in Los Angeles County" addressed aim three.

CHAPTER 5

MANUSCRIPT 1: EARLY GESTATIONAL WEIGHT GAIN IS ASSOCIATED WITH PREGNANCY-INDUCED HYPERTENSION[1]

[1] L. Zhan, J. Liu, B. Cai, T.A. Merchant, and X. Sui to be submitted to Epidemiology.

Abstract

Background: Studies on the association between gestational weight gain (GWG) and pregnancy-induced hypertension (PIH) are inconsistent.

Methods: Data came from women who were free of chronic hypertension and gestational diabetes from the 1988 National Maternal and Infant Health Survey with twice prenatal records in both early pregnancy (8-20 weeks of gestation) and after 20 weeks' gestation (N=3,332). Linear mixed models and generalized equation models with Poisson regression were used to examine the associations between GWG trajectories in early pregnancy and blood pressure changes and PIH after 20 weeks of gestation.

Results: Latent class growth model identified four distinct GWG trajectories in early pregnancy: low growth (2.3%), low normal growth (39.7%), normal growth (48.2%), and high growth (9.9%) groups. Women in high growth group had 1.7 mmHg increases in systolic blood pressure (95% confidence interval (CI), 0.9, 2.6), and 0.9 mmHg in diastolic blood pressure (95% CI, 0.2, 1.7), compared to women in normal growth group. In contrast, women in low growth group were protected from subsequent blood pressure increase. Women in high growth group also had higher risk of PIH (RR: 2.0, 95% CI, 1.4, 2.9) compared to those in normal growth group. These associations were independently of weight gain after 20 weeks' gestation.

Conclusion: These results suggest that appropriate weight management in early pregnancy holds promise to control blood pressure and reduce the risks of pregnancy-induced hypertension.

Introduction

Hypertensive disorders are the most frequent cardiovascular events during pregnancy, occurring in about 10% of all pregnancies.(Steegers et al. 2010; Hutcheon et al. 2012) Pregnancy-induced hypertension (PIH), the most frequent type of hypertensive disorders during pregnancy, has increased 1.8 times from 1987 to 2004.(Wallis et al. 2008) To date, it has become a leading cause of maternal and fetal mortality affecting about 5% to 7% of all pregnancies.(Lindheirmer et al. 2009)

There is no effective treatment for PIH, thus more knowledge on how to prevent or lower the risk of PIH is essential. High prepregnancy body mass index (BMI) is a potentially modifiable risk factor because it is associated with increased risk for PIH during pregnancy.(Thadhani et al. 1999; Duckitt and Harrington 2005; Poon et al. 2009) Gestational weight gain (GWG) has been hypothesized to be another potentially modifiable risk factor of PIH in pregnancy. Yet existing studies are inconclusive about the association between GWG and PIH.(Abrams and Selvin 1995; Thorsdottir et al. 2002; Brennand et al. 2005; Jensen et al. 2005; DeVader et al. 2007; Crane et al. 2009; Beyerlein et al. 2011; Gaillard et al. 2011; Heude et al. 2012; Thangaratinam et al. 2012; Gaillard et al. 2013; Li et al. 2013; Macdonald-Wallis et al. 2013) The inconsistency might be attributed to several methodological limitations. First, many studies, (Thorsdottir et al. 2002; Brennand et al. 2005; Jensen et al. 2005; DeVader et al. 2007; Crane et al. 2009; Beyerlein et al. 2011; Gaillard et al. 2011; Hutcheon et al. 2012) that used total GWG, the difference between maternal weight gain at delivery and prepregnancy weight, is a measure with some intrinsic limitations. Edema is prevalent in women who developed PIH, which further leads to extra weight gain in late pregnancy.

As a result, total GWG is limited due to the unclear temporal sequence between total GWG and PIH.(Abrams et al. 1995; Abrams and Selvin 1995; Thorsdottir et al. 2002; Jensen et al. 2005; Khalil et al. 2009) Also total GWG that fails to account for gestational duration,(Brennand et al. 2005; DeVader et al. 2007; Beyerlein et al. 2011; Gaillard et al. 2011; Gaillard et al. 2013) resulting in bias due to this confounding. Second, some studies used a constant weekly rate of GWG,(Gaillard et al. 2011; Heude et al. 2012) which cannot reflect the sigmoidal growth of GWG. Thus, the weekly rate of GWG can bias the estimation because of GWG measurement errors. (Institute of Medicine(IOM) and National Research Council(NRC) 2009) To overcome these limitations in measuring GWG, Hutcheon et al.(Hutcheon et al. 2012; Hutcheon et al. 2013) suggested the trajectory of GWG is the most appropriate way to assess the effect of weight gain during pregnancy on health outcomes.

Early pregnancy (i.e., before 20 weeks gestation) has been considered as a potential window for interventions to prevent hypertensive disorders because substantial blood pressure rise occurs after 20 weeks' gestation. Yet most studies usually do not have data on serial weight records during pregnancy. Thus, previous studies are limited in differentiating weight gain in different periods (American College of Obstetricians and Gynecologists(ACOG) October 2007) and depicting the changing rate, non-linear increasing trend and total amount of GWG in early pregnancy, an important and sensitive period of pregnancy.(Larsen 2001; Institute of Medicine(IOM) and National Research Council(NRC) 2009) To our knowledge, only two European studies examined the association between GWG in early pregnancy and the risk of hypertensive disorders in mid- or late- pregnancy.(Gaillard et al. 2013; Macdonald-Wallis et al. 2013) Macdonald-

Wallis et al.(Macdonald-Wallis et al. 2013) described the GWG trajectory of early pregnancy but they did not examine the potential non-linear increasing trend during this period, which may generate inaccurate findings.(Institute of Medicine(IOM) and National Research Council(NRC) 2009) Also this study did not account for the effect of late GWG, which would bias the independent effect of GWG in the early pregnancy on PIH. Lastly, the positive association between GWG in early pregnancy and PIH in those two European studies may not be generalizable to the U.S. population because of different racial composition and different trends and prevalence in prepregnancy obesity, PIH, and excessive GWG.

Our study has two objectives: 1) to describe the natural growth trajectory of GWG during early pregnancy (8-20 weeks gestation) and its correlates and 2) to examine the independent association of the trajectories of GWG during early pregnancy on the subsequent development of PIH and blood pressure change. The results will provide important evidence on whether appropriate GWG in early pregnancy is beneficial to reduce the risk of PIH.

Methods

Study design and Subjects

This was a retrospective cohort study using the data from the 1988 National Maternal and Infant Health Survey (NMIHS), which was conducted by the National Center for Health Statistics (NCHS) to study the factors related to poor pregnancy outcomes. It collected nationally representative sample of U.S. mothers who delivered a baby in 1988. The survey consisted of three parts: the 1988 birth certificates, prenatal care provider and/or hospital administrator questionnaires and mother's questionnaire. Mother's questionnaires were administrated postpartum with a mean interval of 17 months between delivery time and interview. In total, 13,417 live births were randomly drawn from vital records from 48 states, the District of Columbia, and New York City. Black infants and low birth weight infants (<1500 gram, 1500-2499 gram, 2500+ gram) were oversampled. Each record was assigned a final weight to reflect the complex survey design.(Sanderson and Gonzalez 1998) The overall response rate was 71%. The details of NMIHS were presented elsewhere.(Sanderson and Gonzalez 1998)

We included 9953 participants who gave live births and had a complete hospital/provider form.(Schieve et al. 2000) We further restricted to 7903 women who delivered a singleton birth between 20-44 weeks and were free of preexisting medical conditions such as diabetes and hypertension, and gestational diabetes in this pregnancy. These women were excluded because those preexisting conditions and related medical interventions might modify weight gain during pregnancy. To examine longitudinal change of GWG in early pregnancy and to relate it with PIH in mid-to-late pregnancy, we restricted the participants who had at least twice prenatal care visits in either early pregnancy (8 to 20 weeks) or mid-to-late gestation (after 20 weeks' gestation). The above inclusion and exclusion criteria resulted in 3,332 women remaining in the final analyses.

Gestational weight gain measure

Data elements such as gestational age (GA) at each prenatal visit, mothers' prepregnancy weight and weight gain at each prenatal visit were used to produce the trajectories of GWG in early pregnancy from 8 to 20 week's gestation. Records before 8 weeks were not used because very few women had data at that early period and maternal weights do not change much before 8 weeks of gestation.(Hutcheon et al. 2013; Macdonald-Wallis et al. 2013) GA at each prenatal visit was computed as the number of weeks between the last menstrual period (LMP) and the date of prenatal visits.(Schieve et al. 2000) Data on mother's prepregnancy weight were primarily obtained from the prenatal care provider/hospital forms (87.6%), then supplemented by records in birth certificates (12.4%).(World Health Organization 2012) Maternal weight at each prenatal visit and delivery was abstracted from the hospital/provider forms (Schieve et al. 2000) and was used to compute maternal weight gain at each prenatal visit by subtracting mother's prepregnancy weight. We calculated total weight gain in early gestation by mother's weight at delivery room less the last record of mother's weight before 20 week's gestation (average of 18 week, interquartile range [IQR]:16-19 week), and total weight gain in mid-to-late gestation (after 20 weeks' gestation) by mother's weight at delivery room less her total weight gain during early gestation. We incorporated the last measurement prior to 20 weeks to calculate the rate of weight gain during mid-to-late gestation (i.e., weight gain after early gestation divided by weeks after early gestation).(Khalil et al. 2009) Furthermore, total GWG during the entire pregnancy were categorized into inadequate, adequate and excessive GWG, based on 2009 Institute of Medicine's recommendation.(Bodnar et al. 2004; Bodnar et al. 2010) This will help to understand the transition of GWG from early gestation to delivery. In addition, to minimize effects of data entry or recording errors, implausible GWG values at certain prenatal visits (weight gain >80 lbs or < -30 lbs) were recoded as missing values.(Hutcheon et al. 2013)

Blood pressure, PIH and Preeclampsia

Provider/hospital records in NMIHS included data on serial systolic and diastolic blood pressure measurements and urine protein test results.(Gunderson et al. 2000) PIH was defined as having at least two occasions of systolic blood pressure (SBP) equal or greater than 140 mmHg or diastolic blood pressure (DBP) equal or greater than 90 mmHg, and without proteinuria after the 20th week of gestation.(Leeman and Fontaine 2008) Preeclampsia was further defined as the development of PIH and proteinuria after the 20th week of gestation. Due to lack of data, our definition of preeclampsia could not take into account organ function, as recently suggested by the American Congress of Obstetricians and Gynecologists (ACOG).(American College of Obstetricians and Gynecologists 2013) Hypertensive disorders in this study were defined as women with either PIH or preeclampsia.

Covariates

Many covariates were considered in our analyses. Data on mother's age, race/ethnicity, education attainment, marital status, smoking status before pregnancy, and parity came from birth certificates. Data on family income and physical activity during pregnancy were taken from mother's questionnaire. Women were defined as 'none exerciser' if they responded "no" to the question "Did you exercise or play sports at least three times a week after you found out you were pregnant?" Among women who reported exercising during the pregnancy, they were further classified as exercising <5 months or ≥5 months' gestation based on reported duration of exercise during pregnancy. Women's BMI was calculated by prepregnancy weight in kilograms divided by the square of measured height in meters, and further categorized as underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), and obese (≥30).(Druzin et al. 2008) To assess the independent effects of GWG in early pregnancy on blood pressure or PIH after 20 weeks gestation, last blood pressure records (i.e., SBP, DBP) before 20 weeks gestation and rate of GWG after 20 weeks gestation were also included as covariates.

<u>*Statistical analyses*</u>

Trajectories of GWG in early pregnancy. Latent class growth modeling (LCGM) was used to describe the longitudinal gestational age-associated changes in GWG from 8 to 20 weeks of gestation. The LCGM approach identified latent groups of individuals with similar trajectories on the basis of the raw data distribution.(Nagin DS 2005) Women were grouped according to their instantaneous rates of GWG. Models with the smallest values of AIC, BIC and CAIC were selected as best fitting models.(Heather Andruff et al. 2009; Institute of Medicine(IOM) and National Research Council(NRC) 2009) The details of this approach have been described elsewhere.(Llabre et al. 2004; Andruff H et al. 2009; Choi et al. 2012; Berlin et al. 2014) Weight gain was log-transformed to satisfy normality assumption. A constant of 15 was added to ensure nonnegative observations.(Hutcheon et al. 2013) PROC TRAJ with sample weight was performed to produce the GWG trajectory. We further described the characteristics of women by their trajectories of weight gain in early pregnancy using basic descriptive statistics such as frequencies, means (±standard deviations), and percentages. Chi-square or t-tests were used to examine any group differences where appropriate. Weighted multinomial logistic regression was used to examine the correlates of GWG trajectory in early pregnancy.

Association between GWG trajectories in early pregnancy and blood pressure change after 20 weeks of gestation. This analysis was restricted to normotensive women during the entire pregnancy (n=3069), because pregnant women in hypertension were mandatory to take medicines to keep blood pressure normal. Linear mixed models (LMM) was used to describe the longitudinal blood pressure measurements (SBP and DBP) as a function of the trajectories of GWG in early pregnancy, respectively; these models can accommodate unbalanced, unequally spaced observations over time. Mother's gestational age (>20 weeks) was included as a measure of time. Random effects were specified for the model intercept and gestational age, with a component symmetric covariance structure. Because the interaction term between gestational age (continuous) and rate of weight gain in mid-to-late pregnancy (>20 weeks) was statistically significant ($p<0.001$), we stratified our analyses into two groups based on delivery dates (≥ 37 and <37 weeks of gestation). We first examined the crude association between GWG in early pregnancy and blood pressure change. The second model additionally included maternal characteristics and behavioral factors.

Association between GWG trajectories in early pregnancy and the development of PIH and preeclampsia. Generalized estimating equations (GEE) method with a Poisson distribution and log link was used to model the development of PIH and preeclampsia while taking into account the repeated measurements and the approximate Poisson distribution for PIH and preeclampsia outcomes.(Sagiv et al. 2005) The independent working correlation matrix was chosen by Quasi-Akaike Information Criterion (QIC) values. We first built a crude model and then added the rate of GWG after 20 weeks and all covariates to the adjusted model.

All analyses were done using SAS software (version 9.3, SAS Institute, Cary, NC) and were weighted; p-values were two-tailed and values that less than 0.05 were considered as a statistical significance.

Results

As shown in Table 1, compared to the 7,903 women with singleton live births and without chronic conditions, our analytical final sample (n=3,332) were older, had a higher proportion of being non-Hispanic white, college graduated, married, and with a higher family income (≥$25K). The results were in the expected direction, because the inclusion criteria were related to prenatal care utilization and health status.

Trajectories of GWG in early pregnancy. Four latent groups were identified and named as low (2.3%), low-normal (39.7%), normal (48.2%), and high growth (9.9%) groups, representing women with the lowest to the highest rate of GWG in early pregnancy (Figure 1, Table 2). Women in the normal growth group on average gained 15.0 pounds at the 20th week of gestation ($E[Ln(GWG)]=(2.8-0.01*GA+0.001*GA^2)-15$). Women who experienced a low-normal growth trajectory gained a total of 5.1 pounds during the same period, but their rate of weight gain were smaller than that of normal growth group women ($E[Ln(GWG)]=(2.4+0.03*GA)-15$). Other women underwent two extreme growth trajectories. In the high growth group, women gained about 16.3 pounds at the 8th week of gestation and increased to 28.8 pounds at the 20th week of gestation ($E[Ln(GWG)]=(3.2+0.03*GA)-15$). In contrast, women in the low growth group showed a flat U-shape of growth, as they lost 8.7 pounds weight in the first trimester (≤ 13 weeks' gestation), and regained weight gradually in the following 7 weeks (total weight lost= 3.8 pounds, $E[Ln(GWG)]=(3.9-0.31*GA+0.01*GA^2)-15)$.

All maternal characteristics and health behaviors except parity and exercise status during pregnancy were significantly related to the trajectories of GWG in early pregnancy in the bivariate analysis (Table 2). Thirty two percent of women in the normal growth group gained adequate weight and over half of them gained excessive weight at delivery. Compared to normal growth group, more women in high growth group gained excessive weight (90.0 %), while women in the low growth group were more likely to gain inadequate weight (70.7%) at delivery. Women in normal growth group had the highest proportion of preterm delivery (7.4%), compared to the other three groups. The percentages of developing PIH were lowest in women of low growth trajectory and highest among women of high growth trajectory (p value for trend <0.001).

Table 3 showed the correlates of the trajectories of GWG during early pregnancy. After adjusting all covariates, the odds of being in low growth group were higher among non-Hispanic black and overweight or obese women, but it was lower in women exercised over 5 months of gestation and smoked before pregnancy, compared to the odds of being in the normal growth group. Younger age (≤24 years), multiparous status (=1), living in less income family (<$49,999), and being obese and non-smokers before pregnancy were high risk factors for women being in low-normal growth group. The findings in women with high growth trajectory were similar to that reported in women with low growth trajectory as the odds were higher among non-Hispanic black and overweight or obese women. We additionally found underweight or non-smokers before pregnancy were protective factors from being in high growth group.

Association between the trajectory of GWG during early pregnancy and subsequent blood pressure changes in normotensive women. Due to rates of GWG after 20 weeks were different between women with full term births and preterm births, we conducted stratified analyses by preterm delivery status. Among women with full term births, those in the high growth group on average had a significant mean increases of 1.74 mmHg (95% CI, 0.87, 2.60) of SBP and 0.92 mmHg (95% CI, 0.19, 1.65) of DBP after 20 weeks of gestation than those in normal growth group. In contrast, women in low growth group had lower subsequent blood pressure increase after week 20. As well as these independent associations between GWG during early pregnancy and blood pressure change, we observed similar association between the rate of GWG after 20 weeks' gestation and concurrent SBP(mean difference: 1.90, 95% CI, 1.33,2.47) and DBP(mean difference: 0.98, 95% CI, 0.50,1.46) changes. In addition, higher baseline SBP and DBP, nulliparity and overweight and obesity status were associated with both SBP and DBP rises after 20 weeks of gestation. Underweight status was associated with lower SBP and younger age (≤24 years), less than high school education and smoked before pregnancy were associated with lower DBP.

Among women with preterm births, being high growth of weight gain during early pregnancy was not associated with SBP and DBP changes. However, the rate of GWG after 20 weeks of pregnancy was independently associated with an average of 1.58 mmHg (95% CI: 0.52, 2.64) increase in SBP and 1.21 mmHg (95% CI: 0.33, 2.09) increase in DBP. Women in obese and higher level of blood pressure before pregnancy were positively associated with subsequent blood pressure increases. Hispanics women showed a lower diastolic blood pressure compared to non-Hispanic whites women. (Table 3)

Trajectories of GWG during early pregnancy and subsequent development of PIH and hypertensive disorders. The rates of hypertensive disorders in high growth group were higher than women in normal growth group (PIH: adjusted rate ratio (ARR): 2.02, 95% CI, 1.39, 2.94; Hypertensive disorders: ARR: 1.91, 95% CI: 1.43, 2.55). Per one pound increase in rate of GWG after 20 weeks' gestation was associated with an increased risk of developing PIH (ARR, 2.01, 95% CI, 1.52, 2.65) and hypertensive disorders (ARR:1.81, 95% CI, 1.48, 2.21). Other significant risk factors for PIH included non-Hispanic black race, multiparous gestation, and overweight or obese status before pregnancy.

Discussion and Conclusions

Latent class growth models revealed four trajectories of GWG in early pregnancy (8-20 weeks of gestation), which represented four distinct subsets of pregnant women: low, low-normal, normal, and high growth groups. Women in normal growth group experienced a steady weight gain of 15.0 pounds at the 20th week of gestation. Women in high growth group gained a total of 16.3 pounds at the 8th week of gestation and their weights increased to 28.8 pounds at week 20. Women in low growth group displayed a flat-U shape with weight loss before 13 weeks' gestation. We further found that women in high growth group in early pregnancy had significantly higher SBP and DBP, and were more likely to develop PIH and hypertensive disorders compared to women in normal growth group. Low growth and low-normal group displayed a protective effect on subsequent blood pressure changes and hypertensive disorders. These findings were independent of prepregnancy BMI status, GWG after 20 weeks of pregnancy, and other covariates.

First of all, the latent groups provided insight into the GWG trajectories in early pregnancy. (Schieve et al. 2000; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Hutcheon et al. 2013) Women in normal growth group showed a quadratic change, with a relatively slower rate in the first trimester (≤13 weeks) of weight gain. The amount of GWG (15.0 pounds) and rate of weight gain in early pregnancy in 1988 are very close to those reported in other studies.(Brown et al. 1986; Hediger et al. 1990; Institute of Medicine (Subcommittees on Nutritional Status and Weight Gain During Pregnancy and Dietary Intake and Nutrient Supplements During Pregnancy 1990; Hickey et al. 1996; Carmichael et al. 1997; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Hutcheon et al. 2013) For instance, Carmichael et al.(Carmichael et al. 1997) reported a total of 13.2 pounds of weight gain at the 20th week of gestation in women who delivered between 1980 and 1990 from the San Francisco's Perinatal Database. The small difference might be attributed to the different sample characteristics in terms of higher proportion of white and normal weight women, and involving women with hypertensive disorders or having large for gestational age's infants in our study. These were reported to associate with high GWG in the first or second trimester three decades ago.(Abrams et al. 1995; Abrams and Selvin 1995; Caulfield et al. 1996; Thorsdottir et al. 2002; Jensen et al. 2005; Institute of Medicine(IOM) and National Research Council(NRC) 2009) Moreover, we identified two risk trajectories of GWG of hypertensive disorders, which displayed as fast, linear increase of GWG in high growth group and a flat U-shape change of weight lost in low growth group. To our knowledge, no study has produced those extreme trajectories of weight gain based on the raw data distribution. However, similar extreme values of GWG can be observed in a study that was conducted in normal weight women delivered from 1998 to 2008. (Hutcheon et al. 2013)

Second, both the trajectory of GWG observed in early pregnancy and rate of GWG after 20 weeks gestation were independently related with subsequent blood pressure change, and the development of hypertensive disorders. These results were in agreement with previous studies.(Crane et al. 2009; Gaillard et al. 2011; Heude et al. 2012; Gaillard et al. 2013; Macdonald-Wallis et al. 2013) In the unique study that examined the impact of the trajectory of early GWG on hypertensive disorders,(Macdonald-Wallis et al. 2013) researchers found an average of 0.44 pounds per week gestational weight gain before 18 weeks of gestation was associated a significant mean increase in SBP (0.04 mmHg, 95% CI 0.00,0.07) and DBP (0.03 mmHg, 95% CI 0.00,0.05) in mid pregnancy (18-29 weeks), and significant higher risks of PIH (1.37, 95% CI 1.16,1.38) and preeclampsia (1.31, 95% CI 1.07,1.61). This phenomenon is physiologically plausible because the more women weigh, the more blood they will need to supply oxygen and nutrients to their tissues. As a result, the volume of blood circulated through their blood vessels increases and the pressure in their artery would be raised. Pregnancy in this process plays a role on both GWG and blood pressure change and may further catalyze the development of obesity and hypertensive disorders.(Callaway et al. 2007) Moreover, we observed similar positive associations between rate of GWG after 20 weeks gestation and hypertensive disorders as that reported in previous studies.(Gaillard et al. 2011; Heude et al. 2012) However, the results were limited in predicting the causal effects because it was difficult to determine the temporal sequence between weight gain and hypertensive disorders. Future studies with accurate measurements of weight gain attributed by edema are needed to investigate the causal relationship.

Lastly, our study has many novel findings, which will shed light on future research and intervention programs for pregnant women. First, our study identified latent growth trajectories in GWG in early pregnancy and describing characteristics of each group. These were helpful in targeting high risk women in intervention programs. For example, the results suggest that weight monitoring interventions during early pregnancy were encouraged among non-Hispanic black, overweight or obese, and smoked women. Second, we found a protective effect of women in low growth group on SBP and DBP rises, and observed a strong reduction effect of hypertensive disorders as well. However, due to low growth group only had 103 women and only eight of them developed hypertensive disorders, we were unable to detect the significant effect. Further observational studies with large sample size and intervention trials are needed, especially in overweight or obese women, to identify the causal association and to quantify the weight loss during the first 20 weeks of pregnancy. GWG is a modifiable factor, until such evidences become available, obstetricians and primary care practitioners can provider weight management suggestions to women in high risk of hypertensive disorders.(Seely EW and Maxwell C 2007) Thirds, different results were shown between women with full term births and preterm births, regarding the trajectories of GWG on blood pressure changes. We additionally assumed that the associations may vary by subtypes of preterm births (i.e., spontaneous preterm births and medically-indicated preterm births), because different mechanisms may exist between those subtypes and GWG and hypertensive disorders.(Kramer et al. 1995; Siega-Riz et al. 1996; Spinillo et al. 1998; Ehrenberg et al. 2003; Stotland et al. 2006; Rudra et al. 2008; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Carnero et al. 2012; Fujiwara et al. 2014) As such, a study with sufficient preterm delivery women were urgently needed, as simultaneously being preterm delivery and hypertensive disorders may double maternal and fetal mortality and morbidity. Lastly, we observed a 16.3-pound increase of weight among full term births' women of high growth trajectory at the 8^{th} week of gestation. Considering those women were in high risk of hypertensive disorders, the finding revealed an importance of managing weight gain at the very early stage of pregnancy. Therefore, in practices, health providers are encouraged to counsel women who intended to pregnancy or have pregnancy at initial stage with weight management, in order to lower the risks of hypertensive disorders.

The main strength of this study is the use of LCGM to identify GWG trajectories in early pregnancy and examined its associations with subsequent blood pressure change and PIH incidence. This method overcame the limitations in traditional methods of describing GWG (Gaillard et al. 2011; Hutcheon et al. 2012; Hutcheon et al. 2013; Macdonald-Wallis et al. 2013), and provided a unique advantage of discovering meaningful trajectories that may not be identified in prior recommendations.(Nagin DS 2005; Institute of Medicine(IOM) and National Research Council(NRC) 2009) For our study, results showed that 90% of women, who were classified in the high growth trajectory, were defined as excessive GWG based on 2009 IOM's recommendations.

However, in the post hoc analysis by using those categorical measurements of GWG at early pregnancy, we did not find a significant association between excessive GWG and hypertensive disorders (results not shown). This indicated that using cut-off points from certain guidelines alone were insufficient to lead weight-gain interventions on preventing adverse health outcomes.(Carmichael et al. 1997; Institute of Medicine(IOM) and National Research Council(NRC) 2009) Instead, a natural growth trajectory that can be identified in women with similar characteristics provides potential approach in health care practices. In addition, this study used a longitudinal design, which was superior in exploring the causal relationship between GWG and blood pressure change. Although our results are insufficient to prove the causality, they revealed temporality by showing that GWG precedes the blood pressure increase and the development of PIH. Findings are also plausible from the perspective of maternal physiological change that weight gain, especially abdominal fat accumulation increased both cardiac output and systemic vascular resistance increases, either of which would further induce blood pressure rise.(Institute of Medicine(IOM) and National Research Council(NRC) 2009)

Some methodological issues needed to be considered. Selection bias may occur in our analysis. First, after excluding participants without sufficient prenatal visit records, our final sample was reduced by 50% and their characteristics were different comparing to all eligible participants. Therefore, our results would be applicable to those women receiving routine prenatal care. Second, our results were generated from 1988 NMIHS data, and therefore may not reflect the contemporary situation. For example, we found non-Hispanic white and high-income women had a high rate of PIH, which was conflicting from current findings.(Gaillard et al. 2011; Liu et al. 2014) However, in spite of being a historic dataset, the 1988 NMIHS is still the latest**,** nationally representative database for American women. Also, using the data with few medical interventions to limit GWG and collected before the 1990 IOM's guidelines of GWG, our results were able to reflect the natural association between GWG and hypertensive disorders. Finally, information bias and residual confounding cannot be ruled out. For example, women's prepregnancy weight that available from health provider and hospital forms may be self-reported, which would result measurement error, particularly in high BMI status women.(Kuczmarski et al. 2001; Fattah et al. 2009) As a result, we may have overestimated amount of weight gain, especially in our lower and higher growth groups. However, we conducted sensitivity analyses by correcting prepregnancy weight in regression calibrations, which were created by comparing the measured and self-reported data in the Third National Health and Nutrition Examination Survey and have been applied in perinatal health research; (Burkhauser and Cawley 2008; Margerison Zilko et al. 2010) yet the association remained unchanged.

In conclusion, early GWG predicted blood pressure changes. Women in high growth group of GWG in early pregnancy were more likely to increase both SBP and DBP, and further increase the rate of PIH and hypertensive disorders. This strong and independent effect indicates that appropriate weight management during early pregnancy contributes to blood pressure control and reduces the development of PIH and preeclampsia. Intervention trials are needed to examine effective methods to assist women gain proper weight in early pregnancy in order to reduce risk of hypertensive disorders. The results will assist health providers provide individualized preconception or prenatal counseling to women about their weight gain during pregnancy.

Table 5.1. Maternal characteristics of women who included and excluded from the study

Characteristics	Included (n=3332)* N (%)	All(n=7903)* N (%)	P-value†
Maternal age			
≤20	340 (7.6)	1374 (12.8)	<0.001
20-24	861 (25.1)	2343 (28.4)	
25-29	1113 (35.2)	2230 (31.5)	
30-34	752 (23.7)	1415 (19.6)	
≥35	266 (8.4)	541 (7.7)	
Race/Ethnicity			
Hispanic	255 (9.2)	691 (12.8)	
Non-Hispanic white	1844 (77.3)	3150 (67.1)	<0.001
Non-Hispanic black	1121 (9.1)	3828 (15.7)	
Other	112 (4.4)	234 (4.4)	
Education			
<High school graduates	487 (11.7)	1861 (19.2)	<0.001
Some college graduates	1330 (39.4)	3183 (39.3)	
≥College graduates	1515 (48.9)	2859 (41.6)	
Parity status			
0	1137 (34.9)	2607 (34.8)	0.145
1	1031 (31.7)	2261 (30.4)	
≥2	1164 (33.5)	3006 (34.8)	
Missing		29	
Family income			
<10K	716 (14.2)	2601 (22.0)	<0.001
10K-<25,000	977 (28.4)	2454 (31.0)	
25K-<49,999	1141 (39.3)	2042 (32.8)	
≥49,999	498 (18.1)	806 (14.2)	
Marital status			
Yes	2457 (84.6)	4603 (74.0)	<0.001
No	875 (15.4)	3300 (26.0)	
Prepregnancy body mass index (kg/m^2)			
<18.5	290 (8.2)	797 (9.0)	0.200
18.5-24.9	2116 (67.8)	4956 (66.3)	
25-29.9	628 (16.4)	1410 (16.6)	
≥30	298 (7.6)	740 (8.1)	
Exercise during pregnancy			
No exercise	1979 (58.9)	4653 (57.3)	0.205
Exercise ≤5 months	471 (12.8)	1136 (13.2)	
Exercise >5 months	882 (28.3)	2114 (29.6)	
Smoking before pregnancy			
Yes	952 (28.7)	5514 (69.4)	0.151
No	2380 (71.3)	2389 (30.6)	

* The frequency within each cell was presented in unweighted number; all percentages within each cell were weighted.
† P value was based on χ^2 test of independence.

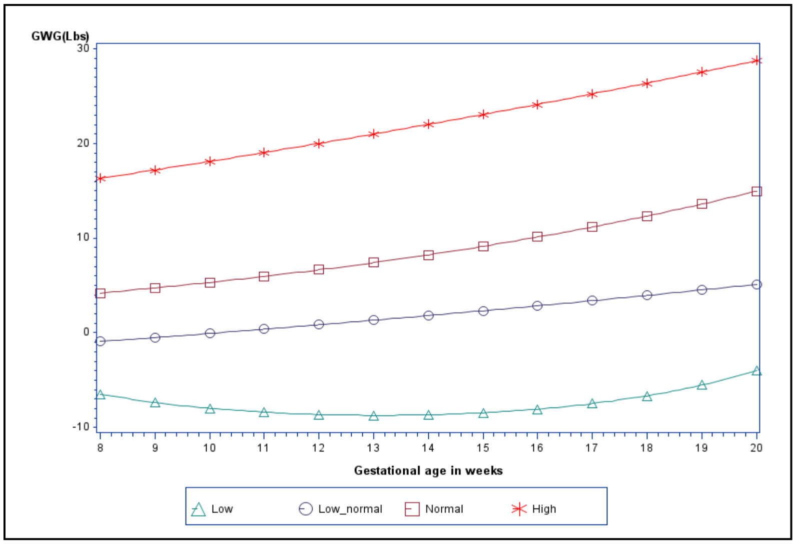

Figure 5.1. Four trajectories of weight gain in early pregnancy (8-20 weeks of gestation) among 3332 pregnant women in Unite States, 1988 National Maternal and Infant Health Survey

Table 5.2. Characteristics of participants by trajectories of GWG during early pregnancy (N=3332)[*]

Characteristics	Low N (%)[*]	Low-normal N (%)[*]	Normal N (%)[*]	High N (%)[*]	P-value[†]
Total	103(2.3)	1335(39.7)	1507(48.2)	387(9.9)	
Predicted GWG(95%CI) (at the 20th week)	-4.0 (-5.8,-1.8)	5.1(4.2,6.1)	15.0 (13.8,16.2)	28.8 (25.9,31.9)	<0.001
Total GWG at delivery[‡]					
Inadequate	72 (70.7)	546 (37.3)	191 (11.0)	10 (1.9)	
Adequate	20 (18.8)	494 (39.5)	476 (32.4)	31 (8.1)	<0.001
Excessive	11 (10.5)	295 (23.2)	840 (56.7)	346 (90.0)	
Maternal age					
<20	20 (16.2)	166 (8.6)	114 (5.9)	40 (9.9)	0.005
20-24	41 (33.2)	370 (28.7)	350 (21.8)	100 (25.1)	
25-29	30 (33.2)	423 (33.3)	529 (36.9)	131 (35.4)	
30-34	6 (11.1)	274 (22.0)	386 (26.3)	86 (20.2)	
≥35	6 (6.2)	102 (7.5)	128 (9.1)	30 (9.5)	
Race/Ethnicity					
Hispanic	10 (12.4)	104 (9.3)	112 (9.2)	29 (8.6)	<0.001
Non-Hispanic white	39 (58.6)	722 (76.1)	925 (80.4)	158 (70.7)	
Non-Hispanic black	50 (21.1)	454 (9.1)	427 (7.1)	190 (16.4)	
Other	4 (7.8)	55 (5.5)	43 (3.3)	10 (4.3)	
Education					
< High school graduates	25 (24.3)	206 (12.1)	179 (9.5)	77 (18.9)	<0.001
Some college Graduates	46 (43.5)	532 (39.9)	591 (38.7)	161 (39.5)	
≥College Graduates	32 (32.2)	597 (48.1)	737 (51.8)	149 (41.6)	
Parity status					
0	42 (39.0)	461 (33.9)	520 (35.2)	114 (36.4)	0.190
1	25 (21.7)	425 (34.6)	453 (30.7)	128 (27.1)	
≥2	36 (39.3)	449 (31.6)	534 (34.1)	145 (36.5)	
Family income					
<$10K	39 (29.6)	293 (13.7)	265 (12.4)	119 (21.5)	<0.001
$10K-<$25K	39 (29.0)	391 (29.5)	439 (27.8)	108 (27.3)	
$25K-<$49,999	21 (36.0)	484 (41.3)	514 (38.0)	122 (38.1)	
≥$49,999	4 (5.4)	167 (15.5)	289 (21.9)	38 (13.0)	
Marital status					
Yes	62 (74.6)	973 (85.2)	1170 (85.9)	252 (78.2)	0.004
No	41 (25.4)	362 (14.8)	337 (14.1)	135 (21.8)	
Prepregnancy body mass index (kg/m^2)					
<18.5	2 (0.4)	123 (8.1)	145 (9.4)	20 (4.5)	<0.001
18.5-24.9	45 (43.0)	826 (66.7)	1019 (70.5)	226 (64.3)	
25-29.9	33 (39.1)	255 (16.1)	243 (14.7)	97 (20.8)	

≥30	23 (17.5)	131 (9.1)	100 (5.4)	44 (10.4)	
Exercise during pregnancy					
No exercise	69 (71.3)	792 (58.6)	873 (57.7)	245 (63.3)	0.187
≤5 months	13 (13.4)	174 (11.9)	232 (13.8)	52 (10.6)	
>5 months	21 (15.3)	369 (29.5)	402 (28.5)	90 (26.1)	
Smoking before pregnancy					
Yes	21 (17.9)	346 (25.4)	446 (29.1)	139 (42.8)	<0.001
No	82 (82.1)	989 (74.6)	1061 (70.9)	248 (57.2)	
Preterm delivery					
<37 wks	19 (4.9)	239 (5.5)	284 (7.4)	65 (5.2)	0.047
≥37 wks	84 (95.1)	1096 (94.5)	1223 (92.6)	322 (94.8)	
Pregnancy-induced hypertension					
Yes	5 (4.0)	90 (6.6)	115 (7.9)	53 (16.1)	<0.001
No	98 (96.0)	1245 (93.4)	1392 (92.1)	334 (83.9)	
Preeclampsia					
Yes	3 (1.4)	48 (3.1)	52 (3.1)	23 (4.5)	0.497
No	100 (98.6)	1287 (96.9)	1455 (96.9)	364 (95.5)	

IQR: interquartile range; *GWG*: gestational weight gain; *wks*: weeks.

[*] The frequency within each cell was presented in unweighted number; all percentages within each cell were weighted.

[†] P value was based on χ^2 test of independence.

[‡] Gestational age was accounted for the determination of adequacy of GWG using the 2009 Institute of Medicine's recommendations.

Table 5.3. Correlates of the trajectories of GWG during early pregnancy (N=3332)*

	Low†		Low-normal†		High†	
Characteristics	AOR	(95%C.I.)	AOR	(95%C.I.)	AOR	(95%C.I.)
Maternal age						
<20	2.84	0.99, 8.12	2.12	1.35, 3.34	1.19	0.62, 2.29
20-24	1.76	0.88, 3.52	1.62		1.04	0.69, 1.57
25-29			Ref			
30-34	0.47	0.16, 1.38	0.93	0.72, 1.19	0.86	0.57, 1.29
≥35	0.67	0.18, 2.49	0.91	0.63, 1.32	1.15	0.65, 2.01
Race/Ethnicity						
Hispanic	0.96	0.37, 2.51	1.01	0.71, 1.42	0.94	0.54, 1.65
Non-Hispanic white			Ref			
Non-Hispanic black	2.19	1.14, 4.19	1.26	0.99, 1.60	2.38	1.68, 3.39
Other	3.60	1.07, 12.12	1.97	1.22, 3.20	1.89	0.83, 4.31
Education						
< High school graduates			Ref			
Some college Graduates	0.41	0.16, 1.05	0.87	0.61, 1.24	0.55	0.33, 0.94
≥College Graduates	0.52	0.23, 1.20	0.84	0.60, 1.17	0.55	0.35, 0.89
Parity status						
0			Ref			
1	0.73	0.34, 1.55	1.33	1.04, 1.69	0.86	0.58, 1.26
≥2	1.14	0.54, 2.40	1.14	0.89, 1.47	0.91	0.61, 1.35
Family income						
<$10K	1.16	0.48, 2.83	0.80	0.57, 1.12	1.10	0.68, 1.78
$10K-<$25K	0.76	0.35, 1.67	0.87	0.69, 1.11	0.83	0.56, 1.24
$25K-<$49,999			Ref			
≥$49,999	0.34	0.09, 1.27	0.70	0.53, 0.92	0.68	0.42, 1.11
Marital status						
Yes			Ref			
No	0.76	0.39, 1.50	0.85	0.62, 1.17	0.90	0.55, 1.46
Prepregnancy body mass index(kg/m^2)						
<18.5	0.06	0.01, 0.40	0.88	0.63, 1.23	0.43)	0.22, 0.86
18.5-24.9			Ref			
25-29.9	4.55	2.40, 8.63	1.19	0.91, 1.54	1.48	1.01, 2.17
≥30	4.57	2.01, 10.36	1.81	1.25, 2.61	1.74	1.01, 3.00
Exercise during pregnancy						
No exercise			Ref			
≤5 months	0.63	0.28, 1.45	0.81	0.61, 1.08	0.66	0.41, 1.07
>5 months	0.39	0.19, 0.80	1.03	0.83, 1.27	0.85	0.60, 1.22
Smoke before pregnancy						
Yes	0.38	0.18, 0.83	0.77	0.62, 0.96	1.73	1.25, 2.40
No			Ref			

CI, confidence interval.
*Significant effect P values <0.05. †AOR normal growth group was used as base outcome.

Table 5.4. Associations of the trajectories of GWG during early pregnancy with subsequent blood pressure change among normotensive women with full-term and preterm deliveries (N=3069)

	Full term birth (2507)				Preterm term birth (562)			
	Systolic blood pressure		Diastolic blood pressure		Systolic blood pressure		Diastolic blood pressure	
	Mean difference (95% C.I.)		Mean difference (95% C.I.)		Mean difference (95% C.I.)		Mean difference (95% C.I.)	
Trajectories of GWG (during early pregnancy)								
Low	-1.67	-3.20, -0.14	-1.22	-2.50, 0.06	2.43	-1.27, 6.12	1.89	-1.20, 4.97
Low-normal	-0.21	-0.76, 0.33	0.33	-0.13, 0.78	0.27	-1.09, 1.64	-0.10	-1.24, 1.04
Normal	Ref		Ref		Ref		Ref	
High	1.74	0.87, 2.60	0.92	0.19, 1.65	1.72	-0.54, 3.98	1.27	-0.61, 3.15
Rate of GWG (>20 wks)	1.90	1.33, 2.47	0.98	0.50, 1.46	1.58	0.52, 2.64	1.21	0.33, 2.09
Gestational age (at each prenatal visit)	0.37	0.34, 0.39	0.39	0.38, 0.41	0.41	0.32, 0.49	0.39	0.32, 0.46
Blood pressure (≤20 wks)	0.39	0.37, 0.42	0.21	0.19, 0.23	0.43	0.38, 0.49	0.20	0.15, 0.25
Maternal Age								
<20	0.01	-1.11, 1.13	-1.07	-2.01, -0.13	-1.54	-4.10, 1.02	-1.11	-3.25, 1.02
20-24	-0.26	-0.95, 0.42	-0.97	-1.54, -0.40	-1.66	-3.44, 0.11	-1.34	-2.83, 0.14
25-29	Ref		Ref		Ref		Ref	
30-34	0.31	-0.38, 0.99	0.16	-0.42, 0.73	-0.15	-1.93, 1.62	0.38	-1.10, 1.87
≥35	0.60	-0.41, 1.60	0.82	-0.02, 1.66	-1.04	-3.47, 1.39	-0.11	-2.16, 1.93
Race								
Hispanic	-0.93	-1.89, 0.03	0.43	-0.38, 1.24	-2.29	-4.59, 0.01	-2.42	-4.35, -0.49
Non-Hispanic white	Ref		Ref		Ref		Ref	
Non-Hispanic black	-0.65	-1.35, 0.04	-0.22	-0.80, 0.36	-1.09	-2.71, 0.52	-0.82	-2.16, 0.53
Other	-1.65	-2.99, -0.30	-0.21	-1.34, 0.93	-2.55	-6.23, 1.13	-2.00	-5.08, 1.08
Education								
<HS graduates	-0.74	-1.66, 0.17	-1.15	-1.92, -0.39	0.15	-1.97, 2.27	-1.34	-3.10, 0.43
Some college graduates	0.19	-0.39, 0.77	-0.19	-0.67, 0.30	-0.49	-2.06, 1.08	-0.88	-2.19, 0.43
≥College graduates	Ref		Ref		Ref		Ref	

Parity status								
0	0.91	0.23, 1.58	1.17	0.60, 1.73	1.38	-0.29, 3.04	1.37	-0.02, 2.76
1	-0.07	-0.70, 0.55	0.07	-0.46, 0.59	0.36	-1.24, 1.96	-0.25	-1.59, 1.09
≥2	Ref		Ref		Ref		Ref	
Family income								
<$10K	-0.55	-1.39, 0.29	-0.26	-0.97, 0.45	1.00	-1.03, 3.03	0.60	-1.09, 2.29
$10K-<$25K	0.01	-0.63, 0.66	-0.10	-0.64, 0.45	0.46	-1.22, 2.13	-0.15	-1.55, 1.26
$25K-<$49,999	Ref		Ref		Ref		Ref	
≥$49,999	-0.05	-0.82, 0.72	0.32	-0.33, 0.97	0.07	-2.12, 2.27	0.32	-1.52, 2.16
Marital status								
Yes	Ref		Ref		Ref		Ref	
No	0.06	-0.73, 0.84	-0.06	-0.72, 0.60	0.21	-1.49, 1.90	-0.12	-1.53, 1.30
Prepregnancy body Mass Index(kg/m^2)								
<18.5	-1.37	-2.28, -0.46	-0.55	-1.31, 0.21	-0.96	-3.13, 1.20	-0.39	-2.19, 1.42
18.5-24.9	Ref		Ref		Ref		Ref	
25-29.9	2.32	1.63, 3.01	1.71	1.13, 2.29	0.59	-1.09, 2.27	1.12	-0.28, 2.52
≥30	3.76	2.79, 4.74	2.46	1.64, 3.28	3.61	1.18, 6.04	3.81	1.78, 5.84
Exercise during pregnancy								
No exercise	Ref		Ref		Ref		Ref	
≤5 months	0.21	-0.55, 0.97	-0.11	-0.75, 0.53	0.14	-1.60, 1.88	-0.12	-1.57, 1.33
>5 months	0.01	-0.56, 0.58	-0.03	-0.51, 0.45	-1.16	-2.77, 0.44	-0.83	-2.19, 0.52
Smoke before pregnancy								
Yes	0.56	-0.03, 1.14	-0.58	-1.07, -0.09	0.30	-1.07, 1.67	-1.11	-2.25, 0.04
No	Ref		Ref		Ref		Ref	

C.I., confidence interval; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *GWG*, gestational weight gain; wks, weeks.

*Significant effect P values <0.05.

Table 5.5. Association of the trajectories of GWG during early pregnancy and the risk of PIH and preeclampsia (N=3332)

	Pregnancy- Induced Hypertension		Hypertensive disorders[†]	
	Adjusted RR (95% C.I.)		Adjusted RR (95% C.I.)	
Trajectories of GWG(during early pregnancy)				
Low	0.50	0.17, 1.48	0.52	0.25, 1.08
Low-normal	0.90	0.65, 1.24	0.95	0.75, 1.21
Normal	Ref		Ref	
High	2.02	[illegible]	[illegible]	[illegible]43, 2.55
Gestational age (at each prenatal visit)	1.04	[illegible]	[illegible]	[illegible]98, 1.04
Rate of GWG (>20 wks)	2.01	1.52, 2.65	1.81	1.48, 2.21
Maternal Age				
<20	1.20	0.68, 2.15	1.21	0.77, 1.90
20-24	1.11	0.75, 1.64	1.21	0.90, 1.63
25-29	Ref		Ref	
30-34	1.33	0.91, 1.96	1.27	0.95, 1.70
≥35	1.39	0.80, 2.39	1.62	1.10, 2.41
Race/Ethnicity				
Hispanic	0.82	0.49, 1.39	0.73	0.48, 1.11
Non-Hispanic white	Ref		Ref	
Non-Hispanic black	0.58	0.37, 0.90	0.72	0.53, 0.98
Other	1.09	0.53, 2.24	0.84	0.46, 1.53
Education				
<HS graduates	0.91	0.53, 1.55	1.21	0.81, 1.79
Some college graduates	1.10	0.79, 1.52	1.18	0.93, 1.50
≥College graduates	Ref		Ref	
Parity status				
0	Ref		Ref	
1	0.71	0.51, 0.98	0.73	0.56, 0.93
≥2	0.55	0.38, 0.77	0.60	0.46, 0.77
Family income				
<$10K	0.88	0.52, 1.48	0.83	0.56, 1.23
$10K-<$25K	0.94	0.64, 1.37	1.05	0.79, 1.39
$25K-<$49,999	Ref		Ref	
≥$49,999	1.36	0.92, 2.01	1.35	1.00, 1.83
Marital status				
Yes	Ref		Ref	
No	1.00	0.62, 1.62	0.84	0.58, 1.21
Prepregnancy BMI status (kg/m^2)				
<18.5	0.56	0.25, 1.25	0.52	0.27, 0.99
18.5-24.9	Ref		Ref	
25-29.9	2.26	1.63, 3.12	2.46	1.94, 3.12
≥30	3.63	2.44, 5.40	3.56	2.65, 4.79

Exercise				
No exercise	Ref		Ref	
≤5m	0.80	0.51, 1.26	0.92	0.67, 1.26
>5m	0.75	0.52, 1.06	0.80	0.61, 1.04
Smoke before pregnancy				
Yes	0.95	0.69, 1.30	0.84	0.66, 1.07
No	Ref		Ref	

CI, confidence interval; *RR*, rate ratio; *GWG*, gestational weight gain; wks, weeks.
[*]Significant effect P values <0.05.
[†]Hypertensive disorders include PIH and preeclampsia.

CHAPTER 6

MANUSCRIPT 2: ASSOCIATIONS OF GESTATIONAL WEIGHT GAIN AND SUBTYPES OF PRETERM DELIVERIES ESTIMATED WITH MARGINAL STRUCTURAL MODELS[2]

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Abstract

Background: The association between gestational weight gain (GWG) and preterm births is largely unknown. We proposed to 1) describe GWG in early pregnancy (≤20 weeks' gestation) and mid-late pregnancy (>20 weeks' gestation) and explore their correlates and 2) to estimate the total effect of GWG in early and mid-late pregnancy on the odds of preterm birth while considering hypertensive disorders as an intermediator.

Method: Data came from the 1988 National Maternal and Infant Health Survey, restricting to women free of chronic hypertension and gestational diabetes, with ≥1 prenatal records in early pregnancy and ≥2 records in mid-late pregnancy. Marginal structural models were used to adjust for time-dependent confounding by hypertensive disorders, pregnancy induced hypertension and preeclampsia.

Result: Only 16.4% and 30.4% of women gained adequate weight in early pregnancy and mid-late pregnancy, respectively. The percentages of developing hypertensive disorders were lowest among women of inadequate GWG and highest among women of excessive GWG (p for trend <0.001) in both periods of pregnancy. Among normal weight women, both inadequate and excessive GWGs in mid-late pregnancy were associated increased risk of spontaneous preterm births, while excessive GWG in mid-late pregnancy increased risk of medically indicated preterm births. Among overweight and obese women, women with inadequate weight gain in early pregnancy were protected from medically indicated preterm births.

Conclusion: These results suggest that appropriate weight gain in pregnancy holds promise to reduce the risks of preterm births. Our method also provides an alternative approach of low costs and free of ethical concern to examine causal associations.

Introduction

Preterm birth, defined as delivery occurring before 37 weeks of gestation, and is further categorized into three clinical conditions: medically indicated preterm births, preterm premature rupture of membranes, and spontaneous preterm births.(Carmichael et al. 1997; Blackmore-Prince et al. 1999; Schieve et al. 2000) Preterm birth is a major cause of neonatal morbidity and mortality and has long-term adverse consequences on the health of surviving infants.(Lawn et al. 2005; Kaempf et al. 2006; Morgan et al. 2008; Saigal and Doyle 2008) However, each year, one out of every eight infants in the United States (U.S.) was delivered preterm and more than $26 billion was cost for caring for those preterm births.(Martin JA et al. 2012; American College of Obstetricians and Gynecologists 2013; Martin et al. 2013) Thus, more knowledge on how to prevent or lower the risk of preterm births is warranted.

Both prepregnancy body mass index (BMI) and gestational weight gain (GWG) are potential modifiable risk factors for preterm births.(Berkowitz et al. 1998; Rudra et al. 2008; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Wise et al. 2010; Gawade et al. 2011; Carnero et al. 2012; American College of Obstetricians and Gynecologists 2013; Masho et al. 2013; Fujiwara et al. 2014; Park et al. 2014) However, compliance with weight loss interventions is low, and therefore, strategies are needed to encourage women to adhere to the interventions.(Flodgren et al. 2010) Pregnancy provides a "teachable moment" as women at that time are more self-conscious about their health conditions.(Phelan 2010) Yet, the association between GWG and preterm births remains unclear, partly due to methodological issues in studying this question. One of problems is that the subtypes of preterm births have different pathophysiological mechanisms.(Savitz 2008) Previous studies have shown a strong association between excessive GWG and an increased risk of medically indicated preterm births via cesarean delivery.(Berkowitz et al. 1998; Rudra et al. 2008; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Wise et al. 2010; Gawade et al. 2011) However, the findings are inconsistent with the effect of inadequate GWG on both spontaneous and medically indicated preterm births. (Carnero et al. 2012; Masho et al. 2013; Fujiwara et al. 2014; Park et al. 2014) Furthermore, analyzed approaches used in previous studies are problematic. First, weight gain changes during pregnancy; thus total GWG at delivery, a frequently used measure, is not measured accurately because weight gain in the second or third trimesters has a stronger associations with preterm births rather than weight gain in the first trimester.(Hickey et al. 1995; Rudra et al. 2008; Wise et al. 2010) Second, as GWG by definition changes over the course of pregnancy, GWG measured in the second and third trimesters is prone to time varying confounding. For example, as shown in Figure 1, hypertensive disorders can be affected by earlier GWG, and affect subsequent GWG and preterm births.(Hickey et al. 1995; Thangaratinam et al. 2012; Drehmer et al. 2013; Gaillard et al. 2013; Masho et al. 2013; Xinxo et al. 2013; Fujiwara et al. 2014) Thus, it is likely to be a confounder and intermediate variable, simultaneously. In addition, it is biologically plausible that hypertensive disorders may modify the effect of GWG on preterm birth. As a result, traditional methods of evaluating the relation between GWG and preterm births are criticized at two levels: first, adjustment for hypertensive disorders (an intermediate variable) leads to bias; and second, those methods fail to account for possible interaction between GWG and hypertensive disorders on preterm births.(Robins et al. 2000; Richiardi et al. 2013)

To address the gaps in literature, this study has two objectives: 1) to describe GWG pattern in early pregnancy (≤20 weeks' gestation) and mid-late pregnancy (>20 weeks' gestation) and explore the correlates of GWG, and 2) to estimate the overall causal effect of GWG during pregnancy, a time-varying exposure, on the odds of preterm births. Marginal structural models (MSMs) were used to adjust for time-dependent confounding by hypertensive disorders.(Robins et al. 2000; Bodnar et al. 2004)

Methods

Study design and Subjects

This was a prospective cohort study using data from the 1988 National Maternal and Infant Health Survey (NMIHS), a survey which was designed to study the factors related to poor pregnancy outcomes and conducted by the National Center for Health Statistics (NCHS). In total, a nationally representative sample of U.S. mothers who delivered a baby in 1988 was randomly drawn from vital records from 48 states, the District of Columbia, and New York City (13,417 live births). Black infants and low birth weight infants (<1500 gram, 1500-2499 gram, 2500+ gram) were oversampled. The survey consisted of three parts: mother's questionnaire, the 1988 birth certificates, and prenatal care provider and/or hospital administrator questionnaires. Mother's questionnaires were administrated postpartum with a mean interval of 17 months between delivery and interview. The overall response rate was 71%. Each record was assigned a final weight to reflect the complex survey design.(Sanderson and Gonzalez 1998) The details of NMIHS were presented elsewhere.(Sanderson and Gonzalez 1998)

We included 9953 participants who gave live births and had a complete hospital/provider form.(Schieve et al. 2000) We further restricted to 7106 women who delivered a singleton birth between 20-44 weeks, were free of chronic diabetes, chronic hypertension, gestational diabetes in this pregnancy, and with prepregnancy BMI above 18.5 kg/m^2. Women with preexisting medical conditions were excluded because related medical interventions might modify weight gain during pregnancy. We focused on normal and overweight or obese women and provided provisional data for underweight women (Table 4), due to the small sample size of underweight women (N=328) and nine underweight women being diagnosed with hypertensive disorders. To examine the changing rate of GWG during pregnancy and its associations with hypertensive disorders and preterm births, participants were required to 1) have at least one prenatal care visits between 8 to 20 weeks' gestation and at least two prenatal care visits after 20 weeks' gestation (excluding records on delivery day) (N=3433), and 2) have available data (i.e., records of labor and rupture of membranes) to define the subtypes of preterm birth. The above inclusion and exclusion criteria resulted in 3320 women remaining in the final analyses.

Preterm births

Preterm birth was defined as less than 37 weeks of gestation. Gestational age at delivery was abstracted from vital records. We abstracted data from hospital and care providers to determine two clinical subtypes of preterm birth: spontaneous or medically indicated preterm birth.(Carmichael et al. 1997; Blackmore-Prince et al. 1999; Schieve et al. 2000) If the record showed a woman experienced premature rupture of membranes or her labor began spontaneously (not medically induced), the woman was defined as having a spontaneous preterm birth. Medically indicated preterm births were defined as those having either artificial rupture of membranes to induce labor, drugs used to induce labor in the absence of ruptured membranes, or having a cesarean section in the absence of either spontaneous preterm births.(Carmichael et al. 1997)

Gestational weight gain

Serial weight measurements at each prenatal visit and associated gestational ages were recorded on the hospital/provider questionnaires.(Schieve et al. 2000) Gestational age at each prenatal visit was computed as the number of weeks between the last menstrual period (LMP) and the date of prenatal visits. Data on mother's prepregnancy weight were primarily obtained from the prenatal care provider/hospital questionnaire (87.6%), which was supplemented by prepregnancy weight from birth certificates (12.4%) when data were missing in provider questionnaire.(World Health Organization 2012)

To consider the time varying effect of GWG on preterm birth, with hypertensive disorders being an intermediate factor on the pathway from GWG to preterm births, GWG was calculated for early (≤20 weeks) and mid-late (>20 weeks) pregnancy, respectively. GWG in early pregnancy was computed by the last record of mother's weight before 20 week's gestation (average of 18 week, interquartile range [IQR]:17-19 week) less mother's prepregnancy weight. Women's GWG in mid-late pregnancy was calculated as mother's weight at delivery room less the last record of mother's weight before 20 week's gestation. Adequacy ratio of GWG was adopted to categorize GWG in each period as: inadequate, adequate and excessive gain. Specifically, according to the 2009 Institutes of Medicine (IOM) guidelines, it assumes that normal weight (18.5–24.9

kg/m^2) women typically gain 4.4 lbs during the first 12 weeks of pregnancy, while overweight (25.0–29.9 kg/m^2) women gain 2.2 lbs and obese (≥30.0 kg/m^2) women gain 1.1 lbs.(Institute of Medicine(IOM) and National Research Council(NRC) 2009) These assumptions as well as the weight gain in second and third trimester were used to obtain the adequacy of GWG in relation to 2009 IOM guidelines. (Bodnar et al. 2004; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Bodnar et al. 2010) We considered this measurement is independent with gestational age, which reduces the misclassification of GWG as the results of inconsistent cut off points between two pregnancy periods among women. In addition, to minimize effects of data entry or recording errors, implausible GWG values at certain prenatal visits (weight gain >80 lbs or < -30 lbs) were recoded as missing values (n<30).(Hutcheon et al. 2013) How many measurements of GWG were made? Maybe sub-headings will make that more clear? E.g. *GWG early pregnancy:*

Pregnancy-induced hypertension and preeclampsia

As we hypothesized early, hypertensive disorders can be an intermediator on the pathway from GWG to preterm births. Provider/hospital questionnaires included data on serial systolic and diastolic blood pressure measurements and urine protein test results.(Gunderson et al. 2000) PIH was defined as having at least two occasions of systolic blood pressure equal or greater than 140 mmHg or diastolic blood pressure equal or greater than 90 mmHg, and without proteinuria after the 20th week of gestation.(Leeman and Fontaine 2008) Preeclampsia was further defined as the development of PIH and proteinuria after the 20th week of gestation. Due to lack of data, our definition of preeclampsia could not take into account organ function, which is included in the new American Congress of Obstetricians and Gynecologists (ACOG) definition of preeclampsia.(American College of Obstetricians and Gynecologists 2013) Hypertensive disorders were defined as women developed either PIH or preeclampsia (Mean=31 weeks of gestation, interquartile range, 25 to 36 weeks of gestation).

Covariates

Data on mother's age, race, highest education, marital status, smoking status before pregnancy, and parity were obtained from vital records. Data on family income and physical activity before pregnancy were taken from mother's questionnaire. Women were defined as 'none exerciser' if they responded "no" to the question "Did you exercise or play sports at least three times a week after you found out you were pregnant?" Women's prepregnancy body mass index (BMI) was calculated by dividing prepregnancy weight in kilograms by the square of measured height in meters, and further categorized as underweight (<18.5), normal weight (18.5–24.9), overweight (25.0–29.9), and obese (≥30).(Druzin et al. 2008) The categorizations of these variables were shown in Table 1.

Statistical analyses

Motivation for MSMs. We aimed at studying the total causal effect of maternal GWG on preterm births via both direct and indirect pathways through hypertensive disorders (Figure 1). The causal effect is defined as the contrast in an individual with two potential outcomes (preterm vs not preterm births). MSMs create a pseudo population in which factors influenced by the initial exposure do not predict subsequent exposure. The counterfactual contrast obtained in this way represents the difference in the outcome when all individuals were exposed versus none were exposed. In the context of this study, GWG in the mid-late pregnancy would not be affected by hypertensive disorders in the pseudo population. MSMs would estimate the counterfactual difference in preterm births if all individuals had inadequate or excessive GWG versus all had adequate weight gain.(Robins et al. 2000; Bodnar et al. 2004) More details are described below.

Effect of GWG on preterm birth. MSMs were completed in a three-stage process. In stage I, baseline exposure (GWG_1 in Figure 1) was modeled as an outcome. After adjusting all covariates mentioned above (L_1), a probability of associated with certain category of GWG_1 would be estimated. Then, based on those probabilities, each woman was assigned with a stabilized inverse-probability-of GWG category weights (IPW_1) (1). The lower the IPW_1 of a woman assigned, the higher the probability that the woman was in the certain category of GWG in the pseudo population and vice-versa. The purpose of allocating IPW_1 to each woman was to weight covariate distributions for women in different GWG categories. In the other words, this process created a pseudo population in which GWG category and the covariates were no longer associated with each other. In stage 2, similar procedure was applied by modeling the secondary exposure effect (GWG_2 in Figure 1) as an outcome. All baseline covariates, GWG_1 category (i.e., inadequate, adequate and excessive GWG during early pregnancy), PIH were incorporated in the regression model to derive secondary probabilities for each woman. Correspondingly, each woman was assigned stabilized inverse-probability of GWG categories weights at mid-late pregnancy (IPW_2) (2). To estimate the causal association of two exposures (i.e., GWG before and after 20 weeks' gestation) through MSMs, we recomputed final inverse probabilities weight (IPW) by multiplying IPW_1 and IPW_2. The details have been described in previous studies.(Robins et al. 2000; Bodnar et al. 2004)

$$IPW_1=P(GWG_1=gwg_{1i})/P(GWG_1=gwg_{1i}|L_1=l_{1i}) \quad (1)$$

$$IPW_2=P(GWG_2=gwg_{2i}|GWG_1=gwg_{1i})/P(GWG_1=gwg_{0i}|GWG_0=gwg_{0i},L_1=l_{1i},PIH=pih_{2i}) \quad (2)$$

In stage 3, we employed a marginal model with weighted function of the stabilized IPW and two exposures (GWG_1 and GWG_2) on the outcome of preterm births in this final pseudo population to obtain the causal parameters. Under the stabilized IPW, all the covariates and potential mediator were no longer associated with GWG. We then performed interaction test between hypertensive disorder and GWG_1 and $GWG_{2,}$ respectively (P-values >0.05).

Analysis plans. Analyses were done using SAS software (version 9.3, SAS Institute, Cary, NC). PROC GENMOD was applied to model the marginal effects. Because PROC GENMOD is often used for binary outcomes, analyses were performed in term births' mothers and spontaneous preterm births' mothers or term births' mothers and medically indicated preterm births' mothers. Specifically, to examine the effect of GWG on spontaneous preterm births, we excluded women with medically indicated preterm births from analysis (N=143) or vice versa. Although the interaction term between prepregnancy BMI and GWG was not significant in any preterm birth subtypes, we stratified all models by prepregnacy BMI based on previous reports,(Spinillo et al. 1998; Schieve et al. 2000; Dietz et al. 2006; Smith et al. 2007) the theoretical plausibility of such effect modification, as well as the importance of the maternal prepregnancy BMI identified in previous reports and recommendations.(Institute of Medicine(IOM) and National Research Council(NRC) 2009) We focused on the pathway through hypertensive disorders of PIH and preeclampsia, but also provide analysis on the pathway through PIH. Finally, we tested interaction between hypertensive disorders and GWG. All P-values were two-tailed, and values that less than 0.05 were considered to indicate statistical significance.

Results

Our final analytical sample (N=3322) had higher proportions of women who were aged ≥25 years, non-Hispanic white, college graduates, married, coming from households with an income ≥$25K, comparable to the 7106 women with singleton live births, with prepregnancy BMI ≥18.5, and without preexisting medical conditions and gestational diabetes in this pregnancy (Table 1).

In early pregnancy (<20 weeks), only 16.4% of women gained adequate weight and the percentage increased to 30.4% in mid-late pregnancy (20-44 weeks). Compared to women with adequate GWG in early pregnancy, women with inadequate GWG were younger (<25 years), more likely to be Black, obese, poor, and less educated. In mid-late pregnancy, more black, multiparous (≥2) and obese women had inadequate GWG, while younger, White, nulliparous, and overweight or obese women had excessive GWG in mid-late pregnancy compared to women with adequate GWG. Hypertensive disorders were the lowest among women with inadequate GWG and highest among women with excessive GWG (p for trend <0.001) in both periods of pregnancy.

Association between GWG and preterm birth using MSMs. Table 3 shows the adjusted odds ratios with stabilized weighting in marginal structure models by prepregnancy BMI status. We focus on hypertensive disorders as the mediator; however, results were similar as we repeated our analyses by individual PIH. Among normal weight women, spontaneous preterm birth was more likely among those with inadequate GWG (OR=1.57 95% CI, 1.08, 2.22), and excessive GWG (OR=1.46, 95% CI, 1.02, 2.09), compared to women with adequate GWG. Regard to medically indicated preterm birth, it was more likely among women with excessive GWG in mid-late pregnancy compared to women with adequacy GWG (OR=1.94, 95% CI, 1.12, 3.36). Among overweight or obese women, medically indicated preterm birth was less likely among those with inadequate GWG (OR, 0.4, 95% CI, 0.12, 0.98), compared to women with adequate GWG. In addition, the interaction between hypertensive disorders and GWG was insignificant and all above results remained unchanged when we stratified by hypertensive disorders' status.

Discussion and conclusions

In a prospective analysis using MSMs, spontaneous preterm birth was more likely among normal weight women who had inadequate or excessive GWG in mid-late pregnancy (>20 weeks). In this group of women excessive GWG in mid-late pregnancy was associated with increased risk of medically indicated preterm birth. Among overweight or obese women, inadequate GWG in early gestation was associated with reduced risk of medically indicated preterm birth. There was no evidence of effect modification by hypertensive disorders. The use of MSMs estimated causal effects by correcting for time-dependent confounding.

In this study, we examined the GWG in two periods of pregnancy and its correlates. We applied MSMs and found weight gain in mid-late pregnancy was associated with increased risk of both types of preterm birth among normal weight women. A U-shape association of both inadequate and excessive GWG in mid-late pregnancy was positively associated with spontaneous preterm births.(Kramer et al. 1995; Siega-Riz et al. 1996; Spinillo et al. 1998; Schieve et al. 1999; Ehrenberg et al. 2003; Dietz et al. 2006; Stotland et al. 2006; Han et al. 2011; Carnero et al. 2012; Fujiwara et al. 2014) Excessive GWG in mid-late pregnancy increased the odds of having medically indicated preterm births(Berkowitz et al. 1998; Rudra et al. 2008; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Wise et al. 2010; Gawade et al. 2011). Among overweight and obese women, we found that women who gained inadequate weight in early pregnancy were protected from medically indicated preterm births.(Rudra et al. 2008)

These findings were consistent with, those from previous studies. (Kramer et al. 1995; Siega-Riz et al. 1996; Berkowitz et al. 1998; Spinillo et al. 1998; Schieve et al. 1999; Ehrenberg et al. 2003; Dietz et al. 2006; Stotland et al. 2006; Rudra et al. 2008; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Wise et al. 2010; Gawade et al. 2011; Han et al. 2011; Carnero et al. 2012; Fujiwara et al. 2014) First, the association between GWG and subtypes of preterm births is physiologically plausible. GWG during early pregnancy is largely attributed to the expansion of maternal tissues, while GWG from mid-late pregnancy reflects mostly fetal and placental growth and amniotic fluid accumulation.(Neufeld et al. 2004) The increased odds of spontaneous preterm births among women with inadequate GWG in mid-late pregnancy can be explained by the placental dysfunction theory. Inadequate weight gain in mid-late pregnancy may be the result of malnutrition, resulting in placental growth retardation, which stimulates stress hormones such as norepinephrine and cortisol release, resulting in prostaglandin production, inducing uterine contractions and subsequent preterm delivery.(Tsukamoto et al. 2007; Durie et al. 2011; Wang et al. 2011) Excessive spontaneous preterm births among women with excessive GWG may be attributed to the increased levels of inflammatory proteins,(Romero et al. 2006) which promote cervical ripening, but their overproduction may weaken amniotic membranes, cause myometrium' contractions, and further induce preterm delivery.(Romero et al. 1998; Goldenberg et al. 2000; Institute of Medicine (IOM) 2007) Previous studies have shown that visceral fat mass increases during pregnancy is associated with the rise of inflammatory proteins.(Soltani and Fraser 2000; Ramsay et al. 2002; Wisse 2004) Reasons for excessive GWG inducing medically indicated preterm births are complicated, which may be the remedial action when labor was failure to progress or caused by clinical concerns for the infant or the mothers, such as hypertensive disorders and macrosomia.(Stotland et al. 2004; Oken et al. 2009) Yet, many of the reasons were associated with excessive weight gain during pregnancy, which are consistent to our findings of increased odds of medically indicated preterm births among women who gained excessive in mid-late pregnancy. (Abrams et al. 1995; Abrams and Selvin 1995; Thorsdottir et al. 2002; Jensen et al. 2005; Khalil et al. 2009)

Second, a protective effect of inadequate GWG on medically indicated preterm births was found in early pregnancy among overweight and obese women.(Rudra et al. 2008; Cnattingius et al. 2013) Maternal obesity before pregnancy is a strong risk factor for medically indicated preterm births.(Berkowitz et al. 1998; Rudra et al. 2008; Institute of Medicine(IOM) and National Research Council(NRC) 2009; Wise et al. 2010; Gawade et al. 2011; Cnattingius et al. 2013) Hypertensive disorders have been considered to play an important role on this pathway.(Nohr et al. 2007; Khatibi et al. 2012) Among overweight and obese women, the effect of overweight on preterm birth may be larger than the indirect effect via hypertensive disorders. Studies have shown that restrained GWG in early pregnancy, particularly in overweight and obese women, benefits hypertensive disorders risk reduction.(Gaillard et al. 2013; Macdonald-Wallis et al. 2013) Therefore, as fewer women developed hypertensive disorders, the indirect effect of GWG in early pregnancy and preterm births via hypertensive disorders decreased. However, MSMs estimate the total effect GWG on preterm birth, and hence we could not separate the direct and indirect effects in this analysis. Future studies using time-varying exposure mediation analysis are warranted to examine the exact amount of the reduced indirect effect.(VanderWeele TJ and Vansteelandt S 2009; VanderWeele 2010; VanderWeele 2013)

Lastly, correlates of GWG differed in two periods, suggesting that weight management intervention should be tailored by the stages of pregnancy. For instance, before pregnancy and early pregnancy, adolescent mothers could be encouraged to achieve good nutritional status in order to ensure fetal growth needs.(Groth 2006) However, as observed in ours and other related studies(Institute of Medicine(IOM) and National Research Council(NRC) 2009), more young mothers (<20 years) gained excessive GWG in the mid-late pregnancy or at delivery. This on one hand informs proper weight control programs should be designed for adolescent mothers, because high weight gain is a major reason for an increased risk of obesity those mothers.(Groth 2006) One the other hand, IOM recommendations are needed to be re-examined to recommend enough weight gain in adolescents. Furthermore, parity only played a role in mid-late pregnancy, which suggests that health intervention of GWG in mid-late pregnancy should be differentiated by nulliparous and multiparous women. By tailoring the intervention activities by women characteristics and pregnancy process, improve the effectiveness of health counselling or interventions in practice.

As discussed above, main strengths of this study are the use of MSMs to examine the periodic effect of GWG on different types of preterm births. By separating GWG into early and mid-late pregnancy, we precluded the impact of lateral hypertensive disorders associated edema on the early GWG. This provided a unique way to identify independent effects of GWG in early gestation on preterm births. We further applied MSMs to account for the possible effect modification by hypertensive disorders. Moreover, this study used a longitudinal design, which was superior in exploring the causal relationship between GWG and subtypes of preterm births. The results suggest that interventions encouraging GWG management in the mid-late pregnancy among normal weight women may be beneficial and clinically relevant. Health counselling of weight reduction during early pregnancy is beneficial to overweight and obese women to reduce medically indicated preterm births.

Although this study has multiple strengths as discussed above, our study has several limitations. First, after excluding participants without sufficient prenatal visit records, our sample size was only half of participants and their characteristics were different comparing to all eligible participants. Therefore, our results would only be appropriate to those women receiving routine prenatal care. Second, our results were generated from 1988 NMIHS data, and therefore may not reflect the contemporary situation.(Gaillard et al. 2011; Liu et al. 2014) To our knowledge, the 1988 NMIHS is still the last available nationally representative sample in the US on pregnancy. This database provided a unique opportunity to observe the natural association between GWG and preterm births in 1988 when medical interventions on GWG were limited in the US. Also, the assumed weight gain for specific prepregnancy BMI in the first trimester was based on the data from the mid-late 1980s,(Siega-Riz et al. 1994; Abrams et al. 1995) thus NMIHS is an appropriate dataset that helps to preclude biases because of the measurement assumption. Finally, information bias and residual confounding cannot be ruled out. The prepregnancy weight may have measurement error, particularly in women with high BMI.(Kuczmarski et al. 2001; Fattah et al. 2009) However, we conducted sensitivity analyses by correcting prepregnancy weight in regression calibrations, which were created by comparing the measured and self-reported data in the Third National Health and Nutrition Examination Survey and have been applied in perinatal health research.(Burkhauser and Cawley 2008; Margerison Zilko et al. 2010) The association remained unchanged.

In brief, excessive GWG after 20 weeks' gestation was positively associated with both spontaneous and medically indicated preterm births among normal weight women, and inadequate GWG before 20 weeks' gestation was inversely related to medically indicated preterm births among overweight or obese women in causal models from a longitudinal study using MSMs. The findings are clinically important because they identify a possible window for health interventions to reduce preterm births.

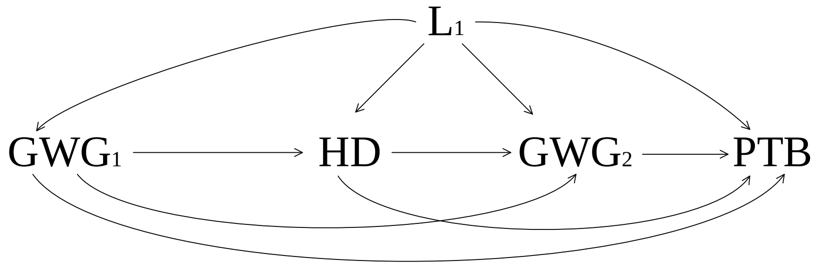

Figure 6.1. Directed acyclic graph for GWG and preterm birth. The graph depicts the assumed association between study varaibles. L_1=historic covariates including characteristics and health behaviors; HD= hypertensive disorders during pregnancy, time-varying covariates; GWG_1=GWG in early pregnancy; GWG_2=GWG in mid-late pregnancy; PTB=preterm births. Time-dependent confounding occurs through HD variables, which are part of directed path from GWG_1 to PTB, but a back-door path from GWG_2 to PTB.

Table 6.1. Sample characteristics of included study participants in comparison to total

Characteristics	Included (N=3,322) N (%)†	Total (N=7,106)* N (%)†	P-value‡
Maternal age			
≤20	370 (8.6)	1,175 (12.2)	<.0001
20-24	871 (25.5)	2,074 (28.0)	
25-29	1,093 (34.6)	2,017 (31.7)	
≥30	988 (31.2)	1,840 (28.2)	
Race/Ethnicity			
Hispanic	264 (10.1)	633 (13.1)	<.0001
Non-Hispanic white	1,780 (76.0)	2,845 (67.3)	
Non-Hispanic black	1,174 (9.8)	3,430 (15.5)	
Other	104 (4.2)	198 (4.1)	
Education			
< High school graduates	516 (12.5)	1,627 (18.4)	<.0001
Some college graduates	1,334 (40.1)	2,862 (39.6)	
≥College graduates	1,472 (47.4)	2,617 (42.0)	
Parity			
0	1,103 (34.3)	2,283 (34.1)	0.0330
1	1,033 (31.7)	2,054 (30.4)	
≥2	1,186 (34.0)	2,741 (35.5)	
Family income			
<25K	1,752 (44.5)	4,496 (52.3)	<.0001
≥25K	1,570 (55.5)	2,610 (47.7)	
Marital status			
Yes	2,384 (83.3)	4,205 (74.9)	<.0001
No	938 (16.7)	2,901 (25.1)	
Prepregnancy BMI status (kg/m^2)			
18.5-24.9	2,309 (73.5)	4,956 (72.9)	0.5216
25.0-29.9	675 (17.8)	1,410 (18.3)	
≥30.0	338 (8.8)	740 (8.6)	
Physical activity before pregnancy			
No exercise	1,750 (53.3)	4,191 (57.3)	0.2068
Exercise	1,572 (46.6)	2,915 (42.7)	
Smoking before pregnancy			
Yes	966 (29.1)	2,111 (29.9)	0.2143
No	2,356 (70.9)	4,995 (70.1)	

* Total were defined for those women who delivered a singleton birth between 20-44 weeks, were free of chronic diabetes, chronic hypertension, gestational diabetes in this pregnancy, and with prepregnancy BMI above 18.5 kg/m^2.

† The frequency within each cell was presented in unweighted number; all percentages within each cell were weighted.

‡P value was based on χ^2test of independence.

Table 6.2. Socio-demographic characteristics and health behaviors by GWGs in early (≤20 weeks) and mid-late (>20 weeks) pregnancy (unweighted N=3,322)

	GWG in early pregnancy[†]			P-value[*]	GWG in mid-late pregnancy[†]			P-value[*]
	Inadequate N (%)[‡]	Adequate N (%)[‡]	Excessive N (%)[‡]		Inadequate N (%)[‡]	Adequate N (%)[‡]	Excessive N (%)[‡]	
Total	1174(34.6)	518(16.4)	1630(49.0)		922(23.9)	944(30.4)	1456(45.7)	
GWG in early pregnancy[†]								
Inadequate GWG	-	-	-	-	343 (36.9)	359 (37.5)	472 (31.5)	0.0019
Adequate GWG	-	-	-		142 (14.1)	163 (19.1)	213 (15.8)	
Excessive GWG	-	-	-		437 (49.0)	422 (43.4)	771 (52.7)	
Maternal age								
≤20	186 (11.3)	51 (7.4)	133 (7.2)	<.0001	104 (6.9)	93 (8.3)	173 (9.8)	0.0131
20-24	358 (30.5)	137 (26.7)	376 (21.6)		221 (24.4)	226 (22.2)	424 (28.3)	
25-29	368 (33.7)	155 (31.4)	570 (36.3)		285 (34.5)	329 (35.6)	479 (34.0)	
≥30	262 (24.5)	175 (34.5)	551 (34.9)		312 (34.2)	296 (33.9)	380 (27.9)	
Race/Ethnicity								
Hispanic	93 (9.3)	52 (13.6)	119 (9.5)	0.0090	55 (9.1)	92 (11.4)	117 (9.7)	0.0046
Non-Hispanic white	613 (74.7)	289 (75.2)	878 (77.2)		432 (72.1)	529 (76.4)	819 (77.8)	
Non-Hispanic black	421 (10.2)	161 (8.1)	592 (10.0)		404 (13.5)	292 (8.2)	478 (8.9)	
Other	47 (5.8)	16 (3.1)	41 (3.4)		31 (5.3)	31 (4.1)	42 (3.6)	
Education								
<High school graduates	218 (14.9)	68 (11.0)	230 (11.2)	0.0500	178 (14.7)	138 (12.2)	200 (11.5)	0.2070
Some college graduates	479 (41.4)	204 (40.5)	651 (39.0)		388 (41.8)	362 (38.5)	584 (40.3)	
≥College graduates	477 (43.7)	246 (48.5)	749 (49.8)		356 (43.5)	444 (49.3)	672 (48.2)	
Parity								
0	393 (32.7)	191 (37.1)	519 (34.5)	0.2480	246 (27.8)	279 (29.3)	578 (41.1)	<.0001
1	382 (34.7)	143 (28.7)	508 (30.6)		278 (31.7)	308 (33.9)	447 (30.3)	
≥2	399 (32.6)	184 (34.2)	603 (34.9)		398 (40.5)	357 (36.8)	431 (28.6)	
Family income								
<25 K	683 (49.8)	235 (37.0)	834 (43.3)	0.0002	529 (44.6)	466 (42.7)	757 (45.7)	0.4706

≥25 K	491 (50.2)	283 (63.0)	796 (56.7)		393 (55.4)	478 (57.3)	699 (54.3)	
Marital status								
Yes	800 (81.5)	394 (85.1)	1190 (83.9)	0.2361	617 (81.1)	710 (85.6)	1057 (82.9)	0.0848
No	374 (18.5)	124 (14.9)	440 (16.1)		305 (18.9)	234 (14.4)	399 (17.1)	
Prepregnancy BMI(kg/m^2)								
18.5-24.9	887 (78.7)	392 (79.8)	1030 (67.7)	<.0001	692 (81.1)	710 (78.2)	907 (66.3)	<.0001
25.0-29.9	185 (12.9)	97 (16.9)	393 (21.5)		131 (10.1)	164 (15.7)	380 (23.2)	
≥30.0	102 (8.4)	29 (3.2)	207 (10.9)		99 (8.8)	70 (6.1)	169 (10.5)	
Physical activity before pregnancy								
Yes	551 (46.0)	258 (48.3)	763 (46.6)	0.7757	419 (44.0)	443 (45.4)	710 (48.9)	0.1418
No	623 (54.0)	260 (51.7)	867 (53.4)		503 (56.0)	501 (54.6)	746 (51.1)	
Smoking before pregnancy								
Yes	307 (26.1)	154 (28.9)	505 (31.4)	0.0551	329 (32.9)	249 (27.3)	388 (28.3)	0.0860
Pregnancy-induced hypertension								
Yes	65 (5.9)	37 (6.8)	171 (10.9)	0.0006	50 (4.1)	45 (4.8)	178 (13.2)	<.0001
No	1109 (94.1)	481 (93.2)	1459 (89.1)		872 (95.9)	899 (95.2)	1278 (86.8)	
Hypertensive disorders[τ]								
Yes	75 (6.4)	46 (8.2)	197 (11.7)	0.0006	58 (4.3)	54 (5.8)	206 (14.3)	<.0001
No	1099 (93.6)	472 (91.8)	1433 (88.3)		872 (95.9)	899 (95.2)	1278 (86.8)	

GWG, gestational weight gain.

[*] P value was based on χ^2test of independence.

[†] Gestational age was accounted for the determination of adequacy of GWG using the 2009 Institute of Medicine's recommendations.

[‡] The frequency within each cell was presented in unweighted number; all percentages within each cell were weighted.

[τ] Hypertensive disorders include pregnancy-induce hypertension and preeclampsia.

Table 6.3. Effect of GWG in early and mid-late pregnancy on spontaneous PTB and medically indicated PTB, mediated through hypertensive disorders, 1988 NMIHS (unweighted N=3322)

	Preterm births		Marginal Structure model with stabilized weight	
GWG[†]	n	%[*]	OR	95% C.I.
Normal weight (N=2309)				
Spontaneous PTB	241	(4.3)		
≤20 weeks' gestation				
Inadequate GWG	89	(4.0)	0.78	(0.52, 1.18)
Adequate GWG	44	(4.7)	Ref	
Excessive GWG	108	(4.3)	0.82	(0.55, 1.24)
>20 weeks' gestation				
Inadequate GWG	84	(4.5)	1.57	(1.08, 2.22)
Adequate GWG	63	(4.5)	Ref	
Excessive GWG	94	(3.9)	1.46	(1.02, 2.09)
Medically indicated PTB	96	(1.3)		
≤20 weeks' gestation				
Inadequate GWG	37	(0.6)	1.35	(0.67, 2.71)
Adequate GWG	13	(1.3)	Ref	
Excessive GWG	46	(1.3)	1.31	(0.66, 2.60)
>20 weeks' gestation				
Inadequate GWG	22	(0.9)	1.19	(0.59, 2.40)
Adequate GWG	21	(0.8)	Ref	
Excessive GWG	53	(1.2)	1.94	(1.12, 3.36)
Overweight or Obese (N=1013)				
Spontaneous PTB	107	(4.5)		
≤20 weeks' gestation				
Inadequate GWG	29	(4.4)	1.01	(0.46, 2.19)
Adequate GWG	14	(3.1)	Ref	
Excessive GWG	64	(4.8)	1.27	(0.62, 2.60)
>20 weeks' gestation				
Inadequate GWG	36	(7.2)	1.40	(0.77, 2.56)
Adequate GWG	26	(3.8)	Ref	
Excessive GWG	45	(4.0)	0.87	(0.51, 1.49)
Medically indicated PTB	61	(2.1)		
≤20 weeks' gestation				
Inadequate GWG	12	(1.0)	0.40	(0.12, 0.98)
Adequate GWG	9	(0.8)	Ref	
Excessive GWG	40	(3.0)	0.68	(0.28, 1.67)

>20 weeks' gestation				
Inadequate GWG	12	(2.4)	2.28	(0.84, 6.23)
Adequate GWG	10	(1.4)	Ref	
Excessive GWG	39	(2.4)	1.49	(0.67, 3.33)

PTB, preterm births; GWG, gestational weight gain.
[*] The frequency within each cell was presented in unweighted number; all percentages within each cell were weighted and reflected the prevalence of preterm births in each GWG category.
[†] Gestational age was accounted for the determination of adequacy of GWG using the 2009 Institute of Medicine's recommendations.

Table 6.4. Effect of GWG in early and mid-late pregnancy on spontaneous PTB, mediated through hypertensive disorders, among underweight women (unweighted N=314**)**, 1988 NMIHS

	Preterm births		Marginal Structure model with stabilized weight	
GWG[†]	n	%[*]	OR	95% C.I.
Underweight weight				
Spontaneous PTB	55	(5.3)		
≤20 weeks' gestation				
Inadequate GWG	25	(6.2)	1.09	(0.46, 2.57)
Adequate GWG	12	(3.2)	Ref	
Excessive GWG	18	(5.9)	1.02	(0.43, 2.44)
>20 weeks' gestation				
Inadequate GWG	23	(4.8)	0.67	(0.34, 1.34)
Adequate GWG	24	(7.5)	Ref	
Excessive GWG	8	(3.3)	0.38	(0.14, 1.03)

PTB, preterm births; GWG, gestational weight gain.
[*] The frequency within each cell was presented in unweighted number; all percentages within each cell were weighted.
[†] Gestational age was accounted for the determination of adequacy of GWG using the 2009 Institute of Medicine's recommendations.

CHAPTER 7

MANUSCRIPT 3: INFLUENCE OF PERSONAL CAPITAL ON IMPROVING PERINATAL HEALTH SERVICE USES IN LOS ANGELES COUNTY[3]

[3] L. Zhan and J. Liu to be submitted to Maternal and Child health Journal

Abstract

Background: The purpose was to investigate the associations of personal capital and the use perinatal health services, defined as the receipt of preconception counseling and the late initiation of prenatal care (> 13 week of gestation).

Method: Data came from the 2007 and 2010 Los Angeles Mommy and Baby (LAMB) study (unweighted N=7,597). Personal capital was measured by a composite score, covering a set of multidimensional resources including internal resources (self-esteem and mastery), partner and social support, and neighborhood support (social cohesion and reciprocal exchange). Multilevel models were used to account for potential confounding at individual and neighborhood levels.

Results: Personal capital varied by race, with Whites having the highest score (53.8), followed by Asians (50.8), Blacks (48.4) and Hispanics (48.0). Whites also had the highest proportions of using perinatal health services, followed by Asians, Blacks and Hispanics. Higher personal capital score was associated with higher odds of receiving preconception counseling in Whites and Asians and was negatively associated with late prenatal care initiation in Hispanics, Blacks and Asians. For preconception care, internal resources were significant correlates in Whites, Hispanics, and Asians. Partner support was a significant correlate in Whites and Hispanics. Neighborhood supports were significant correlates in Whites, Blacks and Asians. For prenatal care, internal resources were significant correlates in Whites, Blacks, and Asians. Partner support was a significant correlate in Hispanics, Blacks and Asians. Social support was a significant correlate for Asians, and neighborhood supports were significant correlates in Hispanics, Blacks and Asians.

Conclusions: The findings indicated that increasing personal capital can be a useful strategy to improve the use of perinatal health services. The intervention strategies should be tailored for different racial groups.

Introduction

In Unite States (U.S), improving the well-being of mothers, infants and children is an important public health goal.(US Department of Health Human Services 2011) However, to date, in nearly one-third pregnancies women experienced some types of perinatal complications such as pregnancy-induced hypertension (PIH) and preterm delivery, (Berg et al. 2010) which has caused about 650 deaths in pregnant women each year (Berg et al. 2010) and over 40% of neonatal deaths. (Heron 2012; Martin et al. 2013)

Prenatal care was considered as the foremost strategies to lower morbidities and mortality and to reduce health disparities in mothers, infants and children. (Showstack et al. 1984; Murray and Bernfield 1988; Luke et al. 1993; Curry et al. 1998; Lu and Halfon 2003) A number of studies reiterated that initiating prenatal care earlier improved birth weights and decreased the risk of preterm birth.(Quick et al. 1981; Greenberg 1983; Peoples and Siegel 1983; McLaughlin et al. 1992) After years of efforts, over 73% of U.S. women who gave birth began prenatal care within the first trimester, while approximately one million women began prenatal care after the first trimester. (Higgins et al. 1994; Ta and Hayes 2010; Leal et al. 2011) The initiation of prenatal care within the first trimester was the highest among White and Asian women (78.8 % and 77.8%, respectively), followed by Hispanic (68.3%) and Black women (63.4 %). (Kramer et al. 2000; Lu and Halfon 2003) Thus, more efforts are needed to further increase early start of prenatal care and to eliminate the disparity in its utilization.

Preconception counseling (six month before pregnancy) is a novel concept which was proposed after recognizing that even early prenatal care is too late to prevent some birth defects and current prenatal strategies are not sufficient to explain the persistent racial disparities in birth outcomes.(Abrams et al. 1995; Lu and Halfon 2003; Atrash et al. 2006; Moore LK et al. 2008; Macdonald-Wallis et al. 2013) Preconception care has been integrated in *Healthy People* 2020 objectives and U.S. Center for Disease Prevention and Control recommended that all women at reproductive ages should receive this primary care.(Atrash et al. 2006; Johnson et al. 2006; US Department of Health and Human Services 2010; World Health Organization 2012) However, to date only around 18.4% of women received the preconception care, and its prevalence varied by race and geographic areas. (Williams et al. 2012; Robbins et al. 2014) Studies are warranted to explore the strategies to disseminate this new health concept increase its utilization.

Personal capital defined on a multi-dimensional scale, including self-esteem and mastery ability at the individual level; partner support and social network support at the interpersonal level; and neighborhood social cohesion and reciprocal exchange at the community level (Wakeel et al. 2013) (Appendix 1). Personal capital is known to impact individual's psychosocial and behavioral risk factors, (Dunkel Schetter 2011) and further associated with maternal and child health outcomes. For example, high self-esteem and high mastery ability of mothers are associated with higher birth weight and reduced risk of intrauterine growth retardation among their offspring. Partner support, social network support and neighborhood support are positively associated with better labor progress.(Goldenberg RL et al. 1991; Collins et al. 1993; Rini et al. 1999; Feldman et al. 2000; Bell et al. 2006) As a composite score, personal capital has also been related to the decrease in adverse birth outcomes such as preterm birth in recent studies.(Wakeel et al. 2013; Wakeel et al. 2013)

However, personal capital, as a potential strategy, has been rarely linked with perinatal health services. Studies found that improving personal capital contributed to better use of primary health care (Grootaert and Van Bastelaer 2002; Laporte et al. 2008), and mental health services use. (Van der Linden et al. 2003; Maheshwari and Steel 2012) A few studies reported that contextual social capital and social support were significant determinants for prenatal care use.(St Clair et al. 1989; Leal et al. 2011) However, to our knowledge no studies have used a multidimensional measure of personal capital to assess its overall impact on prenatal care and on preconception counseling. In addition, no studies have examined whether the associations between personal capital and perinatal health services vary by racial groups. Cultural and sociodemographic differences in racial groups may result in differences in personal capitals. (Norbeck and Anderson 1989; West et al. 1998; Twenge and Crocker 2002; Chandra and Skinner 2003; Diaz et al. 2007; Wakeel et al. 2013) These different personal capitals may further cause disparities in maternal and child health outcomes. In all, better knowledge on whether personal capital might be a protective factor for perinatal health service utilization and how its impact might vary by racial groups will be useful to the design of programs aiming at improving perinatal health care use and narrowing racial disparities in maternal and child health outcomes.

Our study had two objectives. First, we examined the association between personal capital and perinatal health services use. We hypothesized that personal capital was positively associated with preconception counseling and prenatal care utilization, and the effect might vary by racial groups. Second, we further studied the roles of each component in personal capital on perinatal health services use. We hypothesized that some dimensions of personal capital might be more important for one racial group than other racial groups. The knowledge on the roles of sub-components of personal capital in each racial group will be useful in targeting different elements among racial groups in the efforts to improve perinatal health service utilization.

Data and Methods

Data source

Data came from the 2007 and 2010 Los Angeles Mommy and Baby (LAMB) study, a cross-sectional, population-based mail or telephone survey of women who had recently delivered a live birth in Los Angeles (LA) county in 2007 and 2010. The survey focused on preconception, prenatal, and postpartum correlates of adverse maternal and child health outcomes. The 2007 LAMB Study was a collaboration between the University of California, Los Angeles (UCLA) and the Maternal, Child, and Adolescent Health Program (MCAH) of LA county's Department of Public Health. The 2010 LAMB survey was administered and sponsored by LA county's Department of Public Health.

The 2007 LAMB study employed multi-stage and clustered design in which all census tracts in LA county were divided into two strata that corresponded to high and low perinatal health risk. MCAH had identified 150 high-risk zip codes within the county using six perinatal indicators including the number and proportion of women of reproductive age living on incomes below 200% of poverty, births to mothers receiving Medi-Cal, births to mothers age 18 and under, low birth weight births, and percent of late onset or no prenatal care, and infant mortality rate. All census tracts within these high-risk zip codes were categorized as high-risk tracts and the remaining tracts in LA county were low-risk tracts. Women giving birth to low birthweight (<2500 grams) and preterm (<37 completed weeks' gestation) babies were oversampled. The response rates in 2007 were 56%.(Los Angeles Maternal) The 2010 LAMB study a population-based survey that utilizes a stratified random sampling method, by Service Planning Area, race and age. It oversampled African American and teenage mothers to ensure an adequate sample for subgroup analysis. The response rate in 2010 was 57%.(Los Angeles County Department of Public Health et al. 2012)

The data we used for analysis is the combined 2007 and 2010. It identified 14 Best Start communities as the high need areas of LA county by assessing the risk indicators such as low-birth weight, low-performing schools and poverty, and evaluating the strengths and capacity of each community including its leadership infrastructure and its potential for partnership. To get a representative picture of the mothers who gave birth in LA county in 2007 and 2010, a weight was created by post-stratifying on selected maternal and infant characteristics to minimize selection and response bias due to different sampling frames in 2007 and 2010. (Los Angeles County Department of Public Health and Maternal) Specific factors selected in post-stratification included community level (14 communities and other), mother's race/ethnicity, mother's age, mother's education and infant's birth outcome status (low birth weight). The designation of survey respondents to each of the 14 communities were based on census tract correspondence tables (2000 census tract for 2007 data and 2010 for 2010 data). (Los Angeles County Department of Public Health and Maternal) The LAMB survey collected detailed information regarding preconception counseling and women's health behaviors prior to the pregnancy or in early pregnancy, which provided a unique opportunity to examine the proposed questions.

Prenatal care and preconception counseling

The LAMB survey asked women to report whether she talked to a doctor, nurse, or other health care worker during the six months before she got pregnant with the new baby. This was used to create the binary exposure of preconception counseling. LAMB survey also asked pregnant women about the time when they had their first prenatal care visit. Information was used to classify early prenatal care initiation (within 13 weeks of gestation) or late prenatal care initiation (after 13 weeks of gestation). (Los Angeles Maternal)

Personal capital

Personal capital was measured by four components based on Bronfenbrenner's ecological model.(Bronfenbrenner 1977; Bronfenbrenner 2009; Wakeel et al. 2013; Wakeel et al. 2013) (Table 1, Appendix A) LAMB survey used 28 questions to assess women internal resources (7 items) of self-esteem (3 items) and mastery ability (4 items), partner support (6 items), social supports (7 items), neighborhood support (10 items) of social cohesion (5 items) and social reciprocal exchange (5 items). Specifically, self-esteem was defined based an overall evaluation of an individual's value.(Jesse et al. 2006) Mastery evaluated the ability of one's control over her life.(Rini et al. 1999) Partner and social supports considered physical and emotional support from the baby's father or her kin and close friends, respectively.(Smart 1977; Fragile Families and CHild Wellbeing Study 2003) Neighborhood support included neighborhood social cohesion and reciprocal exchange and concerned a mutual assistance and support among neighbors.(Buka et al. 2003) This definition summarized an individual's total personal capital at three levels: 1) internal resources at individual level, 2) partner support and social network support at interpersonal, and 3) neighborhood support at community level. According to Bronfenbrenner's conceptual model, internal resources had the largest and most direct impact on individuals, followed by partner support, social network support and neighborhood support. Therefore, after those item-specific scores (with different range) were summed up to form component scores, they were first weighted to reflect the different impacts of each component on individuals and then summed to calculate the total personal capital score (with higher scores reflecting greater levels). As applied in previous study (Wakeel et al. 2013; Wakeel et al. 2014), internal resources, partner support, social network support, and neighborhood support were weighted to represent 32.5, 27.5, 22.5, and 17.5% of the overall score, respectively. Finally, the weighted personal capital score was standardized to range from 1 to 100, with a mean of 50 and a standard deviation of 10. Cronbach's tests were used to identify the internal consistency of all items included in each component.

Covariates

Same-ethnic density effect. Same-ethnic density was defined as the proportion of one ethnic group living in each census tract of an individual woman. Because cultural influence would vary in neighborhoods depending on same-ethnic density level, which may further result in different personal capital and different health outcomes.(Faris and Dunham 1939; Pickett et al. 2005; Shaw et al. 2010; Bécares et al. 2012) Thus, in our analyses, we considered the same-ethnic density as a potential confounder or effect modifier in the relationship between personal capital and perinatal health services use. In our study, it was measured by the percentage of Whites, Hispanics, Blacks, Asians living in each census tract based on 2010 U.S. Census and initially categorized into five levels as 0%-0.99%, 1%-4.99%, 5%-14.99%, 15%-49.99%, and ≥50%.(Pickett et al. 2009) Because small cell sizes in some categories, we further categorized it into three levels (0%-14.99%, 15%-49.99%, and ≥50%) for Hispanic density.

Socio-demographic factors. We considered mother's age, parity, marital status, education, health insurance, nativity, and pregnancy intendedness as the potential confounder.

Medical problems and adverse obstetric conditions. Those medical issues were related with both personal capital and perinatal health service uses and therefore were included as potential confounders in analyses. (Goldenberg RL et al. 1991; Collins et al. 1993; Rini et al. 1999; Feldman et al. 2000; Bell et al. 2006) LAMB survey asked all participants to report whether they had the following conditions in the 6 months before the pregnancy: depression, anxiety, high blood pressure (hypertension), high blood sugar (diabetes), anemia (poor blood, low iron), heart problems, problems with gums or teeth, and asthma. We examined grouped these medical problems into 0, 1, and ≥ 2 conditions. Regarding adverse obstetric history before last pregnancy, LAMB survey asked women whether they have one or more obstetric problems, including preterm birth, delivering low birth weight infant, miscarriage, stillbirth, abortion, and infant death and defects. This was further grouped into: 1) preterm birth and/or low birth weight infant, 2) miscarriage and /or still birth, 3) abortion, and 4) infant death and/or defects. In our analysis, we also created a dichotomous variable for adverse obstetric history (yes versus no).

Statistical analyses

All analyses were conducted using SAS 9.3 (SAS Institute Inc., Cary, NC) and were weighted to account for the complex survey design and non-responses. One-way ANOVA tests compared the mean scores for overall personal capital and components for covariates. Chi-square tests of independence were used to examine differences in maternal characteristics among Whites, Hispanics, Blacks and Asians. Statistical significance was set at $p<0.05$. Next, late prenatal care initiation (adverse event) and the receipt of preconception counseling (good event) were chosen as the outcome of interest. We chose to model late prenatal care initiation because around 90% of sampled population initiated prenatal care within the 13 weeks of gestation and thus, to identify the risk factor for the late initiation of prenatal care is more straightforward for public health interventions. Also, it prevented from a biased odds ratio as the results of very high prevalence of the interested outcome. On the other hand, the receipt of preconception counselling has a low prevalence, thus targeting potential risk factors to improve its utilization are more relevant. Multilevel logistic regression models were used for each outcome while considering the confounding by same-ethnic density, maternal demographics, health behaviors and individual medical and adverse obstetric history factors. We additionally adjusted preconception counseling when used late prenatal care initiation as outcome. Furthermore, to better understand the role of each component of personal capital on perinatal health services and provided potential intervention strategies, we ran separate models by including the four components of personal capital in different weights one at a time. Lastly, to examine whether those effects would vary by racial groups, we conducted stratified regression analyses for two outcomes.

Results

Sample characteristics. A total of 6,179 women and 6,590 women responded to the 2007 and 2010 LAMB surveys, respectively. After excluding women who delivered twin births (n=225) and who had missing data on preconception care (n=300), prenatal care (n=655), personal capital components (n=1011), and other covariates (n=3042), our analytic sample included 7,597 women. Among the 2,118 census tracts shown in our sample, 309 census tracts had only one woman, and over 34% of census tracts had more than 5 women living in the same census tract.

As shown in Table 2, most of our study population were aged 25 years old or more at interview (73.1%), Hispanic (61.6%), and multiparous (68.6%). About half of women had more than high school education (48.5%), were married at the time of interview (58.1%), and were U.S. born (55.4%). Over one-third (34.5%) of women had no health insurance before last pregnancy. Over one-fourth (26.9%) women reported one medical problem in 6 months before pregnancy and 13.1% reported 2 or more medical problems prior to their pregnancy. About one-third (28.5%) of women reported having some adverse obstetric conditions prior to this pregnancy.

Personal capital. Personal capital varied by race, with Whites having the highest score (53.8), followed by Asians (50.8), Blacks (48.4) and Hispanics (48.0). (Table 2) It was significantly higher in women who were college education or more, were married, and were U.S.-born, and had private medical insurance, intended pregnancy, and no medical problems prior to their pregnancy.

Sample characteristics by racial groups. As shown in Table 3, most Hispanics (62.6%) lived in census tracts had half or more Hispanics, while only about 33.7% of Whites, 10% of Blacks and 9.4% of Asians lived in census tracts had half or more residents with the same race as themselves, respectively. Compared to Whites, Hispanic and Black women were younger, having lower education, more likely to be unmarried, and having no health insurance, having unintended pregnancy, and having more medical problems prior to their pregnancy. Aforementioned characteristics were distributed similarly in Asians and Whites, however, more of Asians were reported to be nulliparous (44.7%) and be foreign born (76.1%). Only about half of Hispanics (48.9%) were born in U.S. and 75.0% of Hispanics experienced healthy obstetric conditions prior to this pregnancy.

Associations between personal capital and the receipt of preconception counseling. Whites had the best use of perinatal health services, followed by Asians, Blacks and Hispanics. (Table 2) As shown in Table 4, overall personal capital was associated preconception counseling use in Whites and Asians. Specifically, every five-point increase in personal capital was associated with a 26% increase in the odds of preconception counseling use in Whites (95% Confident Interval (C.I.), 1.16, 1.38) and a 14% increase in Asians (95% C.I., 1.05, 1.24), respectively. Regarding the effect of sub-components of personal capital, among Whites, more internal resources, partner support and neighborhood support were associated with an increased use in preconception counseling. Among Hispanics, more internal resources and partner support were associated with an increased use in preconception counseling. Among Blacks, more neighborhood support was associated with an increased use in preconception counseling.

Lastly, among Asians, internal resources and neighborhood support were associated with an increased use in preconception counseling.

Associations between personal capital and late prenatal care initiation. As shown in Table 4, overall personal capital was associated with late prenatal care initiation among Hispanics, Blacks and Asians. Specifically, every five-point increase in personal capital was associated with a 6% decrease in the odds of preconception counseling use in Hispanics (95% Confident Interval (C.I), 0.88, 1.00), a 13% decrease in Blacks (95% C.I., 0.81, 0.94), and a 19% decrease in Asians (95% C.I., 0.73, 0.91), respectively. Regarding the effect of sub-components of personal capital, among Whites, more internal resource was associated with a decrease in late prenatal care initiation. Among Hispanics, more partner support and neighborhood support were associated with a decrease in late prenatal care initiation. Among Blacks, more internal resources, partner support and neighborhood support were associated with a decrease in late prenatal care initiation. Among Asians, increasing any of the four components was associated with a decrease in late prenatal care initiation. Furthermore, In addition, regarding same-ethnic effect, among Whites, compared to living in census tracts with half or more White residents, living in census tracts with 14-49.99% White residents was associated with less preconception counseling use (OR=0.58, 95% C.I. 0.44, 0.76) (Appendix B) and living in census tracts with 0-0.99% White residents was associated with more late prenatal care initiation (OR=2.07, 95% C.I. 1.02, 4.21). Receiving preconception counseling was associated with 37% reduction in odds of late prenatal care initiation in Hispanics. (Appendix C)

Discussion

Using the data from a representative sample of urban population with a high proportion of Hispanic women, this study is the first to relate personal capital with preconception counseling and prenatal care utilization, and therefore filling a critical gap in literature. Our study showed that the prevalence of perinatal health services utilization varied by racial groups. As we hypothesized, personal capital was positively associated with the receipt of preconception counseling among Whites and Asians, while it was negatively associated with late prenatal care initiation among Hispanics, Blacks and Asians. Subcomponents of personal capital had different impacts on preceonception counseling among different races. For preconception care, internal resources were significant correlates in Whites, Hispanics, and Asians. Partner support was a significant correlate in Whites and Hispanics. Neighborhood supports were significant correlates in Whites, Blacks and Asians. For prenatal care, internal resources were significant correlates in Whites, Blacks, and Asians. Partner support was a significant correlate in Hispanics, Blacks and Asians. Social support was a significant correlate for Asians, and neighborhood supports were significant correlates in Hispanics, Blacks and Asians. Receiving preconception counseling helped to reduce the late prenatal care initiation in Hispanics.

Although we are the first study that identifies the beneficial role of personal capital, as a composite construct, on perinatal health services use, the results were comparable to the other studies. First, studies have reported the effect of individual components of personal capitals on health services use and health outcomes. Leal et al and St. Clair et al showed contextual social capital, social support and social network structure were significant for the appropriate use of prenatal care.(St Clair et al. 1989; Leal et al. 2011) Many other studies have reported a protective effect of self-esteem, mastery ability, partner support, social support and neighborhood support on intrauterine growth infant birthweight, and fetal growth. (Goldenberg RL et al. 1991; Collins et al. 1993; Rini et al. 1999; Feldman et al. 2000; Bell et al. 2006) Second, as compsite structure, Wakeel et al showed personal capital was associated with reducing preterm births.(Wakeel et al. 2013; Wakeel et al. 2013). Our study further extended the literature by documenting its protective effects on both prenatal care and preconception counseling utilization.

Based on the mechanisms that reported in previous studies, theoretically, improving personal capital hold promises to provide better perinatal health services delivery. Studies showed that women with strong internal resource in terms of self-esteem and mastery seek out health-related information more actively compared to women with less internal resources.(Rodin 1986; Goldenberg RL et al. 1991; Aspinwall and Brunhart 1996; Rini et al. 1999) Abundant partner support and social support, on one hand, offered more resources (e.g., money and time) that ensures women acquiring health care when necessary. On the other hand, those supports may elevate self-esteem and indirectly improve health services utilization.(Collins et al. 1993) The effect of neighborhood support in terms of social cohesion and reciprocal exchange may be explained by the accountability mechanisms.(Hendryx et al. 2002) Women are more engaged in social activities with neighbors; common values and goals are more likely to travel through the community. As a result, women with good neighborhood support have better access to health care resources.(Kawachi et al. 2008) Furthermore, personal capital, as a composite of all those individual components, not only provides more opportunities to improve perinatal health services, but also take advantage of the interrelated components by addressing one resource to help women increase other critical resources.

Our results identified the protective role of personal capital on perinatal health service use and further suggested that strategies of improving perinatal health services use via personal capital should be tailored by racial groups.

First, we only found significant associations between overall personal capital and preconception counseling among Whites and Asians. This may be explained by the fact that preconception counseling is a new concept that few women knew about it and the degree of acceptance varies by individual socioeconomic status.(Frey and Files 2006; Hillemeier et al. 2008; Oklahoma State Department of Health 2008; Williams et al. 2012; Robbins et al. 2014) Whites and Asians who were from higher socio-economic backgrounds in our study, usually have more regular primary health care visits, which can cause them to have better access to preconception counseling. (Johnson et al. 1983; Komaromy et al. 1996; Campbell et al. 2001) Thus, after initial acceptance of preconception counseling among some residents, more personal capital such as more neighborhood social cohesion and reciprocal exchange can increase exchange of health values among residents and consequently promote the utilization. (Kawachi et al. 2008) In contrast, Hispanic and Black women who were in lower SES reported lower use of preconception counseling. This finding suggests that improving knowledge can be in the first step among those low socio-demographic status residents. This can be done through distributing pamphlets at the clinics and by health education offered by health care providers during clinic visits.

Second, improving personal capital helps to prevent late prenatal care initiation among Hispanics, Blacks and Asians. In general, prenatal care is a well-accepted perinatal health services, and existed studies showed that adequate prenatal care use was significantly associated with social support and neighborhood support.(St Clair et al. 1989; Leal Mdo et al. 2011) Regarding particular racial groups, Asians and Blacks who are considered as minorities in LA county, are likely to isolate from mainstream society and may have fewer social networks.(Massey and Denton 1988) Thus, programs that offer resources such as group-based or couple-based counseling and free or subsidized neighborhood-based perinatal care are likely to be beneficial for improving prenatal care utilization in Asians and Blacks. (Wakeel et al. 2013) Improving internal resources such as self-esteem and mastery in those minorities may complement deficiency in social support and encourage them to seek more health-related information.(Rodin 1986; Goldenberg RL et al. 1991; Aspinwall and Brunhart 1996; Rini et al. 1999) For Hispanics who are the majority of our study population of Los Angeles county (>61%), improving partner and neighborhood support might be important in decreasing late prenatal care initiation. Hispanic women are usually recognized with high partner support. (Norbeck and Anderson 1989; West et al. 1998; Diaz et al. 2007) However, this was not found in our study population. Wakeel et al (Wakeel et al. 2013) who used same 2007 LAMB study, explained that the lower partner support is more related to mothers' socio-economic status rather than race itself. In other word, being unmarried, no insurance, and low education contribute to the lower partner support. (Wakeel et al. 2013) Therefore, future programs should improve access to care by covering health insurance before pregnancy. For example, the Patient Protection and Affordable Care Act should assist all women of reproductive ages to be covered by health insurance plan with affordable coverage. (American Academy of Pediatrics and American College of Obstetricians and Gynecologist 2002) Those programs are also important for other racial groups considering health insurance was an important predictor for perinatal health services use. (Appendix 2,3)

Several potential limitations should be considered when interpreting the findings. First, the generalizability of our findings on the prevalence of preconception counseling to other geographic areas is limited due to our sample characteristics and its geographic location (urban area and in one state). Yet we believe our results provide worthy strategies for improving both preconception counseling and prenatal care among communities with majority Hispanics. Second, our study is also limited in terms of being cross-sectional in nature that we cannot determine the timing of preconception care and those maternal health behaviors before pregnancy. Third, all preconception exposure and outcomes data were collected by self-report after delivery, which are prone for errors and recall bias. Due to our secondary data analysis nature, we cannot evaluate the validity of personal capital for our study population, although personal capital was chosen based on published scales. (Wakeel et al. 2013; Wakeel et al. 2013) Future studies should consider to use prospective cohort design and may cross-validate the contents of counseling with their providers' responses. Fourth, our study included relatively small sample size of Whites, Blacks and Asians from one county, thus our results should be interpreted cautiously. Lastly, the measurement of personal capital may not be suitable for Hispanics.

Reviewing the measurement of each component of personal capital and the conceptual model, they were all generated from datasets, which contained predominantly non-Hispanic Whites. Thus, to examine the accurate effect of personal capital on health and health services uses, further Hispanic-specific measurements of personal capital are needed.

In conclusion, using the data from a population-based surveillance system in an urban area, we found that different associations between personal capital and both prenatal care and preconception counseling among racial groups. Higher personal capital score was associated with higher odds of receiving preconception counseling among Whites and Asians and was negatively associated with late prenatal care initiation among Hispanics, Blacks and Asians. We further suggested that strategies of improving perinatal health services use via internal resources, partner support, social network support and neighborhood support should be tailored by racial groups. Those racial-specific associations are useful for program planners and public health decision-makers to assess the program need and design more effective programs to promote perinatal health services use and further eliminate the racial disparities in maternal and child health outcomes.

Table 6.1. Distribution of personal capital, 2007&2010 LAMB study

	Measures	Number of items	Raw score		Cronbach's alpha[a]
Personal capital score			Mean	Range	
Composite personal capital			52.0 (0.12)	(10-81)	0.471
Internal resources			21.0 (0.05)	(0.0-28.0)	0.802
Self esteem	3-items Rosenberg Self-esteem Scale short form	3	9.7 (0.03)	(0.0-12.0)	0.782
Mastery	4-items Pearlin Mastery Scale short form	4	11.4 (0.04)	(0.0-16.0)	0.697
Partner support	Fragile Families Study	6	5.3 (0.02)	(0.0-6.0)	0.831
Social network support	Pregnancy Risk Assessment Monitoring System	7	5.9 (0.02)	(0.0-7.0)	0.844
Neighborhood support	Project on Human Development in Chicago Neighborhoods	10	19.7 (0.09)	(0.0-40.0)	0.889
Social cohesion		5	11.6 (0.04)	(0.0-20.0)	0.800
Reciprocal exchange		5	8.1 (0.05)	(0.0-20.0)	0.887

[a]Based on weighted personal capital score

Table 6.2. Sample characteristics, and weighted mean personal capital scores by characteristics, the Los Angeles Mommy and Baby Study (LAMB), 2007-2010

	N (%)[a]	Personal capital score (range 0-100)	
		Mean (SE)	P-value[b]
Unweighted	7,597	50.0 (0.1)	
Weighted	178,532	49.3 (0.1)	
Age, years			
<20	632 (7.0)	45.7 (0.5)	0.1533
20-24	1267 (19.9)	47.3 (0.4)	
25-29	1912 (26.6)	48.9 (0.3)	
30-34	2094 (26.5)	50.6 (0.3)	
≥35	1692 (20.0)	51.2 (0.3)	
Race/Ethnicity			
Non-Hispanic white	1897 (18.1)	53.8 (0.2)	<.0001
Hispanic	2961 (61.6)	48.0 (0.2)	
Non-Hispanic black	1350 (8.2)	48.4 (0.3)	
Asian/Pacific Islanders	1389 (12.0)	50.8 (0.2)	
Education			
<High school	1284 (25.9)	45.4 (0.3)	<.0001
High school graduates	1789 (25.6)	47.8 (0.3)	
College education or more	4524 (48.5)	52.1 (0.2)	
Health insurance before pregnancy			
No insurance	2041 (34.5)	46.7 (0.3)	<.0001
Medi-Cal	1567 (21.2)	46.2 (0.3)	
Private	3668 (40.8)	53.0 (0.2)	
Other	321 (3.4)	50.6 (0.6)	
Parity			
0	2690 (31.3)	49.3 (0.2)	0.2375
1	4190 (57.3)	49.8 (0.2)	
≥2	717 (11.4)	46.4 (0.5)	
Marital status			
Married	4532 (58.1)	51.9 (0.2)	<.0001
Unmarried	3065 (41.9)	45.7 (0.2)	
Nativity			
U.S. born	4831 (55.4)	50.5 (0.2)	<.0001
Foreign-born <10 years	1376 (22.3)	46.6 (0.3)	
Foreign-born ≥10 years	1390 (22.3)	48.8 (0.3)	
Pregnancy intendedness			
No	1928 (26.6)	47.1 (0.3)	0.0346
Yes	4562 (58.5)	50.9 (0.2)	
Missing	1107 (14.9)	46.6 (0.4)	
Total number of medical problems[c]			
0 problem	4592 (60.0)	51.2 (0.2)	<.0001
1 problem	2035 (26.9)	47.8 (0.3)	

≥2 problems	970 (13.0)	43.6 (0.5)	
Total number of adverse obstetric conditions[d]			
0 condition	5145 (71.5)	49.4 (0.2)	0.2983
≥1 conditions	2452 (28.5)	48.9 (0.3)	

[a] Unweighted sample sizes and weighted percentages were presented.
[b] Chi-square tests of independence were used to examine the association between receipt of personal capital and each characteristic listed in the table.
[c] Medical conditions were self-reported depression, anxiety, hypertension, diabetes, anemia, health problem, oral problem, and asthma in the 6 months before the pregnancy.
[d] Adverse obstetric history before the pregnancy included self-reported history of preterm birth, low birth weight, still birth, miscarriages, infant deaths, birth defects, and abortion.

Table 6.3. Sample characteristics by racial groups, the Los Angeles Mommy and Baby Study (LAMB), 2007-2010

	White N (%)[a]	Hispanic N (%)[a]	Black N (%)[a]	Asian N (%)[a]	P-values[b]
Unweighted N	1897	2961	1350	1389	
Personal capital score, Mean (SE)	53.8 (0.2)	48.0 (0.2)	48.4 (0.3)	50.8 (0.2)	<.0001
Receipt of preconception counseling					
Yes	747 (40.4)	731 (24.1)	374 (27.7)	489 (34.4)	<.0001
Late prenatal care initiation[c]					
Yes	141 (6.5)	332 (10.7)	183 (14.0)	122 (8.7)	<.0001
Same-ethnic density					
0-0.99%	121 (6.9)	4 (0.1)	217 (15.7)	162 (12.8)	
1-4.99%	223 (12.3)	46 (1.4)	322 (21.2)	211 (14.1)	
5-14.99%	269 (14.1)	251 (7.6)	339 (22.9)	494 (34.5)	
15-49.99%	714 (33.1)	912 (28.3)	374 (30.3)	418 (29.1)	
≥50%	570 (33.7)	1748 (62.6)	98 (10.0)	104 (9.4)	
Age, years					
<20	72 (2.0)	404 (9.4)	126 (8.6)	30 (1.5)	<.0001
20-24	185 (10.3)	667 (24.3)	305 (24.6)	110 (8.4)	
25-29	431 (22.9)	805 (28.4)	367 (27.4)	309 (23.1)	
30-34	614 (32.2)	643 (23.1)	324 (23.5)	513 (37.2)	
≥35	595 (32.6)	442 (14.9)	228 (15.9)	427 (29.8)	
Education					
<High school	60 (2.7)	1062 (39.2)	128 (11.3)	34 (2.5)	<.0001
High school graduates	299 (15.8)	946 (30.4)	374 (29.1)	170 (12.9)	
≥College education	1538 (81.4)	953 (30.3)	848 (59.6)	1185 (84.6)	
Health insurance before pregnancy					
No insurance	232 (12.2)	1272 (45.8)	303 (23.3)	234 (18.2)	<.0001
Medi-Cal	172 (7.8)	763 (25.1)	461 (35.5)	171 (11.8)	
Private	1398 (75.0)	852 (26.9)	541 (38.2)	877 (62.2)	
Other	95 (4.9)	74 (2.2)	45 (3.0)	107 (7.7)	
Parity					
0	678 (37.0)	885 (26.3)	517 (37.5)	610 (44.7)	<.0001
1	1089 (56.2)	1695 (59.6)	676 (49.7)	730 (52.5)	
≥2	130 (6.8)	381 (14.2)	157 (12.8)	49 (2.9)	
Marital status					
Married	1479 (80.3)	1441 (50.1)	459 (31.9)	1153 (83.6)	<.0001
Unmarried	418 (19.7)	1520 (49.9)	891 (68.1)	236 (16.4)	
Nativity					
U.S. born	1613 (81.9)	1584 (48.9)	1244 (92.4)	390 (23.9)	<.0001
Foreign-born<10 years	130 (8.3)	674 (25.6)	58 (4.0)	514 (38.7)	
Foreign-born≥10 years	154 (9.8)	703 (25.5)	48 (3.6)	485 (37.4)	
Pregnancy intendedness					

No	365 (18.1)	886 (30.0)	400 (29.9)	277 (20.3)	<.0001
Yes	1359 (74.2)	1598 (53.2)	650 (47.5)	955 (69.2)	
Missing	173 (7.8)	477 (16.8)	300 (22.6)	157 (10.5)	
Total number of medical problems[d]					
0 problem	1300 (68.9)	1725 (57.9)	633 (47.4)	934 (66.3)	<.0001
1 problem	412 (21.3)	823 (28.0)	464 (34.2)	336 (25.0)	
≥2 problems	185 (9.8)	413 (14.1)	253 (18.4)	119 (8.7)	
Total number of adverse obstetric conditions[e]					
0 condition	1307 (69.3)	2200 (75.0)	667 (50.1)	971 (71.2)	<.0001
≥1 conditions	590 (30.7)	761 (25.0)	683 (49.9)	418 (28.8)	

[a] Unweighted sample sizes and weighted percentages were presented.
[b] Chi-square tests of independence were used to examine the association between receipt of personal capital and each characteristic listed in the table.
[c] Initiating prenatal care after 13 weeks of gestation.
[d] Medical conditions were self-reported depression, anxiety, hypertension, diabetes, anemia, health problem, oral problem, and asthma in the 6 months before the pregnancy.
[e] Adverse obstetric history before the pregnancy included self-reported history of preterm birth, low birth weight, still birth, miscarriages, infant death, defect, and abortion.

Table 6.4. Associations between personal capital and perinatal health services use, the Los Angeles Mommy and Baby Study (LAMB), 2007-2010

	Whites AOR (95% CI)	Hispanics AOR (95% CI)	Blacks AOR (95% CI)	Asians AOR (95% CI)
Receipt of preconception counseling[*]				
Personal capital (Per 5-point increase)	1.26 (1.16, 1.38)	1.04 (0.98, 1.09)	1.03 (0.96, 1.09)	1.14 (1.05, 1.24)
Sub-components of personal capital (Per 5-point increase)[a]				
Internal resources	1.12 (1.07, 1.17)	1.03 (1.00, 1.06)	1.00 (0.96, 1.04)	1.04 (1.01, 1.08)
Partner support	1.05 (1.00, 1.10)	1.02 (1.00, 1.04)	1.01 (0.98, 1.03)	1.03 (0.98, 1.09)
Social support	1.01 (0.98, 1.04)	0.99 (0.98, 1.01)	0.99 (0.97, 1.02)	1.01 (0.98, 1.03)
Neighborhood support	1.07 (1.04, 1.10)	1.02 (0.99, 1.04)	1.04 (1.00, 1.07)	1.08 (1.05, 1.12)
Late prenatal care initiation[*b]				
Personal capital (Per 5-point increase)	0.92 (0.82, 1.03)	0.94 (0.88, 1.00)	0.87 (0.81, 0.94)	0.81 (0.73, 0.91)
Sub-components of personal capital (Per 5-point increase)[a]				
Internal resources	0.94 (0.88, 0.99)	0.98 (0.94, 1.02)	0.92 (0.87, 0.96)	0.94 (0.88, 1.00)
Partner support	0.99 (0.95, 1.04)	0.97 (0.95, 0.99)	0.97 (0.94, 0.99)	0.90 (0.85, 0.94)
Social support	1.00 (0.95, 1.05)	1.00 (0.98, 1.02)	0.99 (0.96, 1.02)	0.97 (0.93, 1.00)
Neighborhood support	0.98 (0.93, 1.03)	0.98 (0.96, 1.00)	0.94 (0.90, 0.98)	0.93 (0.88, 0.99)

AOR, adjusted odds ratio; CI, confident interval, Ref=reference.

[*]Adjustment included variables in the table and rest of variables in Table 2. In late prenatal care initiation, additionally adjusted for preconception counseling.

[a] Run separated model for each sub-component.

[b] Initiating prenatal care after 13 weeks of gestation.

CHAPTER 8

OVERALL SUMMARY AND CONCLUSIONS

The aims of this dissertation were 1) to describe the natural GWG trajectory during early pregnancy and examined its association with PIH; 2) to estimate the causal associations between GWG in early and mid-late pregnancy and subtypes of preterm births; and 3) to identify the role of personal capital in improving perinatal health service uses. Two databases used in this dissertation from 1988 NMIHS- a prospective nationally representative data and 2007 and 2010 LAMB study- a cross-sectional, population-based survey.

Summary of Key Findings

In Study 1, we found there were four trajectories of GWG in early pregnancy (≤ 20 weeks of gestation), representing four distinct subsets of pregnant women who experienced low, low-normal, normal, and high growth of GWG, respectively. The high growth of GWG during early pregnancy was associated with higher SBP and DBP, and higher risk of PIH. Low growth and low-normal growth of GWG in early pregnancy showed a protective effect on those pregnancy outcomes.

In study 2, we found that among normal weight women, the amount of weight gain in mid-late pregnancy was associated with both spontaneous and medically-indicated preterm birth. Both inadequate and excessive GWG in mid-late pregnancy increased the odds of spontaneous preterm births. Excessive GWG in mid-late pregnancy increased the odds of medically-indicated preterm births. Among overweight and obese women, gained inadequate weight in early pregnancy was protected from medically-indicated preterm births.

In study 3, personal capital was positively associated with the receipt of preconception counseling among Whites and Asian, and negatively associated with late prenatal care initiation among Hispanics, Blacks and Asians. The effect of individual components of personal capital on the receipt of preconception counseling and the initiation of prenatal care differed by racial groups. For preconception counseling, we found: 1) more internal resources, partner support, and neighborhood support increased the receipt in Whites; 2) more internal resources and partner support increased the receipt in Hispanics; 3) more neighborhood support increased the receipt in Blacks; and 4) more internal and neighborhood support increased the receipt in Asians. For prenatal care, we found: 1) more internal resources reduced the late initiation in Whites; 2) more partner support and neighborhood support reduced the late initiation in Hispanics; 3) more internal resources, partner support and neighborhood support reduced the late initiation in Blacks; and 4) all of the four components helped to reduce the late initiation in Asians. Preconception counseling was important for Hispanic women initiating prenatal care earlier.

Implications from this dissertation

The results observed in this dissertation were important because they provided useful information to prevent adverse pregnancy outcomes and improve maternal health services uses before and during pregnancy. The findings in the first two studies described the weight gain trajectories by maternal characteristics and found the associations of GWG in different periods of pregnancy on the risks of PIH and preterm births, for which knowledge gap still exists in literature. Advanced statistical methods applied in those two studies overcame the methodological limitations in previous studies and shed a light on how a longitudinal exposure may impact outcomes after considering time-varying covariates or potential mediators in analyses. Our findings also have clinical significance. We found that extra GWG in early pregnancy was associated with blood pressure rise and higher risk of PIH and the role of GWG on subtypes of preterm births varied by period of gestation and prepregnancy BMI status, suggesting modifying GWG can be a promising strategy to reduce the risks of some pregnancy or delivery complications. This adds to the literature by emphasizing the importance of GWG on pregnancy outcomes. This indicates that primary care practitioners or obstetricians can take the advantage the fact that pregnancy provides a "teachable moment" by counseling women about the proper weight gain during pregnancy, monitoring their weight gain, and offering individualized health care plans to pregnant women.

The findings in the third study focused on the possible roles of personal capital in improving women's use of perinatal health services. The results revealed that increasing personal capital can be an approach to be considered in the program aiming at improving preconception counseling and prenatal care utilization. The racial-specific associations between individual component of personal capital and perinatal health services use were useful for program planners and public health decision-makers to design the programs which will target viable components for each race group in the efforts to promote perinatal health services use and further eliminate the racial disparities in maternal and child health outcomes.

In conclusion, the results in this dissertation not only fulfilled literature gaps using advanced methods in epidemiological researches, but also had implications for both clinical practice and public health programming with the aim of improving maternal and child health outcomes and narrowing racial disparities.

Future Studies

Limitations in this dissertation

There were several limitations in this dissertation. First, the latent class growth Model is limited in relating latent trajectories with potential outcomes of interest. Further studies should try other latent growth models such as latent growth curve model (McArdle and Epstein 1987), which not only permits straightforward examination of intra-individual change over time as well as inter-individual variability in intra-individual change, but also allows investigation into the antecedents and consequents of the change. This method is advanced in estimating the quantitative associations. Specifically, it can predict the difference of certain health outcomes caused by every unit change of an exposure under a specific latent trajectory. Those details are also needed in clinical practice. However, the latent class growth modeling provided a unique advantage of discovering meaningful trajectories that may not be identified in prior recommendations.(Nagin DS 2005; Institute of Medicine(IOM) and National Research Council(NRC) 2009) As such, women underwent those meaningful latent trajectories can become targeted population in intervention programs.

Second, marginal structure models are restricted to differentiate direct and indirect effects from total effect.(Robins et al. 2000; Bodnar et al. 2004) In other word, it was not able to separate the effect through the mediator from the total effect. Thus, once the mediator analysis procedures are available for assessing the time-dependent effect, studies are warranted to detail the effects from different pathways. Based on the separated effects, women with and without certain mediators, for example, PIH, could be differentiated and further offered with individualized medical treatments and interventions.

Third, more observational studies conducted from contemporary datasets are needed to supplement our findings in study 1 and study 2, which were generated from a dataset collected in 1988. Those findings based on concurrent datasets are more useful in reflecting the key changes of women's health because the proportions of women gaining excessive weight during pregnancy or entering pregnancy being overweight or obese have increased dramatically (Gaillard et al. 2011; Liu et al. 2014) and the proportions of minorities, particular Hispanics, growing rapidly (e.g., from 2000 to 2010, Hispanics accounted for 56% the population growth) (Passel et al. 2012) in the past decade. In spite of this, we believe that biological mechanism underlying the associations should be the same for old and contemporary populations.

Fourth, with regard to our third research aim, future studies with a prospective cohort design are needed. Our study is limited in terms of being cross-sectional in nature that we cannot determine the timing of preconception care and those maternal health behaviors before pregnancy. Also, all preconception exposure and outcomes data were collected by self-report after delivery, which are prone for errors and recall bias. The validity of personal capital for our study population cannot be evaluated, although personal capital was chosen based on published scales. (Wakeel et al. 2013; Wakeel et al. 2013) Thus, future studies should consider to use prospective cohort design and may cross-validate the contents of counseling with their providers' responses.

Fifth, the measurement of individual component of personal capital and the conceptual model that is applied to create the overall personal capital need to be validated in Hispanic population. Reviewing the measurement of each component of personal capital and the conceptual model, they were all generated from studies that used datasets with predominantly non-Hispanic Whites. Thus, these measurements may not be suitable for Hispanics. Studies are needed to evaluate the validity of personal capital in Hispanics or other minorities.

Lastly, future studies conducted with national representative dataset and in other typical areas are needed to confirm our findings in study 3. We used a dataset from an urban area with high proportion of Hispanics; many results such as personal capital disparities, racial economic disparities in our study were contradicted as that reported in previous studies. Thus, our findings might not be applicable to other places with different social-economic status and racial compositions. As personal capital hold promises to improve perinatal health services use and may be a useful strategy to improve maternal and child health, studies are warranted to ascertain the role in different areas.

Research recommendations

All studies in this dissertation only shed a light in maternal and child health research; several other research recommendations that stem from this dissertation were summarized as following.

First, trajectories of GWG in obese women are needed. Our study identified obese women were more likely to experience the pregnancy-complication related trajectories: the high and low growth trajectories, suggesting that those obese women may undergo distinctive growth trajectories from normal weight women. Also, as obesity becomes an epidemic and more obese women are encountered with pregnancy complications in recent years (Rubenstein 2005; Catalano 2007), future studies are encouraged to conduct in all classes of obese women, stratified by the severity of obesity, to describe the trajectories of GWG, and investigate the antecedents and consequents of the trajectories.

Next, we used 1988 NMIHS, a prospective cohort study, with advanced statistical analysis approaches to examine the impact of GWG on pregnancy or delivery outcomes. Yet, the relationship may still be interfered by unknown confounding variables. Thus, experimental studies, which are considered as “golden standards”, are warranted to assess the causal effect of GWG on certain maternal and childhood outcomes. Furthermore, by comparing the effect from a range of maternal and childhood outcomes, the results will also be useful to weight the trade-off among multiple outcomes and determine the most appropriate GWG values to achieve the lowest risk of adverse health outcomes and best health status among pregnant women.

Third, studies applied advanced statistical analytic methods are encouraged to re-evaluate the inconsistent findings in previous researches and explore the causal associations in future studies. Mediator, which is an annoyance in estimating the association between exposure and outcome, is needed to re-evaluate in existed studies. For example, when assessing birth outcomes, such as low birth weight and preterm delivery, pregnancy complications such as gestational diabetes and hypertensive disorders are encouraged to account as potential mediators in the analyses. Furthermore, studies with applying casual inferences, marginal structure models, and mediation analyses are recommended, as they provided alternative ways, with low costs and free of ethical concerns, yet useful ways to elucidate reliable causal associations.

Last, but not least, in our study, same-ethnic density was treated as a confounder, and due to our relatively homogenous sample, we did not observed the interactive effect with personal capital on perinatal health services use. However, it is worth to investigate the individual effect of same-ethnic density on perinatal health services use and examine the potential interactive effect with personal capital on health and health services outcomes in other study populations. (Figure 8.1) Regarding analyzing the individual effect of same-ethnic density on perinatal health services use, future studies should take into account the personal capital as a potential mediator into the investigations. Cultural and socioeconomic differences lead to different personal capital in specific racial groups, which may cause disparities in health and health services use. Therefore, ethnic density may display the effect through the mediator, personal capital. Regarding examining the interactive effect, if the effect of personal capital on health and health services use varied by ethnic density areas, it suggests that strategies of optimizing personal capital to improve perinatal health services use may be most effective by tailoring women residential experiences.

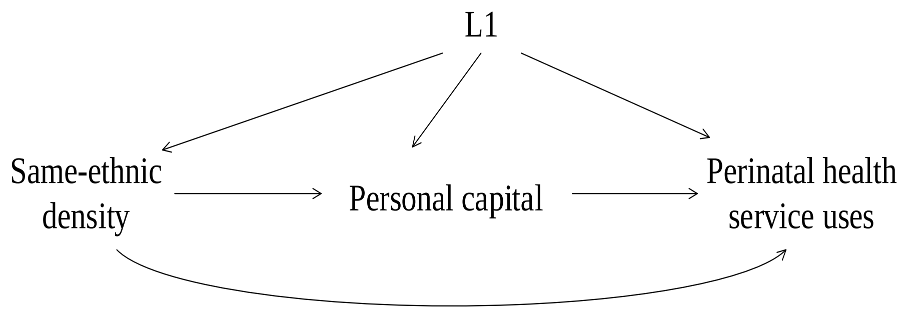

Figure 8.1 Directed acyclic graph for same-ethnic density. The graph depicts the assumed association between study variables. L_1= covariates.

Conclusions

This dissertation implemented a set of new and sophisticated statistical methods to examine three questions in the area of maternal and child health. The information gained from this dissertation provides directions and understandings in promoting healthy weight gain during pregnancy, improving pregnancy outcomes and perinatal care services use. The results from the dissertation are useful for women to self-manage their weight gain during pregnancy, are important for health providers to individualize preconception or prenatal care to women about their weight gain during pregnancy, and are helpful for program planners and public health decision-makers to assess the program need and design more effective programs to promote perinatal health services use and further eliminate the racial disparities in maternal and child health outcomes.

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APPENDIX A: PERSONAL CAPITAL MEASURES

Table A.1. Description of personal capital measures in 2007 and 2010 the Los Angeles Mommy and Baby (LAMB) Study[*]

Measure	Number of items	Items	Possible response (score range)
Internal resources			
Self-esteem	3	I feel that I am 1.a person of worth, 2.able to do things as well as others, 3.satisfied with myself	Strongly disagree (0), disagree (1), neither agree nor disagree(2), agree(3) and strongly agree(4)
Mastery	4	1.I have control over things, 2.have way to solve problems, 3.don't feel pushed around in life, 4.can do anything I set my mind to do	Strongly disagree (0), disagree (1), neither agree nor disagree(2), agree(3) and strongly agree(4)
Partner support	6	Partner 1.gave money/bought things for you, 2.helped you in other ways(taking to doctor, helping with chores), 3.gave emotional support in labor, 4.visited you and baby after delivery, 5.want to put name on birth certificate, 6.said he wanted to help raise baby	Yes(1); no(0)

Social support	7	How often do I have 1.someone to loan me $50, 2.help me if I were sick, 3.take me to the clinic or doctor, 4.give me a place to live, 5.help with me with childcare, 6.help me with household chores, 7.to talk to about my problems	Yes(1); no(0)
Neighborhood support			
Social cohesion	5	People in your neighborhood 1. are willing to help their neighbors, 2. this a close-knot neighborhood, 3.can be trusted, 4.get along with each other, 5.share the same values	Strongly disagree (0), disagree (1), neutral(2), agree(3) and strongly agree(4)
Reciprocal exchange	5	How often do you neighbors 1.do favors for each other, 2.ask each other advice about personal things, 3.have parties where other neighbors are invited, 4.visit in each other's homes/on the street, 5.watch over each other's property	Never (0), almost never(1), sometimes(2), fairly often(3), very often(4)

*Defined according to the 2007 and 2010 LAMB questionnaire and Wakeel et al studies.

Table B.1. Association between personal capital and receipt of preconception counseling by racial groups, the Los Angeles Mommy and Baby Study (LAMB), 2007-2010

	Preconception counseling			
	Whites AOR (95% CI)	Hispanics AOR (95% CI)	Blacks AOR (95% CI)	Asians AOR (95% CI)
Personal capital (per 5-point increase)	1.26 (1.16, 1.38)	1.04 (0.98, 1.09)	1.03 (0.96, 1.09)	1.14 (1.05, 1.24)
Same-ethnic density[a]				
0-0.99%	0.81 (0.50, 1.30)	-	0.63 (0.36, 1.12)	0.72 (0.42, 1.24)
1-4.99%	0.87 (0.59, 1.29)	-	1.15 (0.69, 1.91)	0.85 (0.50, 1.43)
5-14.99%	0.94 (0.65, 1.36)	1.02 (0.74, 1.41)	1.01 (0.61, 1.67)	0.92 (0.58, 1.45)
15-49.99%	0.58 (0.44, 0.76)	0.91 (0.74, 1.13)	1.43 (0.88, 2.30)	0.68 (0.43, 1.09)
≥50%	Ref	Ref	Ref	Ref
Age, years				
<20	0.14 (0.03, 0.77)	0.70 (0.46, 1.06)	1.13 (0.62, 2.04)	0.78 (0.24, 2.55)
20-24	0.59 (0.36, 0.97)	1.11 (0.85, 1.45)	1.02 (0.70, 1.49)	1.00 (0.57, 1.74)
25-29	Ref	Ref	Ref	Ref
30-34	1.12 (0.82, 1.54)	1.24 (0.96, 1.61)	1.17 (0.81, 1.68)	1.31 (0.94, 1.84)
≥35	1.44 (1.04, 1.98)	1.54 (1.14, 2.06)	1.65 (1.11, 2.46)	1.40 (0.98, 2.00)
Education				
<High school	Ref	Ref	Ref	Ref
High school graduates	1.37 (0.47, 4.00)	0.86 (0.68, 1.09)	0.59 (0.37, 0.92)	1.17 (0.43, 3.17)
≥College education	1.63 (0.57, 4.72)	1.17 (0.91, 1.52)	0.65 (0.40, 1.03)	1.22 (0.47, 3.20)
Parity				

0	Ref	Ref	Ref	Ref
1	0.46 (0.36, 0.60)	0.61 (0.48, 0.76)	0.84 (0.61, 1.14)	0.54 (0.41, 0.70)
≥2	0.18 (0.10, 0.33)	0.44 (0.31, 0.63)	1.00 (0.63, 1.60)	0.43 (0.18, 1.02)
Nativity				
U.S. born	Ref	Ref	Ref	Ref
Foreign-born<10 years	0.86 (0.56, 1.31)	0.91 (0.70, 1.19)	1.19 (0.61, 2.30)	0.93 (0.66, 1.30)
Foreign-born≥10 years	1.03 (0.71, 1.51)	0.95 (0.75, 1.20)	0.74 (0.36, 1.53)	0.96 (0.70, 1.33)
Health insurance before pregnancy				
No insurance	Ref	Ref	Ref	Ref
Medi-Cal	5.09 (2.65, 9.79)	3.03 (2.37, 3.87)	2.30 (1.56, 3.38)	4.19 (2.47, 7.11)
Private	3.08 (1.94, 4.88)	1.85 (1.44, 2.40)	1.59 (1.08, 2.36)	3.17 (2.07, 4.83)
Other	3.10 (1.59, 6.02)	2.97 (1.67, 5.25)	2.31 (1.08, 4.93)	2.60 (1.47, 4.60)
Marital status				
Married	1.55 (1.05, 2.27)	1.44 (1.17, 1.77)	1.34 (0.96, 1.86)	1.17 (0.77, 1.76)
Unmarried	Ref	Ref	Ref	Ref
Pregnancy intendedness				
No	Ref	Ref	Ref	Ref
Yes	4.82 (3.29, 7.07)	2.64 (2.10, 3.34)	1.84 (1.35, 2.51)	2.51 (1.74, 3.60)
Missing	1.46 (0.78, 2.72)	1.03 (0.74, 1.42)	1.02 (0.70, 1.50)	1.18 (0.69, 2.03)
Total number of medical problems[b]				
0 problem	Ref	Ref	Ref	Ref
1 problem	1.42 (1.06, 1.89)	1.25 (1.02, 1.55)	1.01 (0.75, 1.35)	0.97 (0.72, 1.32)
≥2 problems	2.08 (1.35, 3.20)	1.56 (1.18, 2.06)	1.69 (1.19, 2.40)	2.43 (1.54, 3.83)
Total number of adverse obstetric conditions[c]				
0 condition	Ref	Ref	Ref	Ref
≥1 conditions	0.83 (0.64, 1.07)	1.17 (0.95, 1.45)	1.21 (0.93, 1.58)	0.97 (0.74, 1.28)

AOR, adjusted odds ratio; CI, confident interval, Ref=reference.

[a] 0-0.99%, 1-4.99% and 5-14.99% were combined into one category (0-14.99%) in Hispanics.

[b] Medical conditions were self-reported depression, anxiety, hypertension, diabetes, anemia, health problem, oral problem, and asthma in the 6 months before the pregnancy.

[c] Adverse obstetric history before the pregnancy included self-reported history of preterm birth, low birth weight, still birth, miscarriages, infant deaths, birth defects, and abortion.

APPENDIX C: STUDY 3 FULL TABLE OF PRENATAL CARE

Table C.1. Association between personal capital and late prenatal care initiation by racial groups, the Los Angeles Mommy and Baby Study (LAMB), 2007-2010

	Late prenatal care initiation[a]			
	Whites AOR (95% CI)	Hispanics AOR (95% CI)	Blacks AOR (95% CI)	Asians AOR (95% CI)
Personal capital (per 5-point increase)	0.92 (0.82, 1.03)	0.94 (0.88, 1.00)	0.87 (0.81, 0.94)	0.81 (0.73, 0.91)
Same-ethnic density[b]				
0-0.99%	2.09 (1.03, 4.24)	-	1.13 (0.57, 2.26)	1.53 (0.63, 3.73)
1-4.99%	0.75 (0.37, 1.56)	-	0.98 (0.51, 1.90)	1.59 (0.67, 3.80)
5-14.99%	0.81 (0.41, 1.58)	0.87 (0.55, 1.39)	0.95 (0.50, 1.82)	1.13 (0.51, 2.53)
15-49.99%	1.21 (0.73, 1.98)	0.90 (0.68, 1.20)	1.02 (0.55, 1.89)	1.87 (0.85, 4.13)
≥50%	Ref	Ref	Ref	Ref
Preconception counseling				
Yes	0.89 (0.54, 1.47)	0.63 (0.44, 0.88)	0.75 (0.50, 1.11)	1.27 (0.82, 1.97)
No	Ref	Ref	Ref	Ref
Age, years				
<20	1.57 (0.53, 4.65)	2.76 (1.76, 4.35)	2.77 (1.39, 5.52)	1.11 (0.30, 4.07)
20-24	1.22 (0.66, 2.26)	1.37 (0.96, 1.95)	1.27 (0.81, 2.00)	0.98 (0.51, 1.90)
25-29	Ref	Ref	Ref	Ref
30-34	0.81 (0.47, 1.42)	0.91 (0.62, 1.35)	0.79 (0.48, 1.28)	0.62 (0.37, 1.04)
≥35	0.72 (0.40, 1.30)	0.74 (0.46, 1.18)	1.04 (0.60, 1.79)	0.68 (0.39, 1.16)
Education				
<High school	Ref	Ref	Ref	Ref
High school graduates	0.40 (0.17, 0.97)	0.93 (0.69, 1.26)	1.02 (0.60, 1.72)	1.50 (0.51, 4.38)

≥College education	0.86 (0.36, 2.06)	0.87 (0.61, 1.25)	0.85 (0.49, 1.49)	1.40 (0.49, 4.01)
Parity				
0	Ref	Ref	Ref	Ref
1	1.33 (0.82, 2.15)	1.02 (0.74, 1.42)	2.33 (1.51, 3.60)	1.51 (0.97, 2.35)
≥2	1.95 (0.90, 4.21)	1.99 (1.25, 3.16)	1.79 (0.95, 3.38)	2.31 (0.90, 5.96)
Nativity				
U.S. born	Ref	Ref	Ref	Ref
Foreign-born<10years	1.17 (0.57, 2.42)	0.36 (0.25, 0.53)	2.78 (1.26, 6.10)	0.96 (0.56, 1.63)
Foreign-born≥10years	1.39 (0.72, 2.69)	0.58 (0.42, 0.81)	1.79 (0.74, 4.30)	0.93 (0.54, 1.60)
Health insurance before pregnancy				
No insurance	Ref	Ref	Ref	Ref
Medi-Cal	0.66 (0.35, 1.25)	0.75 (0.56, 1.02)	0.70 (0.46, 1.07)	0.82 (0.47, 1.43)
Private	0.25 (0.15, 0.43)	0.62 (0.42, 0.90)	0.58 (0.36, 0.92)	0.39 (0.24, 0.64)
Other	0.35 (0.12, 1.00)	0.75 (0.31, 1.82)	0.71 (0.26, 1.95)	0.38 (0.15, 0.95)
Marital status				
Married	0.64 (0.39, 1.07)	0.69 (0.52, 0.92)	0.76 (0.47, 1.21)	0.65 (0.39, 1.08)
Unmarried	Ref	Ref	Ref	Ref
Pregnancy intendedness				
No	Ref	Ref	Ref	Ref
Yes	0.42 (0.26, 0.67)	0.68 (0.51, 0.91)	0.54 (0.36, 0.79)	0.86 (0.53, 1.40)
Missing	0.81 (0.43, 1.54)	0.99 (0.71, 1.38)	0.77 (0.51, 1.16)	1.35 (0.74, 2.47)
Total number of medical problems[c]				
0 problem	Ref	Ref	Ref	Ref
1 problem	1.01 (0.62, 1.64)	0.97 (0.72, 1.31)	1.13 (0.78, 1.65)	1.06 (0.67, 1.67)
≥2 problems	1.14 (0.62, 2.10)	1.82 (1.32, 2.53)	1.58 (1.03, 2.42)	1.01 (0.53, 1.90)
Total number of adverse obstetric conditions[d]				
0 condition	Ref	Ref	Ref	Ref
≥1 conditions	1.42 (0.93, 2.17)	1.32 (1.00, 1.74)	1.64 (1.15, 2.32)	1.04 (0.68, 1.59)

AOR, adjusted odds ratio; CI, confident interval, Ref=reference.

[a] Initiating prenatal care after 13 weeks of gestation.

[b] 0-0.99%, 1-4.99% and 5-14.99% were combined into one category (0-14.99%) in Hispanics.

[c] Medical conditions were self-reported depression, anxiety, hypertension, diabetes, anemia, health problem, oral problem, and asthma in the 6 months before the pregnancy.
[d] Adverse obstetric history before the pregnancy included self-reported history of preterm birth, low birth weight, still birth, miscarriages, infant deaths, birth defects, and abortion.