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Understanding the Relationship of Pregnancy Weight and Weight Change with Infant and Child Health

By

Stephanie Allison R. Leonard

A dissertation submitted in partial satisfaction of the

requirements for the degree of

Doctor of Philosophy

in

Epidemiology

in the

Graduate Division

of the

University of California, Berkeley

Committee in charge:

Professor Barbara Abrams, Chair
Professor Alan Hubbard
Professor Janet King

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Abstract

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Weight and weight change during pregnancy influence fetal growth and development and may have long-lasting effects on offspring health. Additionally, nearly half of women now begin pregnancy overweight or obese and a wide range of weight is gained and lost during and after pregnancy. In response to these concerns, the Institute of Medicine (IOM) revised its gestational weight gain recommendations in 2009 to include a specific, relatively narrow range of recommended gain for women with prepregnancy obesity. Unfortunately, limited scientific evidence and quantitative methods guided these recommendations. The IOM made several research recommendations, including that studies on the impact of gestational weight gain on a range of child outcomes be conducted in large, diverse populations, and that such studies address the extent to which optimal weight gain differs by maternal prepregnancy body mass index (BMI) and other maternal factors, including maternal race/ethnicity.

This dissertation aims to address gaps in our understanding of how pregnancy weight and weight change are associated with child health. The first paper demonstrates two recently developed, quantitative approaches to studying gestational weight gain and determining optimal ranges of weight gain for minimal risk of preterm birth. It also informs whether weight gain recommendations should be tailored to maternal race/ethnicity, which has previously been suggested by the IOM. The second paper identifies longitudinal trajectories of maternal weight from prepregnancy through the postpartum period and assesses the relationship between maternal weight trajectories and offspring obesity in childhood. The third paper determines if maternal history of physical abuse in childhood is related to the risk of offspring overweight in childhood, and whether prepregnancy BMI and gestational weight gain play mediating roles in such an association.

These dissertation papers together provide valuable information to help determine ranges of weight gain during pregnancy that minimize risk of adverse infant and child health outcomes. They also intend to stimulate further research to establish a scientific evidence base for creating effective interventions and clinical gestational weight gain guidelines. Promoting healthy weight and weight gain in pregnancy presents a potentially feasible and effective opportunity to improve infant and child health.

Dedication

This work is dedicated to my soon-to-be daughter.

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Acknowledgments

This work would not have been possible without the generous support of many people. Professor Barbara Abrams served as my dissertation chair and was my mentor over the past three years. She has guided every aspect of my training and devoted many days, nights, and weekends to helping me become the best researcher that I can be. I am also grateful to my other dissertation committee members, Professors Alan Hubbard and Janet King. My biostatistical abilities increased immensely because of Professor Hubbard, who has been extremely helpful and supportive inside and outside of the classroom throughout my doctoral training. Professor King helped me root my doctoral training and this dissertation in nutritional science and policy, and her contributions to this field have been a source of inspiration. I have been fortunate to have several wonderful mentors at UC Berkeley during my doctoral training, including Professors Jennifer Ahern, Jack Colford, and Mahasin Mujahid. I would also like to acknowledge my research colleagues and mentors at other institutions, who have brought diverse perspectives and expertise to my research and training: Professors Lisa Bodnar, Jennifer Hutcheon, Kathleen Rasmussen, David Rehkopf, and Dr. Lorrene Ritchie. Their ideas, input, and support were critical to the papers in this dissertation.

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Chapter 1. Introduction

Prevention of preterm birth and child obesity are national and international public health priorities (1-3). The etiologies of these health outcomes remain poorly understood, but are believed to be rooted in intergenerational pathways (1, 4, 5). In particular, maternal weight and weight change during pregnancy have been identified as likely contributors (6). Because maternal weight is modifiable, it presents a potential opportunity to intervene during a critical period of development to improve the health of infants and children.

Life Course Theory: A Theoretical Framework

Hypotheses relating maternal weight and child health are rooted in the theoretical framework of Life Course Theory. Life Course Theory connects health and disease to exposures earlier in life or across generations (7, 8). The theory grew out of research starting in the late 1980s that connected intrauterine undernutrition with adult chronic disease (9, 10). Based on initial study results at the time, Barker hypothesized that "undernutrition during gestation…permanently changes the body's structure, function and metabolism…"(9) "Barker's hypothesis" developed into the Fetal Origins of Disease Hypothesis and later the field of Developmental Origins of Health and Disease (10). The basic underlying theory is that during developmental periods of plasticity (or "critical and sensitive periods") an organism physiologically adapts to its environment (7, 10). These adaptations can permanently affect development and be adaptive or maladaptive later in life. A particularly critical period is gestation, when the intrauterine environment may stimulate responses such as DNA methylation and altered glucose-insulin metabolism in humans (10).

Life Course Theory goes beyond Developmental Origins, by providing a conceptual framework that helps explain health and disease patterns—particularly health disparities—across populations and over time (8). Following the version of Life Course Theory endorsed by the U.S. Maternal and Child Health Bureau, four key concepts comprise the theory: timeline, timing, environment, and equity (8). Pathways (or trajectories) of health are created over the lifespan and reflect a continuum of exposures and interactions (timeline). Trajectory patterns exist for different population groups. The health pathways are most influenced during critical or sensitive periods (timing). Biological, physical, and social risk factors and protective factors in a person's environment modify the health pathway (environment). Finally, inequality in health reflects more than genetics and personal choice (equity). Risk factors and protective factors exist along the pathway and operate in a person's biological, physical, and social environments. In studying the determinants of child health, Life Course Theory provides a natural framework for developing research questions, designing causal analyses, and interpreting results.

Weight and Weight Change in Pregnancy

Concerns about the risks of gestational weight gain on maternal and child health and the increased prevalence of overweight and obese childbearing women prompted the Institute of Medicine (IOM) in 2009 to revise its recommendations for weight gain during pregnancy (6). The recommendations are specific to a pregnant woman's body mass index (BMI) status before pregnancy, categorized as underweight (< 18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), or obese (≥ 30 kg/m^2). The recommended ranges of weight gain are 12.5-18 kg if underweight, 11.6-16 kg if normal weight, 7-11.5 kg if overweight, and 5-9 kg if

obese. Overall, the ideal pregnancy-related weight change would be a woman who has a normal-weight BMI when she becomes pregnancy, gains 11.5 to 16 kg over a full-term (37 to 41 weeks) pregnancy, and then returns to her prepregnancy weight by six to 12 months after delivery.

Most women in the U.S. are not meeting pregnancy-related weight recommendations (4–6). Approximately one-third of women aged 20 to 39 years old are normal weight, with 26.7% overweight and an additional 31.8% obese (11). Additionally, only one-third of women with full-term pregnancies are meeting gestational weight gain guidelines, with 20.4% gaining below and 47.5% gaining above the recommendations (12). Also most women do not return to their prepregnancy weights; an estimated 25-50% of mothers are more than 10 pounds heavier six to 12 months postpartum than they were before pregnancy (6). Our understanding of whether and how such deviations from pregnancy-related weight recommendations—particularly from weight change recommendations—are related to offspring health is limited (6, 13, 14). A substantial challenge has been disentangling gestational weight gain from gestational duration in studies of weight gain and child health outcomes (13, 15). Shorter pregnancies have less time for weight to be gained, leading to overestimated associations between low weight gain and gestational-age dependent outcomes (15, 16). To address this challenge, our colleagues developed gestational weight gain-for-gestational age z-score and percentile charts, which can be used to study associations independent of gestational duration (16-18). The z-scores have been found to be internally valid, but their external validity is unknown and critical to their adoption outside the source population in Pennsylvania (16, 19). Chapter 2 of this dissertation aims to fill this research need by assessing the generalizability of the z-scores by applying them to the outcome of preterm birth separately in Pennsylvania and California statewide data as well as in several racial/ethnic groups in California. Assessment of the z-scores and preterm birth among racial/ethnic groups also adds to very limited evidence on whether the optimal range of gestational weight gain differs by race/ethnicity.

Chapters 3 and 4 focus on maternal weight and child obesity. Prepregnancy BMI, gestational weight gain, and postpartum weight retention may have distinct effects on the development of child obesity, but their combined effect is not known. To fill this research gap, Chapter 3 describes longitudinal trajectories of maternal weight from prepregnancy through the postpartum period and assesses the relationships between maternal weight trajectories and offspring obesity in childhood in a prospective, national cohort study. Using the same cohort study, Chapter 4 seeks to expand understanding of the life-course etiology of child obesity by determining if women's experience of childhood adversity may contribute to their children's risk of obesity, and whether higher maternal weight and/or weight gain in pregnancy mediate such an association.

The goal of this dissertation is to increase knowledge of how pregnancy-related weight and weight change affect infant and child health. Pregnancy-related weight presents a potential opportunity to intervene during a critical period of development to improve the short- and long-term health of infants and children. Improving research methodologies and pursuing life-course pathways may advance the effectiveness of maternal and child health interventions and policies.

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Chapter 2. Generalizability of pregnancy weight gain z-scores to preterm birth: across populations and by race/ethnicity

Introduction

Preterm birth affects more than 1 in 10 infants and is a leading cause of infant death and long-term disabilities in the U.S. and worldwide (1, 2). Weight gain during pregnancy has long been of interest as a potentially modifiable contributor to preterm birth and related outcomes, but has been difficult to study because women gain more weight as the duration of pregnancy increases (1, 3, 4). To address the need for a weight gain classification independent of gestational duration, our research team developed maternal weight gain-for-gestational age z-score and percentile charts for each week of gestation using a population of women with healthy pregnancy and birth outcomes in Pittsburgh, Pennsylvania (5, 6). We found that the z-score charts enabled estimation of the association between total gestational weight gain and preterm birth in Pennsylvania birth data that is unconfounded by length of pregnancy (7).

The external validity of the z-score charts, however, has been questioned (6, 8) because the source population for the z-scores was not nationally representative. In particular, the convenience sample that we used lacked women of Hispanic and Asian/Pacific Islander race/ethnicity, who make up nearly one-third of births in the U.S. (9). Racial/ethnic variation in gestational weight gain and the possibility that optimal weight gain differs among racial/ethnic groups could affect the generalizability of the z-score chart (9-11). Indeed, in 1990, the Institute of Medicine (IOM) recommended that non-Hispanic black women gain at the upper end of the recommended ranges of gestational weight gain to improve infant outcomes (12). However, the updated 2009 IOM report cited a lack of evidence to support this recommendation (13). Understanding racial/ethnic differences would improve the application of the z-scores in diverse populations and inform future national recommendations for weight gain during pregnancy.

This study had two objectives: (1) to assess the generalizability of the gestational weight gain z-score charts by applying them separately in California and Pennsylvania birth data, and (2) to determine whether maternal race/ethnicity modifies the gestational weight gain range associated with minimal risk of preterm birth by comparing several racial/ethnic groups in California. We accomplished these objectives by applying noninferiority margins, a quantitative method typically used to determine if a new treatment is at least as good as an existing treatment, as a novel approach to determining optimal gestational weight gain z-score ranges.

Methods

Study Aim 1: Application of existing z-score charts to California and Pennsylvania births
A California study population was drawn from the 3,208,204 recorded live births that occurred in the state from 2007 through 2012. In 2007, California adopted the 2003 Revision of the U.S. Standard Certificate of Live Birth, which collects information on prepregnancy weight, delivery weight, and height at the time of delivery. A Pennsylvania study population was drawn from the 1,565,921 recorded live births that occurred in the state from 2003 to 2013, during which time the 2003 revised birth certificate was also used. We retained singleton births with complete, plausible values for gestational age, prepregnancy weight, height, body mass index (BMI),

delivery weight, and gestational weight gain (Supplemental Figure 1). Criteria from the U.S. Centers for Disease Control and Prevention were used to identify biologically implausible values (14). The California sample included 2,744,741 births and the Pennsylvania sample included 1,310,920 births. The State of California Committee for the Protection of Human Subjects, the University of California, Berkeley Committee for the Protection of Human Subjects, and the University of Pittsburgh Human Research Protection Office approved the study.

Preterm birth was defined as a delivery before 37 weeks of pregnancy, using obstetric estimate of gestational age from the birth certificates. Maternal height, prepregnancy weight, and delivery weight were reported on the birth certificates. Maternal prepregnancy body mass index (BMI) was calculated by dividing prepregnancy weight by the square of height (kg/m^2) and classified as underweight (< 18.5), normal weight (≥ 18.5 and < 25), overweight (≥ 25 and < 30), obese class 1 (≥ 30 and < 35), obese class 2 (≥ 35 and < 40), and obese class 3 (≥ 40). Gestational weight gain was the difference between maternal delivery weight and prepregnancy weight. We converted total gestational weight gain to weight gain-for-gestational age z-scores using z-score charts specific to prepregnancy BMI group (5, 6). Confounding variables were determined *a priori* using prior evidence and directed acyclic graphs (15). These variables were selected from available birth certificate fields and included maternal race/ethnicity, maternal age at delivery, height, parity, education level, expected method of payment for delivery, cigarette smoking in the 3 months prior to pregnancy, and trimester of entry to prenatal care (1, 2, 16-24).

Statistical analyses were stratified by state (California and Pennsylvania) and prepregnancy BMI category (because weight gain recommendations vary by BMI) (13, 19-21, 23). Multiple logistic regression models with robust standard errors were used to model the association between maternal weight gain z-score and preterm birth. We used stabilized inverse probability weights to account for missing covariate data in the regression models (25). To capture nonlinear relationships, continuous variables (maternal weight gain z-score, height, and age) were fit with restricted cubic splines using Akaike and Bayesian information criteria to determine the number of knots using Harrell's default placements (26).

We used the models to then predict the marginal probability of preterm birth across weight gain z-scores, with 95% confidence intervals. The probabilities were multiplied by 100 for preterm birth risk per 100 live births, and the nadir of preterm birth risk was identified for each model. To determine ranges of optimal gestational weight gain for the lowest risk of preterm birth, we implemented a noninferiority margin approach described in detail previously (27). We pre-specified a noninferiority risk difference (RD) margin of 1% based on the Healthy People 2020 goal to reduce the prevalence of preterm birth in the U.S. (28). This noninferiority margin represented the range of weight gain z-scores for which the predicted risk of preterm birth was no more than 1 percentage point higher than the lowest observed risk. A noninferiority RD margin of 2% was used as a secondary approach. We identified the z-scores on the lower and upper sides of the nadir at which the upper limit of the 95% confidence interval exceeded the pre-specified margin of noninferiority. Using the z-score charts, we then calculated total gestational weight gain amounts at 28 and 40 weeks' gestation that corresponded to the noninferiority margin z-scores. These ranges reflected ranges of total gestational weight gain ranges associated with minimal risk of preterm birth.

Study Aim 2: Assessing effect modification by maternal race/ethnicity

For the second aim, we used California birth certificate data linked to infants' hospital discharge records that were previously generated via probabilistic linkage by the California Office of Statewide Health Planning and Development (29). We followed the same inclusion criteria as for the first aim, except we additionally excluded births that did not have linked records, had congenital anomalies (identified using patient discharge data), or were missing maternal race and ethnicity information (Supplemental Figure 2). The final sample comprised 2,280,206 California births.

We categorized race/ethnicity as non-Hispanic white, non-Hispanic black, Mexican, other Latin American/Caribbean, Eastern Asian (Chinese, Hmong, Japanese, Korean), South/Southeastern Asian/Pacific Islander (Indian, Cambodian, Filipino, Laotian, Thai, Vietnamese, Guamanian, Hawaiian, Pacific Islander, Samoan), and American Indian/Alaskan Native based on U.S. Census groupings and United Nations regional groupings (30, 31). For stability of statistical models, we also grouped races/ethnicities and combined all obesity classes (BMI $\geq$ 30) with the goal of at least 100 cases. We duplicated Aim 1 analytical procedures for this aim, but additionally stratified analyses by maternal race/ethnicity and adjusted models for maternal nativity (available only in California).

In a secondary analysis, we tested whether optimal ranges of gestational weight gain differed between spontaneous and provider-initiated preterm births. We used patient diagnosis and procedure codes in addition to birth certificates in the California linked dataset to classify preterm birth with premature labor or premature rupture of membranes as spontaneous and all other preterm births as provider-initiated. We used multiple logistic regression models adjusted for all confounding variables, including maternal race/ethnicity and nativity, and stratified by all categories of prepregnancy BMI for this analysis. All analyses were performed using Stata version 13.1 (StataCorp, College Station, Texas).

Results

Study Aim 1

In California, 51% of women were Hispanic, 30% were non-Hispanic white, 13% were Asian/Pacific Islander, and 6% were non-Hispanic black (Supplemental Table 1). In contrast, 73% of women in Pennsylvania were non-Hispanic white, 13% were non-Hispanic black, 9% were Hispanic, and 4% were Asian/Pacific Islander. In both California and Pennsylvania, approximately half of women were normal weight prepregnancy, 45% were overweight or obese, and 70% had a gestational weight gain z-score within a moderate range (-1 to +1 standard deviations). The prevalence of preterm birth was 6.3% in California and 7.7% in Pennsylvania.

The results for the 1% RD noninferiority margin analyses in California and Pennsylvania are shown in Table 1. As an example, in women who were normal weight and delivered in California, the lowest risk of preterm birth was 5.2 per 100 live births and occurred at a gestational weight gain z-score of 0.03. The 95% confidence interval included the 1% RD noninferiority margin from -0.72 to +0.68 z-scores. This range would be equivalent to 7.6–13.3 kg at 28 weeks of pregnancy and 12.5–20.7 kg at 40 weeks of pregnancy, which is full term. In women who were normal weight and delivered in Pennsylvania, the lowest preterm birth risk

was 5.1 per 100 live births and occurred at a z-score of 0.24. The 1% RD noninferiority margin ranged from -0.44 to +0.87 z-scores, which corresponds to 8.6–14.2 kg at 28 weeks of pregnancy and 14.0–22.0 kg at 40 weeks of pregnancy. Figure 1 illustrates these findings by overlaying markers of the 1% and 2% RD noninferiority margins on plots of the predicted marginal probabilities of preterm birth across the weight gain z-scores in California and Pennsylvania.

Weight gain ranges at term corresponding to the 1% RD noninferiority margins in California and Pennsylvania women are shown in Figure 2. The ranges were similar in width and overlapped in all prepregnancy BMI groups, except for underweight and obese class 3, for which there was insufficient statistical power in the Pennsylvania sample to determine the 1% RD noninferiority margins. However, the predicted marginal probability plots for women who were underweight or obese class 3 were similar in the California and Pennsylvania samples (Supplemental Figure 3) and the 2% RD noninferiority margins in underweight women were similar in both samples (Supplemental Table 2). The optimal weight gain ranges for preterm birth were slightly lower in California compared to Pennsylvania across BMI groups. The ranges also consistently decreased with increasing BMI above normal weight in California and above overweight in Pennsylvania. Noninferiority margins for 2% risk differences corresponded to weight gain ranges at 40 weeks of pregnancy that were approximately 4–5 kg wider than for 1% RD noninferiority margins (Supplemental Table 2).

Study Aim 2

Maternal characteristics and preterm birth prevalence varied across maternal racial/ethnic groups within the California linked birth certificate and infant hospital discharge sample (Table 2). Eastern Asian women had the highest prevalence of prepregnancy underweight and American Indian/Alaskan Native women had the highest prevalence of obesity. Low gestational weight gain (< -1 standard deviation) was most common in the Hispanic and Asian groups and high weight gain (> 1 standard deviation) was most common in the American Indian/Alaskan Native and non-Hispanic black groups. The prevalence of preterm birth ranged from 5.2% in Eastern Asian women to 9.2% in non-Hispanic black women.

Among the maternal race/ethnic groups, the ranges established by the noninferiority margins largely overlapped. In women who were normal weight prepregnancy, the total z-score range across racial/ethnic groups for a noninferiority margin of 1% RD was -0.72 to 0.68, equivalent to 11.8–22.2 kg at 40 weeks of pregnancy (Figure 3; Supplemental Table 3). The ranges differed in width, which was likely because of differences in statistical power among subgroups. In racial/ethnic groups with higher statistical power, 95% confidence intervals were narrower causing noninferiority margins to be wider. For detailed results and additional optimal weight gain range plots comparing racial/ethnic groups in California, see Supplemental Tables 3 and 4 and Supplemental Figure 4. Statistical power was insufficient to estimate the noninferiority margins in several combinations of prepregnancy BMI and maternal race/ethnicity, which were therefore excluded. However, Supplemental Figure 5 shows the adjusted predicted marginal probabilities of preterm birth in all prepregnancy BMI-racial/ethnic groups in California. There was no indication of meaningful differences between races/ethnicities, except for extreme weight values in American Indians/Alaskan Natives, which were too sparse to be reliable. As for the first study aim, noninferiority margins of 2% RD resulted in optimal weight gain ranges that

were generally wider by 4–5 kg than for noninferiority margins of 1% RD (Supplemental Table 4).

For the secondary analysis separating spontaneous preterm birth from provider-initiated preterm birth, optimal weight gain ranges were slightly wider for both outcomes and tended to encompass the ranges found for preterm birth overall (Supplemental Table 5). For example, in normal-weight women, the equivalent weight gain ranges at 40 weeks of pregnancy were 12.3–22.5 kg for spontaneous preterm birth (prevalence 4.5%) and 6.3–24.5 kg for provider-initiated preterm birth (prevalence 1.9%).

Discussion

In this population-based study, maternal weight gain z-score charts provided an internally and externally valid approach to studying the association between gestational weight gain and preterm birth. Optimal gestational weight gain ranges for minimal risk of preterm birth, determined using noninferiority margins and the z-score charts, differed by prepregnancy BMI, but did not meaningfully differ between two fundamentally different state populations or by maternal racial/ethnic groups in California.

Serial, measured weights in pregnancy are the gold standard for weight gain classification, but are only available in limited study populations (5, 16-18). Total gestational weight gain is the most widely available measure and has been used in numerous studies on weight gain and preterm birth (13, 19-22). These studies have classified total weight gain using inconsistent approaches, which have been found to overestimate associations between low weight gain and preterm birth (7). Our research team developed the gestational weight gain-for-gestational age z-score and percentile charts as a new way to classify gestational weight gain independent of gestational duration, akin to the well-established use of fetal and pediatric weight-for-age z-score and percentile charts (32, 33). We created the z-scores using serial, measured prenatal weights from women with healthy pregnancy and birth outcomes in Pittsburgh, Pennsylvania (5). Although the z-scores have been applied to Pennsylvania births and national births to non-Hispanic black and non-Hispanic white women (7, 34, 35), this study is the first to directly assess the generalizability of the z-scores to populations with diverse racial/ethnic make-up. The z-scores were similarly associated with preterm birth in two states with highly different population characteristics and among racial/ethnic groups, which supports their use in diverse populations in the U.S. This finding corroborates a recent study of international gestational weight gain z-scores and percentiles in normal-weight women (36), as well as the use of universal fetal and pediatric growth charts among all populations in the U.S. (32, 33).

Non-Hispanic black women in the U.S. are more likely than non-Hispanic white women to deliver infants who are preterm and low birthweight, and, if underweight or normal weight, are more likely to have low gestational weight gain (9-11). These disparities prompted the IOM in 1990 to recommend that non-Hispanic black women gain at the upper end of the recommended gestational weight gain ranges (12), but this recommendation was abandoned in the 2009 IOM revision because of insufficient evidence (13). A few studies that assessed gestational weight gain and preterm birth in relation to race/ethnicity have reported modest and inconsistent differences between non-Hispanic black and non-Hispanic white women (18, 19, 22, 35, 37). In

the current analysis, we extended our assessment of gestational weight gain and preterm birth to seven racial/ethnic groups. There were considerable differences in gestational weight gain amounts and the prevalence of preterm birth among racial/ethnic groups; however, differences in the optimal ranges of gestational weight gain for minimal risk of preterm birth were small and do not substantiate tailoring weight gain recommendations to race/ethnicity.

This study, although limited to the outcome of preterm birth, may be informative for future revisions of the IOM guidelines for weight gain during pregnancy. We applied a unique, quantitative approach to determine optimal weight gain ranges for preterm birth in six prepregnancy BMI categories. Weight gain ranges that corresponded to preterm birth risk within one percentage point of minimum risk, in alignment with the Healthy People 2020 goal for preterm birth, were very comparable to the IOM recommended ranges in underweight, normal-weight, and overweight women (13). The upper limits of the ranges found in this study were higher than the upper limits of the IOM recommended ranges; however, the upper range limits in the IOM guidelines were based primarily on reducing risk of cesarean delivery and large-for-gestational age births (13). Revisions to the IOM guidelines would require consideration of several maternal and child health outcomes, in addition to preterm birth. In its 2009 report, the IOM recommended a single weight gain range for any grade of maternal obesity, but identified the need for more research to determine whether weight gain guidelines should vary by grades of obesity and possibly include weight loss (13). Although we found that the weight gain range associated with the lowest risk of preterm birth for obese class 1 women was consistent with the IOM range for obese women, the optimal weight gain ranges for women with class 2 and 3 obesity were lower than the IOM recommendations and, at the two percent margin of risk, included weight loss. These findings support those in other recent studies of women with prepregnancy obesity (21, 34). Given these findings, separate gestational weight gain recommendations for obesity classes 2 and 3 may be beneficial in guiding weight gain goals and prenatal care that promote healthy birth outcomes. Establishing appropriate guidelines is especially important because of the increasing prevalence of severe obesity (38).

The validity of prepregnancy weight reported on the birth certificate varies by prepregnancy BMI and likely caused some misclassification of prepregnancy BMI and gestational weight gain in this study (39, 40). However, there is little evidence of error in birth certificate-derived delivery weight and a recent systematic review concluded that error in self-reported prepregnancy weight largely did not bias associations with birth outcomes (39, 40). Statistical power in some combinations of prepregnancy BMI and racial/ethnic groups prevented analysis in all subgroups of interest, particularly American Indians/Alaskan Natives and South/Southeastern Asians/Pacific Islanders. More research on maternal weight and weight gain in these racial/ethnic groups is needed. We were also unable to validly distinguish spontaneous and provider-initiated preterm births or exclude infants with congenital anomalies using birth certificate data in the first study aim (24), but did not find any differences after differentiating preterm birth type and excluding congenital anomalies using the California patient discharge data. Our study was observational and limited to births in Pennsylvania and California. It can therefore only demonstrate associations and may not extend to other populations.

This study used two contemporary population-based samples that comprised over 4 million births. Large sample sizes and diverse characteristics enabled us to study a wide range of

gestational weight gain and prepregnancy BMI, and to make comparisons across several racial/ethnic groups. The noninferiority margin method demonstrated an approach to identifying optimal ranges of weight gain during pregnancy that is quantitative, systematic, and reproducible (27). Preterm birth was classified using the obstetric estimate of gestational age on the birth certificates, which has been found to have excellent validity (41). Infant hospital discharge data linked to birth certificate data in California also enabled valid differentiation of spontaneous and provider-initiated preterm birth in a secondary set of analyses.

This study provides evidence to support the generalizability of gestational weight gain z-score and percentile charts created in Pennsylvania to diverse populations in the U.S. The charts may be useful tools to further our understanding of optimal gestational weight gain, which could inform future interventions and weight gain recommendations. Using the z-score charts, we found that low and high weight gain were associated with increased risk of preterm birth and that optimal weight gain ranges for preterm birth decreased as severity of prepregnancy overweight/obesity increased. Additionally, the present findings add to limited evidence that gestational weight gain recommendations tailored to maternal race/ethnicity are not warranted.

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Tables and Figures

Table 1. Adjusted[a] Results in California (*n* = 2,744,741), 2007-2012, and Pennsylvania (*n* = 1,310,920), 2003-2013, Pregnancies using Noninferiority Margins of One Percentage Point in Marginal Risk

Prepregnancy Body Mass Index and U.S. State	Lowest Risk per 100 Live Births	Weight-gain Z-score of Lowest Risk	Lower Margin		Upper Margin		Corresponding Weight Gain at 28 wk (kg)	Corresponding Weight Gain at 40 wk (kg)
			Risk Difference (95% Confidence Interval)	Weight Gain Z-score	Risk Difference (95% Confidence Interval)	Weight Gain Z-score		
Underweight								
CA	6.1	0.20	0.29 (0.11, 0.48)	-0.30	0.31 (0.13, 0.49)	0.75	8.8 – 12.9	13.7 – 19.7
PA	8.5	0.28	NA	NA	NA	NA	NA	NA
Normal weight								
CA	5.2	0.03	0.44 (0.38, 0.49)	-0.72	0.42 (0.36, 0.49)	0.68	7.6 – 13.3	12.5 – 20.7
PA	5.1	0.24	0.40 (0.30, 0.49)	-0.44	0.37 (0.24, 0.49)	0.87	8.6 – 14.2	14.0 – 22.0
Overweight								
CA	5.1	-0.11	0.39 (0.29, 0.49)	-0.87	0.38 (0.29, 0.48)	0.26	5.4 – 11.4	9.8 – 17.9
PA	5.2	0.13	0.33 (0.18, 0.48)	-0.49	0.31 (0.13, 0.49)	0.56	7.2 – 15.3	12.3 – 23.4
Obese Class 1								
CA	6.1	-0.46	0.33 (0.18, 0.47)	-1.20	0.36 (0.23, 0.49)	0.14	1.4 – 8.7	4.4 – 14.1
PA	5.9	0.13	0.27 (0.07, 0.48)	-0.34	0.22 (-0.03, 0.48)	0.45	5.8 – 10.8	10.2 – 16.8
Obese Class 2								
CA	6.2	-0.39	0.26 (0.04, 0.49)	-0.96	0.32 (0.15, 0.49)	0.12	-0.6 – 5.9	2.1 – 11.1
PA	5.9	0.05	0.16 (-0.16, 0.49)	-0.37	0.14 (-0.19, 0.49)	0.29	2.7 – 7.1	6.6 – 12.8
Obese Class 3								
CA	6.9	-0.33	0.17 (-0.15, 0.49)	-0.67	0.26 (0.03, 0.48)	0.05	-1.9 – 3.3	0.3 – 7.4
PA	NA	NA	NA	NA	NA	NA	NA	NA

CA, California; PA, Pennsylvania; NA, not available.

[a] Adjusted for maternal race/ethnicity, maternal age at delivery, height, parity, education level, expected method of payment for delivery, cigarette smoking in the 3 months prior to pregnancy, and trimester of entry to prenatal care.

Table 2. Characteristics of Women Delivering Live Births in California (*n* = 2,280,206), 2007-2012

	Mexican	Non-Hispanic White	Latin American/ Caribbean	South/South-eastern Asian/ Pacific Islander	Non-Hispanic Black	Eastern Asian	American Indian/ Alaskan Native
	n = 1,015,386 %	*n* = 664,456 %	*n* = 227,453 %	*n* = 132,550 %	*n* = 121,386 %	*n* = 110,478 %	*n* = 8,497 %
Pre-pregnancy body mass index (kg/m^2)							
Underweight (<18.5)	2.7	4.3	2.9	8.4	4.1	12.0	2.9
Normal weight (18.5 to <25)	42.0	57.2	44.7	63.8	41.9	72.6	36.7
Overweight (25 to <30)	30.2	22.1	28.5	18.1	26.3	11.8	26.4
Obese (≥ 30)	25.1	16.4	23.9	9.7	27.7	3.7	34.0
Gestational weight gain z-score							
<-1 standard deviation	24.0	14.8	22.4	21.6	18.9	24.3	15.1
-1 to +1 standard deviation	69.2	74.6	70.0	71.3	67.8	71.5	70.4
>+1 standard deviation	6.8	10.7	7.7	7.1	13.3	4.3	14.5
Maternal age at birth							
10-19 y	12.5	4.0	12.2	2.7	13.0	1.2	12.1
20-24 y	26.6	15.9	25.9	11.5	29.4	5.6	29.1
25-29 y	27.3	27.7	27.1	25.2	25.6	19.0	28.1
30-34 y	20.5	30.0	21.3	33.2	19.1	40.0	19.3
≥35 y	13.2	22.3	13.6	27.5	13.0	34.1	11.4
Primiparous	34.0	44.7	39.1	41.5	41.1	48.9	34.1
Maternal education at birth							
Less than high school	42.3	5.8	32.4	6.1	16.7	3.6	23.4
High school graduate	30.9	21.2	31.3	20.9	34.6	10.9	37.6
Some college	19.6	28.6	24.4	30.3	34.9	18.0	28.5
College graduate	7.2	44.4	12.0	42.7	13.9	67.6	10.5
Expected payment for delivery							
Private health insurance	28.0	71.7	32.7	66.8	35.4	72.6	35.7
Other	72.0	28.3	67.4	33.2	64.6	27.4	64.3
Mother born in the U.S.	43.7	87.3	54.7	22.7	90.4	18.8	98.3
Smoked cigarettes in 3 months before pregnancy	1.2	7.3	1.9	2.1	6.0	1.0	14.2
Trimester of prenatal care entry							
1st trimester	80.5	87.7	82.3	83.7	78.1	88.7	69.5

2nd trimester	15.9	10.2	14.4	13.7	17.5	9.4	23.2
3rd trimester or none	3.6	2.1	3.3	2.7	4.4	1.9	7.3
Preterm birth	6.3	5.6	6.9	8.1	9.2	5.2	7.6
Spontaneous preterm birth	4.3	4.0	4.8	5.7	6.4	3.9	5.1
Provider-initiated preterm birth	1.9	1.6	2.1	2.4	2.8	1.3	2.6

Figure 1. Adjusted predicted marginal risks of preterm birth per 100 live births in (A) California and (B) Pennsylvania women who were normal weight (BMI 18.5-24.9 kg/m^2) before pregnancy. Solid curved lines represent point estimates and dashed curved lines represent 95% confidence intervals. The inside vertical lines represent the noninferiority margins for a 1% risk difference and the outside vertical lines represent the noninferiority margins for a 2% risk difference.

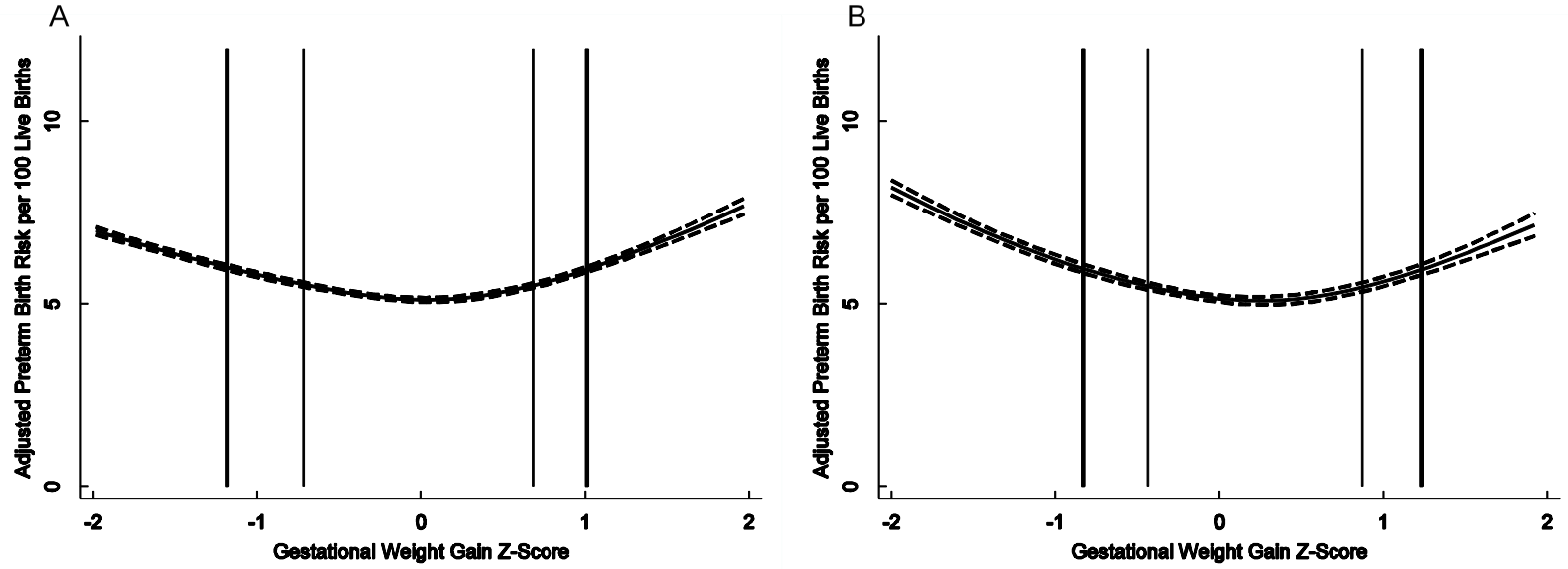


Figure 2. Optimal gestational weight gain ranges at term (40 weeks' gestation) for lowest preterm birth risk corresponding to noninferiority margins of 1% risk difference. Solid lines represent California and dashed lines represent Pennsylvania. Data for low and high weight gains in Pennsylvania underweight and obese class 3 were sparse.

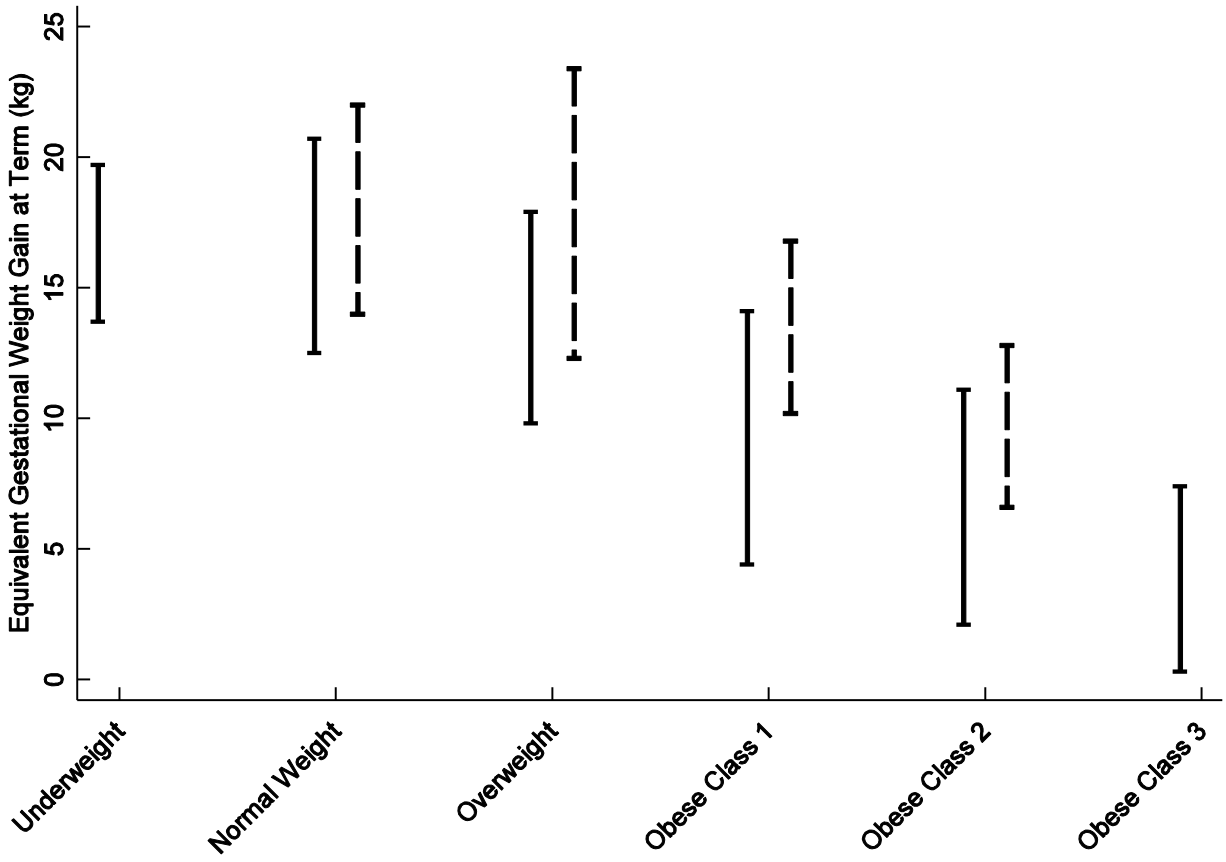
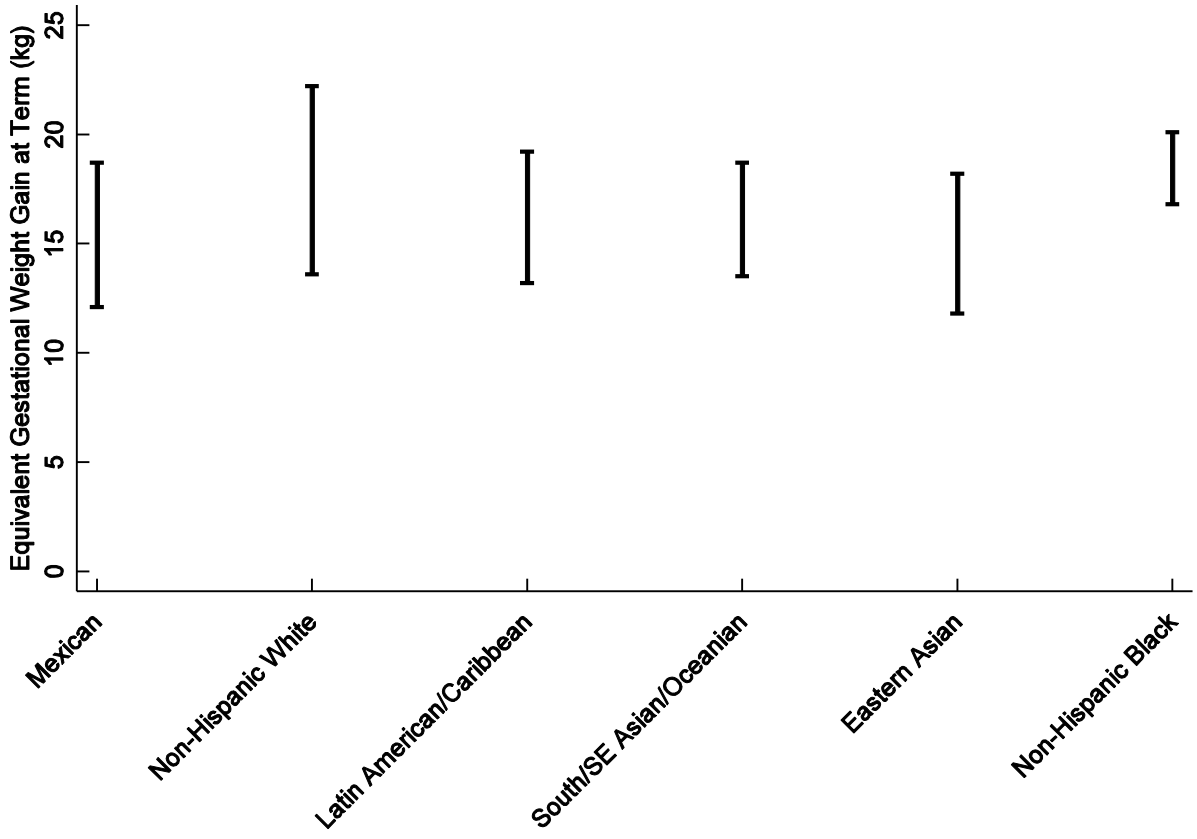


Figure 3. Optimal gestational weight gain ranges at term (40 weeks' gestation) for lowest preterm birth risk corresponding to noninferiority margins of 1% risk difference in California births to women who were normal weight (BMI 18.5-24.9 kg/m^2) before pregnancy.



Supplemental Table 1. Characteristics of Women Delivering Live Births in California (*n* = 2,744,741), 2007-2012, and Pennsylvania (*n* = 1,310,920), 2003-2013.

	California	Pennsylvania
	%	%
Maternal race/ethnicity		
Non-Hispanic white	29.7	73.4
Non-Hispanic black	5.5	13.3
Hispanic	51.4	8.9
Asian/Pacific Islander	13.0	3.6
Other	0.4	0.8
Prepregnancy body mass index (kg/m^2)		
Underweight (< 18.5)	4.1	4.4
Normal weight (18.5 to < 25)	50.1	51.5
Overweight (25 to < 30)	25.7	23.3
Obese class 1 (30 to < 35)	12.4	11.6
Obese class 2 (35 to < 40)	4.9	5.4
Obese class 3 (≥ 40)	2.8	3.7
Gestational weight gain z-score		
<-1 SD	20.9	17.4
-1 to 1 SD	70.9	70.5
>1 SD	8.2	12.1
Maternal age at birth		
10-19 y	8.3	8.6
20-24 y	20.9	22.5
25-29 y	27.0	28.3
30-34 y	25.7	25.8
≥ 35 y	18.1	14.9
Primiparous	39.3	55.6
Maternal education at birth		
Less than high school	24.7	15.0
High school graduate	25.9	26.5
Some college	23.6	26.8
College graduate	25.7	31.7
Expected payment for delivery		
Private health insurance	47.4	63.3
Other	52.6	36.8
Smoked cigarettes in 3 months before pregnancy	3.3	22.3
Trimester of prenatal care entry		
1st trimester	83.5	71.7
2nd trimester	13.5	20.1
3rd trimester or none	3.0	8.2
Preterm birth	6.3	7.7

Supplemental Table 2. Adjusted[a] Results in California (*n* = 2,744,741), 2007-2012, and Pennsylvania (*n* = 1,310,920), 2003-2013, Pregnancies using Noninferiority Margins of Two Percentage Points in Marginal Risk.

	Lower Margin		Upper Margin			
Prepregnancy Body Mass Index and State of Residence	Risk Difference (95% Confidence Interval)	Weight Gain Z-score	Risk Difference (95% Confidence Interval)	Weight Gain Z-score	Corresponding Weight Gain at 28 wk (kg)	Corresponding Weight Gain at 40 wk (kg)
Underweight						
CA	0.79 (0.60, 0.98)	-0.59	0.73 (0.49, 0.99)	1.12	7.8 – 14.5	12.3 – 22.3
PA	NA	NA	NA	NA	NA	NA
Normal Weight						
CA	0.94 (0.87, 0.99)	-1.19	0.91 (0.84, 0.99)	1.01	6.1 – 14.9	10.3 – 23.0
PA	0.87 (0.75, 0.99)	-0.83	0.85 (0.70, 0.99)	1.23	7.2 – 16.1	12.0 – 24.7
Overweight						
CA	NA	NA	0.89 (0.79, 0.99)	0.46	NA – 12.6	NA – 19.6
PA	0.81 (0.62, 0.99)	-1.40	0.80 (0.61, 0.99)	0.83	3.1 – 15.0	6.7 – 23.0
Obese Class 1						
CA	0.77 (0.58, 0.96)	-1.68	0.85 (0.70, 0.99)	0.40	-0.8 – 10.4	1.7 – 16.4
PA	0.71 (0.44, 0.99)	-0.98	0.71 (0.46, 0.98)	0.70	2.4 – 12.5	5.8 – 19.2
Obese Class 2						
CA	0.70 (0.42, 0.99)	-1.41	0.78 (0.56, 0.99)	0.34	-2.7 – 7.5	-0.8 – 13.3
PA	0.57 (0.18, 0.97)	-1.35	0.59 (0.22, 0.98)	0.52	-2.5 – 8.9	-0.4 – 15.3
Obese Class 3						
CA	0.60 (0.25, 0.96)	-1.02	0.73 (0.47, 0.99)	0.28	-4.0 – 5.3	-2.4 – 10.2
PA	NA	NA	NA	NA	NA	NA

CA, California; PA, Pennsylvania; NA, not available

[a] Adjusted for maternal race/ethnicity, maternal age at delivery, height, parity, education level, expected method of payment for delivery, cigarette smoking in the 3 months prior to pregnancy, and trimester of entry to prenatal care.

Supplemental Table 3. Adjusted[a] Results among Maternal Racial/Ethnic Groups using Noninferiority Margins of One Percentage Point in Marginal Risk in the California Linked Birth Sample (*n* = 2,280,206), 2007-2012.

Prepregnancy Body Mass Index and Race/Ethnicity	Lowest risk per 100 live births	Weight-gain z-score of lowest risk	Lower Margin		Upper Margin		Corresponding Weight Gain at 28 wk (kg)	Corresponding Weight Gain at 40 wk (kg)
			Risk Difference (95% CI)	Weight Gain Z-score	Risk Difference (95% CI)	Weight Gain Z-score		
Underweight								
Mexican	6.3	0.19	0.11 (-0.26, 0.49)	-0.12	0.14 (-0.21, 0.49)	0.56	9.4 – 12.0	14.6 – 18.5
Non-Hispanic White	5.8	0.29	0.13 (-0.22, 0.49)	-0.07	0.15 (-0.18, 0.49)	0.72	9.6 – 12.7	14.9 – 19.5
South/Southeastern Asian/Pacific Islander	6.0	0.08	NA	NA	NA	NA	NA	NA
Latin American/ Caribbean	6.8	0.13	NA	NA	NA	NA	NA	NA
Non-Hispanic Black	9.3	0.31	NA	NA	NA	NA	NA	NA
Eastern Asian	3.9	0.10	0.06 (-0.35, 0.48)	-0.12	0.08 (-0.30, 0.49)	0.38	9.4 – 11.3	14.6 – 17.4
American Indian/Alaskan Native	6.1	0.38	NA	NA	NA	NA	NA	NA
Normal weight								
Mexican	5.1	-0.04	0.37 (0.27, 0.48)	-0.81	0.37 (0.25, 0.49)	0.59	7.3 – 11.9	12.1 – 18.7
Non-Hispanic White	4.5	0.18	0.39 (0.29, 0.49)	-0.51	0.38 (0.27, 0.49)	0.89	8.4 – 14.3	13.6 – 22.2
South/Southeastern Asian/Pacific Islander	6.6	-0.01	0.25 (0.02, 0.49)	-0.53	0.20 (-0.09, 0.49)	0.37	8.3 – 11.9	13.5 – 18.7
Latin American/ Caribbean	5.6	-0.01	0.27 (0.07, 0.48)	-0.59	0.22 (-0.028, 0.49)	0.45	8.1 – 12.3	13.2 – 19.2
Non-Hispanic Black	7.0	0.31	0.12 (-0.22, 0.48)	0.07	0.11 (-0.25, 0.49)	0.59	10.6 – 12.9	16.8 – 20.1
Eastern Asian	4.2	-0.21	0.27 (0.05, 0.49)	-0.87	0.22 (-0.02, 0.48)	0.29	7.1 – 11.6	11.8 – 18.2

American Indian/Alaskan Native	5.0	0.42	NA	NA	NA	NA	NA	NA
Overweight								
Mexican	4.9	-0.15	0.36 (0.23, 0.49)	-0.79	0.34 (0.20, 0.47)	0.21	5.8 – 11.1	10.3 – 17.5
Non-Hispanic White	4.4	-0.03	0.31 (0.14, 0.48)	-0.52	0.29 (0.12, 0.46)	0.36	7.1 – 12.0	12.1 – 18.8
South/Southeastern Asian/Pacific Islander	8.0	-0.18	NA	NA	0.02 (-0.44, 0.49)	-0.11	NA – 9.2	NA – 15.0
Latin American/ Caribbean	5.5	-0.15	0.21 (-0.05, 0.48)	-0.58	0.19 (-0.10, 0.49)	0.12	6.8 – 10.5	11.7 – 16.8
Non-Hispanic Black	6.6	0.00	0.12 (-0.23, 0.49)	-0.24	0.05 (-0.36, 0.49)	0.12	8.5 – 10.5	14.0 – 16.8
Eastern Asian	5.3	-0.12	NA	NA	NA	NA	NA	NA
American Indian/Alaskan Native	5.8	-0.61	NA	NA	NA	NA	NA	NA
Obese								
Mexican	5.8	-0.56	0.32 (0.16, 0.49)	-1.24	0.35 (0.23, 0.48)	-0.01	1.2 – 7.8	4.2 – 12.8
Non-Hispanic White	5.5	-0.18	0.22 (-0.03, 0.49)	-0.81	0.26 (0.05, 0.48)	0.26	3.3 – 9.5	6.9 – 15.1
South/Southeastern Asian/Pacific Islander	8.5	0.04	NA	NA	NA	NA	NA	NA
Latin American/ Caribbean	6.3	-0.47	0.11 (-0.25, 0.48)	-0.78	0.21 (-0.05, 0.49)	-0.08	3.4 – 7.3	7.1 – 12.2
Non-Hispanic Black	7.8	-0.35	0.01 (-0.45, 0.49)	-0.42	0.09 (-0.28, 0.49)	-0.10	5.4 – 7.2	9.6 – 12.1
Eastern Asian	7.1	0.10	NA	NA	NA	NA	NA	NA
American Indian/Alaskan Native	6.5	-1.12	NA	NA	NA	NA	NA	NA

CI, confidence interval; NA, not available

[a] Adjusted for maternal nativity, maternal age at delivery, height, parity, education level, expected method of payment for delivery, cigarette smoking in the 3 months prior to pregnancy, and trimester of entry to prenatal care.

Supplemental Table 4. Adjusted[a] Results among Maternal Racial/Ethnic Groups using Noninferiority Margins of Two Percentage Points in Marginal Risk in the California Linked Birth Sample (n = 2,280,206), 2007-2012.

	Lower Margin		Upper Margin			
Prepregnancy Body Mass Index and Race/Ethnicity	Risk Difference (95% CI)	Weight Gain Z-score	Risk Difference (95% CI)	Weight Gain Z-score	Corresponding Weight Gain at 28 wk (kg)	Corresponding Weight Gain at 40 wk (kg)
Underweight						
Mexican	0.60 (0.23, 0.99)	-0.51	0.53 (0.09, 0.99)	0.99	8.1 – 13.9	12.7 – 21.3
Non-Hispanic White	0.61 (0.25, 0.99)	-0.44	0.51 (0.60, 0.99)	1.19	8.3 – 14.9	13.0 – 22.8
South/Southeastern Asian/Pacific Islander	0.39 (-0.17, 0.99)	-0.39	0.41 (-0.14, 0.99)	0.63	8.5 – 12.3	13.3 – 18.9
Latin American/ Caribbean	0.14 (-0.62, 0.99)	-0.23	0.19 (-0.53, 0.99)	0.58	9.0 – 12.1	14.0 – 18.6
Non-Hispanic Black	NA	NA	NA	NA	NA	NA
Eastern Asian	0.52 (0.10, 0.98)	-0.60	0.40 (-0.12, 0.99)	0.79	7.8 – 13.0	12.3 – 20.0
American Indian/Alaskan Native	NA	NA	NA	NA	NA	NA
Normal weight						
Mexican	0.87 (0.75, 0.99)	-1.30	0.85 (0.72, 0.99)	0.94	5.7 – 14.6	9.8 – 22.5
Non-Hispanic White	0.86 (0.73, 0.99)	-0.94	0.83 (0.68, 0.99)	1.3	6.9 – 16.5	11.5 – 25.2
South/Southeastern Asian/Pacific Islander	0.69 (0.39, 0.99)	-1.02	0.65 (0.34, 0.96)	0.70	6.6 – 13.4	11.1 – 20.8
Latin American/ Caribbean	0.71 (0.46, 0.98)	-1.00	0.72 (0.45, 0.99)	0.84	6.7 – 14.1	11.2 – 21.8
Non-Hispanic Black	0.67 (0.36, 0.98)	-0.26	0.59 (0.24, 0.97)	0.97	19.3 – 14.7	14.9 – 22.7
Eastern Asian	0.72 (0.46, 0.97)	-1.38	0.69 (0.41, 0.98)	0.64	5.5 – 13.1	9.5 – 20.4

American Indian/Alaskan Native	NA	NA	NA	NA	NA	NA
Overweight						
Mexican	NA	NA	0.78 (0.63, 0.93)	0.39	NA – 12.2	NA – 19.0
Non-Hispanic White	0.69 (0.40, 0.99)	-1.67	0.80 (0.63, 0.98)	0.64	2.0 – 13.7	5.2 – 21.2
South/Southeastern Asian/Pacific Islander	NA	NA	0.39 (-0.16, 0.98)	0.15	NA – 10.7	NA – 17.0
Latin American/ Caribbean	NA	NA	0.62 (0.30, 0.95)	0.33	NA – 11.8	NA – 18.5
Non-Hispanic Black	0.52 (0.09, 0.98)	-0.55	0.52 (0.07, 0.99)	0.42	6.9 – 12.3	11.9 – 19.3
Eastern Asian	NA	NA	NA	NA	NA	NA
American Indian/Alaskan Native	NA	NA	NA	NA	NA	NA
Obese						
Mexican	0.76 (0.54, 0.99)	-1.68	0.83 (0.67, 0.99)	0.26	-0.8 – 9.5	1.7 – 15.1
Non-Hispanic White	0.67 (0.37, 0.98)	-1.41	0.72 (0.49, 0.95)	0.50	0.4 – 11.1	3.2 – 17.3
South/Southeastern Asian/Pacific Islander	0.21 (-0.49, 0.97)	-0.32	0.14 (-0.61, 0.97)	0.26	5.9 – 9.5	10.4 – 15.1
Latin American/ Caribbean	0.59 (0.21, 0.99)	-1.24	0.61 (0.28, 0.95)	0.19	1.2 – 9.0	4.2 – 14.5
Non-Hispanic Black	0.41 (-0.12, 0.99)	-1.07	0.51 (0.06, 0.99)	0.21	2.0 – 9.2	5.2 – 14.7
Eastern Asian	NA	NA	NA	NA	NA	NA
American Indian/Alaskan Native	NA	NA	NA	NA	NA	NA

CI, confidence interval; NA, not available

[a] Adjusted for maternal race/ethnicity, age at delivery, height, parity, education level, expected method of payment for delivery, cigarette smoking in the 3 months prior to pregnancy, and trimester of entry to prenatal care

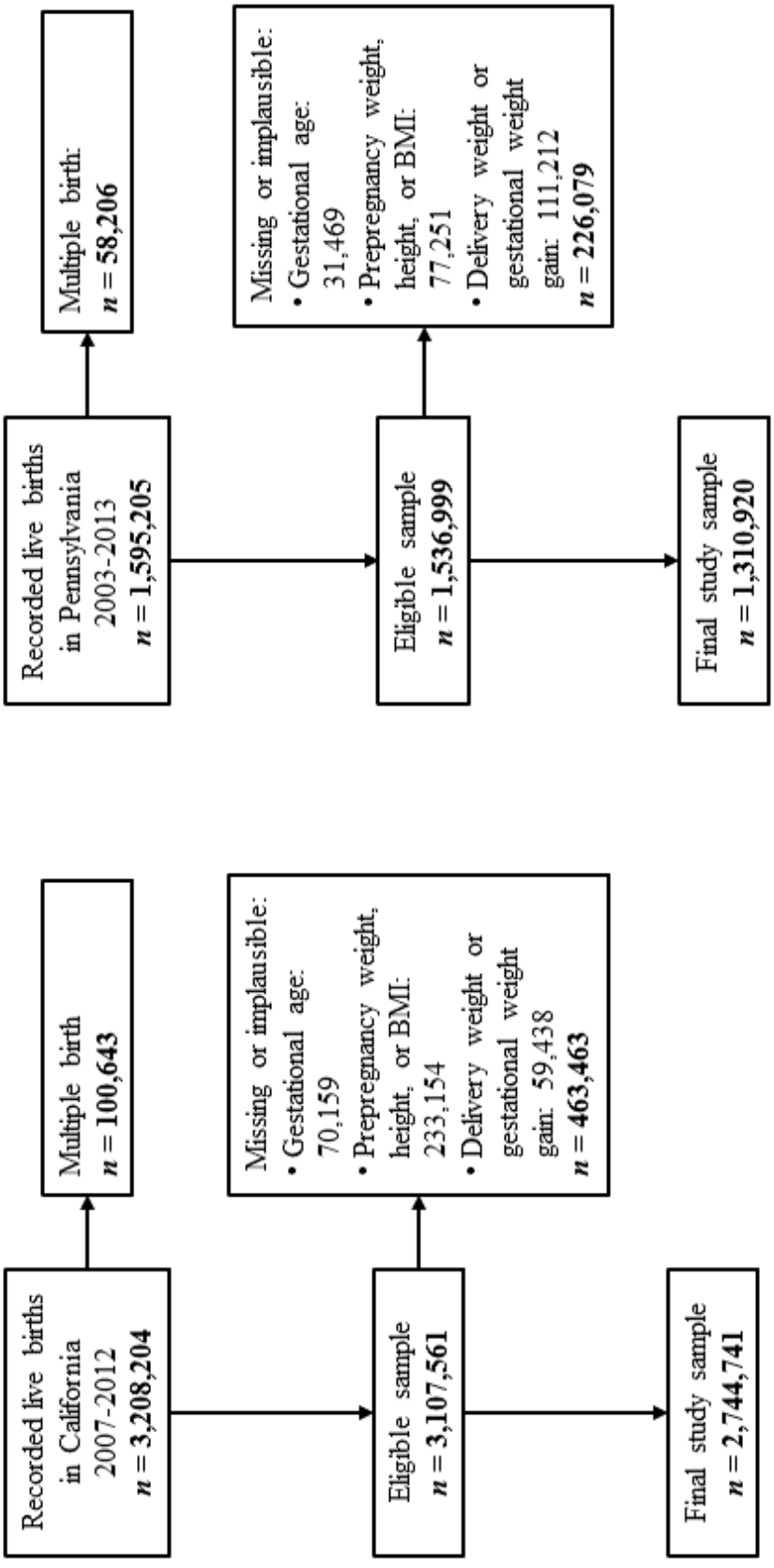
Supplemental Table 5. Adjusted[a] Results for Spontaneous and Provider-initiated Preterm Birth, using Noninferiority Margins of One Percentage Point in Marginal Risk in the California Linked Birth Sample (*n* = 2,280,206), 2007-2012.

Outcome and Prepregnancy Body Mass Index	Lowest Risk per 100 Live Births	Weight Gain Z-score of Lowest Risk	Lower Margin		Upper Margin		Corresponding Weight Gain at 28 wk (kg)	Corresponding Weight Gain at 40 wk (kg)
			Risk Difference (95% CI)	Weight Gain Z-score	Risk Difference (95% CI)	Weight Gain Z-score		
Spontaneous								
Underweight	4.2	0.27	0.33 (0.18, 0.49)	-0.16	0.27 (0.05, 0.49)	1.06	9.3 – 14.3	14.4 – 21.8
Normal Weight	3.6	0.12	0.42 (0.36, 0.48)	-0.77	0.43 (0.37, 0.49)	0.94	7.4 – 14.6	12.3 – 22.5
Overweight	3.4	-0.07	0.42 (0.34, 0.49)	-0.81	0.39 (0.31, 0.48)	0.39	5.7 – 12.2	10.2 – 19.0
Obese Class 1	4.2	-0.29	0.35 (0.22, 0.49)	-1.36	0.36 (0.23, 0.49)	0.38	0.6 – 10.3	3.5 – 16.2
Obese Class 2	4.2	-0.31	0.35 (0.21, 0.49)	-1.36	0.36 (0.23, 0.49)	0.38	-2.6 – 7.8	-0.5 – 13.8
Obese Class 3	4.5	-0.28	0.36 (0.22, 0.49)	-1.37	0.37 (0.24, 0.49)	0.39	-5.9 – 6.3	-4.7 – 11.6
Provider-initiated								
Underweight	1.8	0.03	0.32 (0.17, 0.48)	-1.07	0.32 (0.16, 0.49)	1.27	6.4 – 15.3	10.2 – 23.4
Normal Weight	1.5	-0.23	0.42 (0.36, 0.49)	-2.19	0.44 (0.39, 0.49)	1.20	3.2 – 15.9	6.3 – 24.5
Overweight	1.6	-0.86	NA	NA	0.43 (0.37, 0.49)	0.51	NA – 12.9	NA – 20.1
Obese Class 1	1.7	-0.64	0.37 (0.25, 0.49)	-1.82	0.40 (0.32, 0.49)	0.37	-1.3 – 10.2	0.9 – 16.1
Obese Class 2	1.8	-0.50	0.30 (0.13, 0.49)	-1.53	0.36 (0.24, 0.49)	0.30	-6.6 – 5.5	-5.7 – 10.4
Obese Class 3	2.1	-0.24	0.26 (0.05, 0.49)	-1.00	0.31 (0.14, 0.49)	0.41	-0.8 – 8.0	1.9 – 14.1

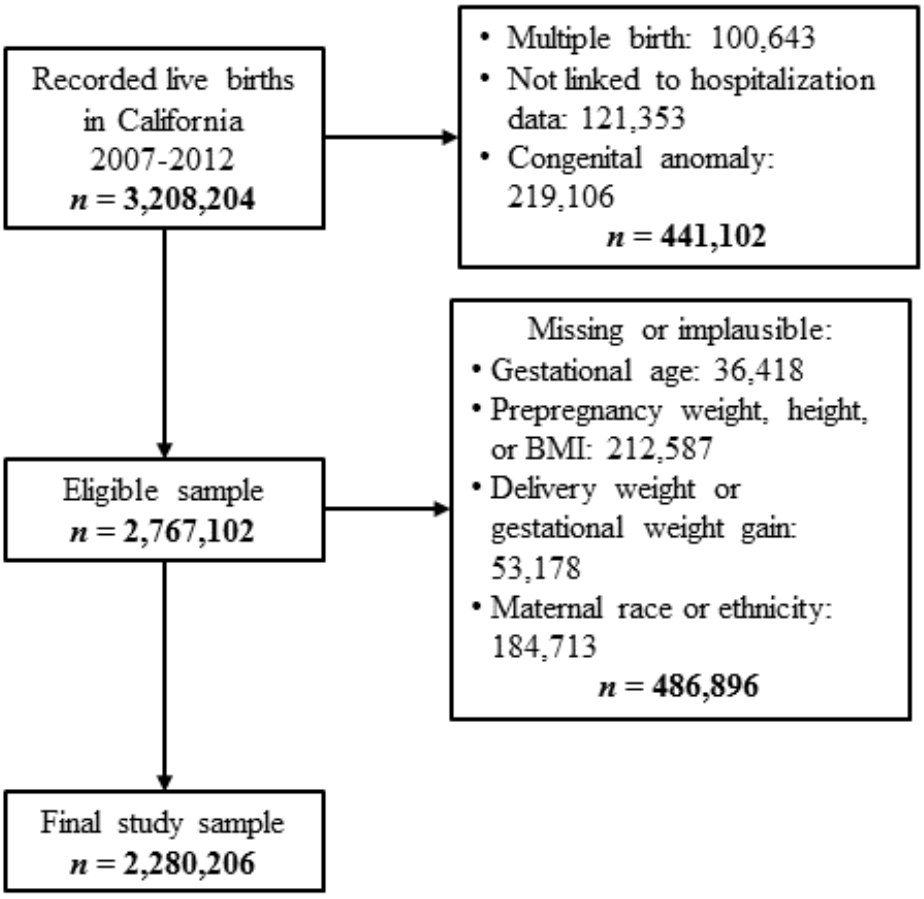
CI, confidence interval

[a] Adjusted for maternal race/ethnicity, maternal age at delivery, height, parity, education level, expected method of payment for delivery, cigarette smoking in the 3 months prior to pregnancy, and trimester of entry to prenatal care.

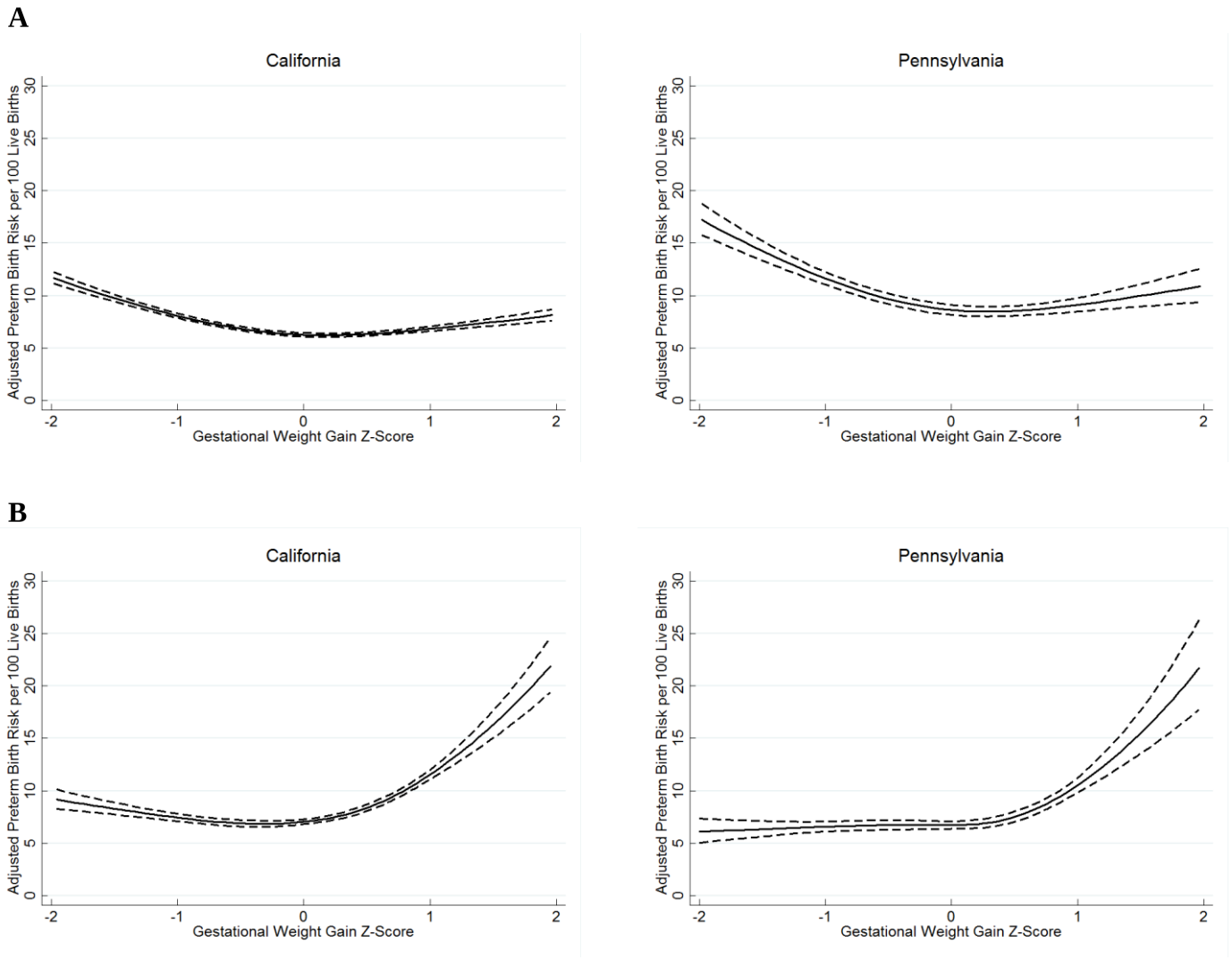
Supplemental Figure 1. Selection of California and Pennsylvania samples for the study's first aim.



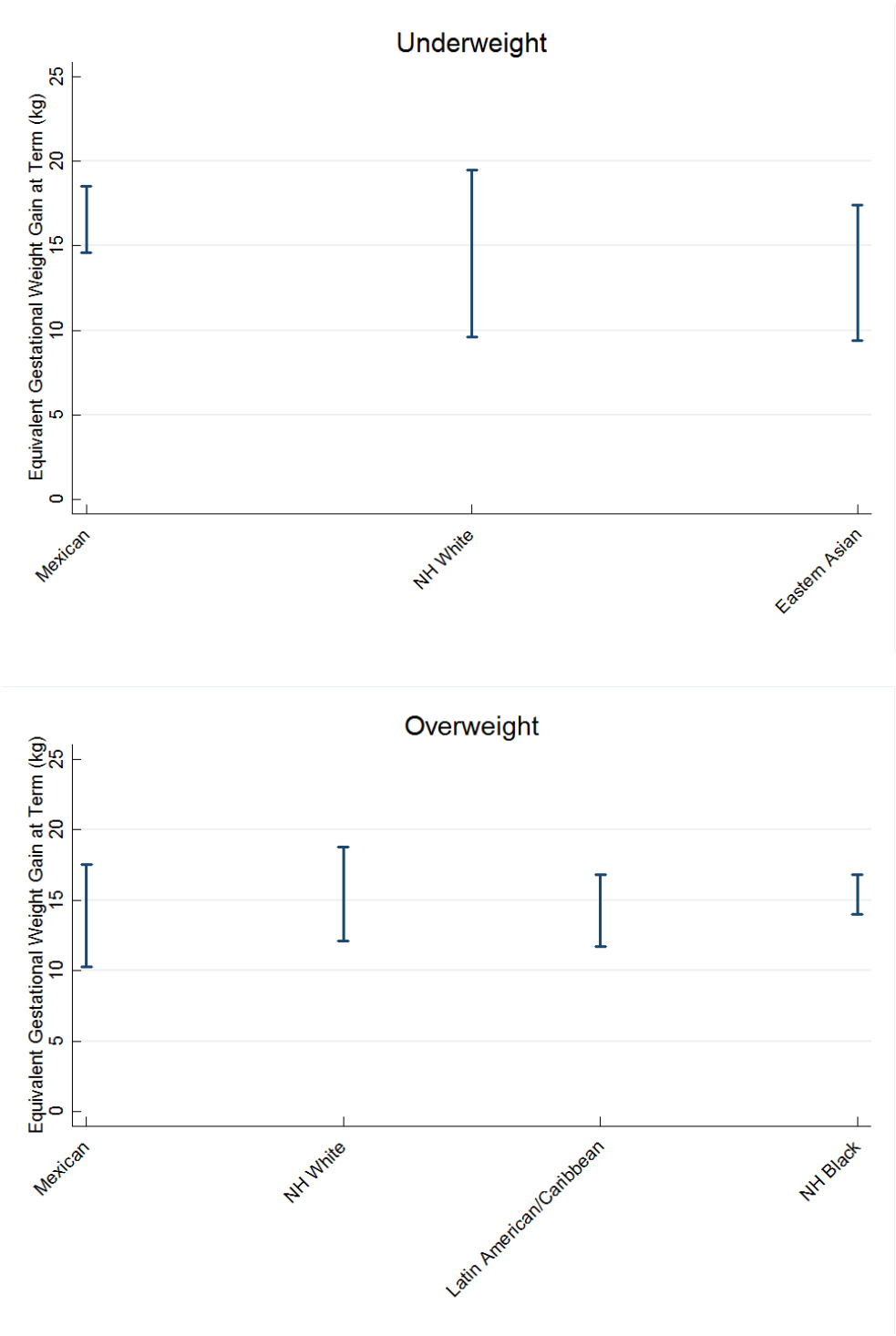
Supplemental Figure 2. Selection of sample for the study's second aim.

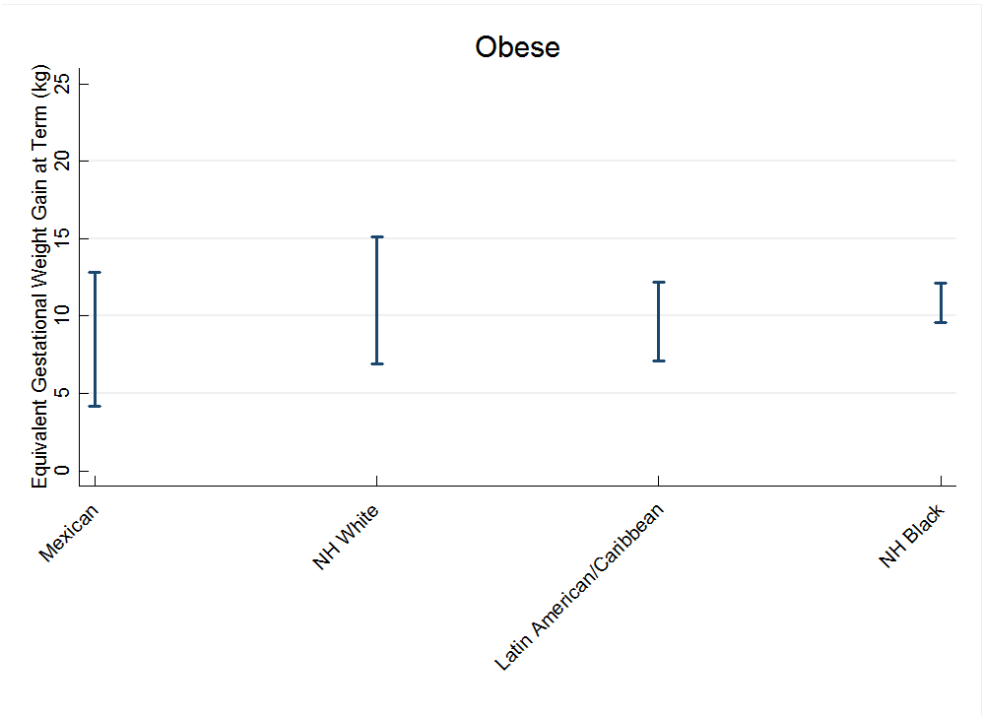


Supplemental Figure 3. Relationship between gestational weight gain z-scores and preterm birth in California and Pennsylvania women who were underweight (**A**) or obese class 3 (**B**) before pregnancy. Solid lines represent adjusted predicted marginal probabilities and dashed lines represent 95% confidence intervals.

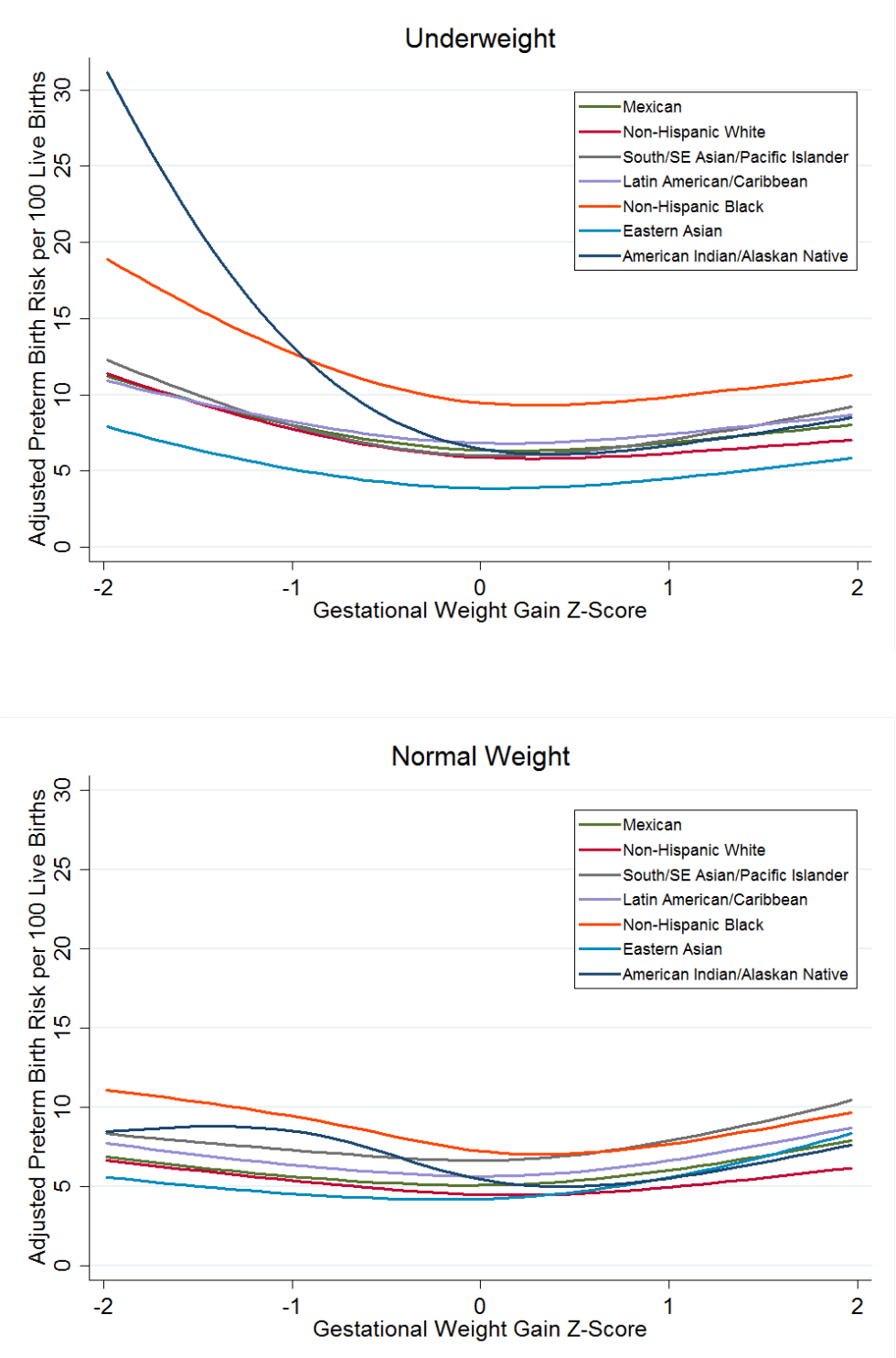


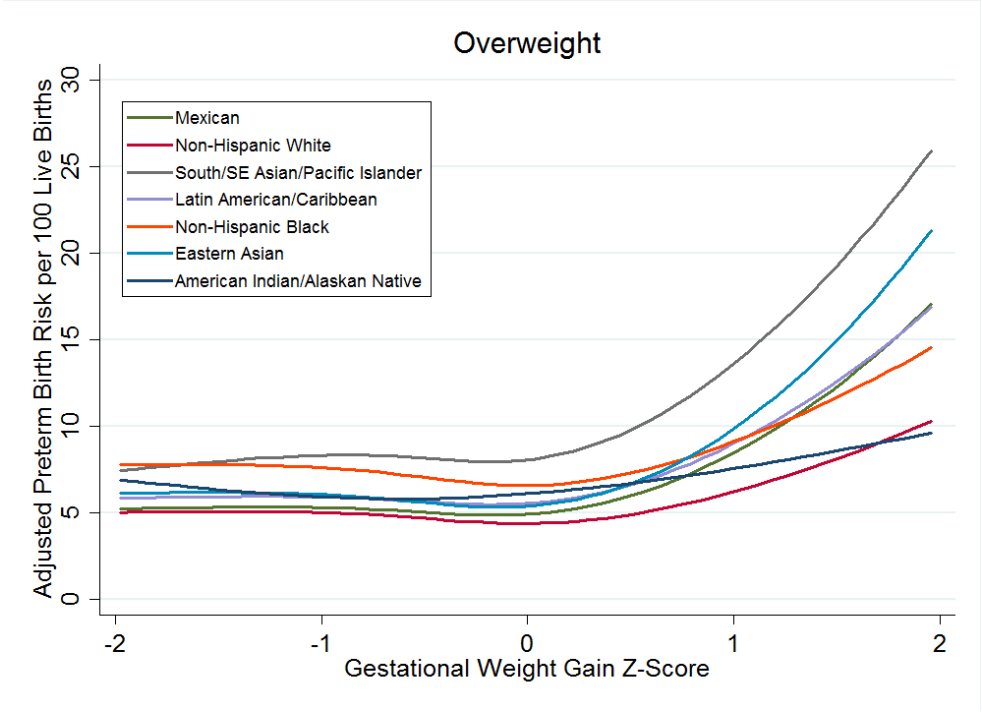
Supplemental Figure 4. Optimal gestational weight gain ranges at term (40 weeks' gestation) for lowest preterm birth risk corresponding to noninferiority margins of 1% risk difference in California births to women who were underweight, overweight, and obese before pregnancy. Maternal racial/ethnic groups with sparse data were excluded.

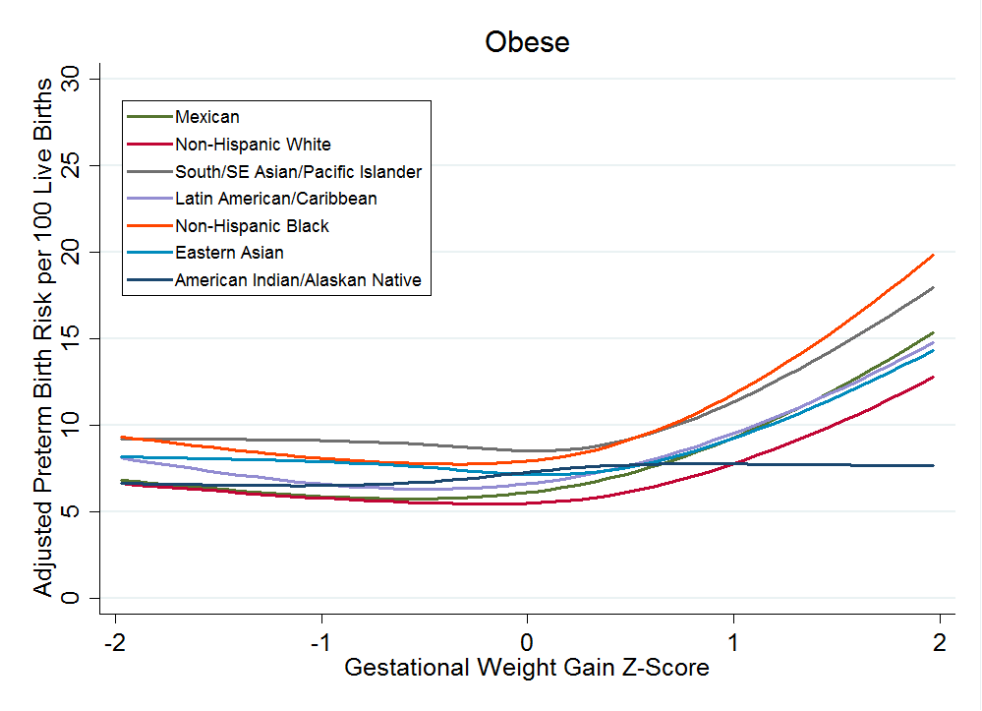



Obese
Equivalent Gestational Weight Gain at Term (kg)
0
5
10
15
20
25
Mexican
NH White
Latin American/Caribbean
NH Black

Supplemental Figure 5. Adjusted predicted marginal probabilities of preterm birth across gestational weight gain z-scores in subgroups of prepregnancy BMI and maternal race/ethnicity, California births (*n* = 2,280,206), 2007-2012.




Overweight
Adjusted Preterm Birth Risk per 100 Live Births
0
5
10
15
20
25
30
Mexican
Non-Hispanic White
South/SE Asian/Pacific Islander
Latin American/Caribbean
Non-Hispanic Black
Eastern Asian
American Indian/Alaskan Native
-2
-1
0
1
2
Gestational Weight Gain Z-Score


Obese
Adjusted Preterm Birth Risk per 100 Live Births
0
5
10
15
20
25
30
Mexican
Non-Hispanic White
South/SE Asian/Pacific Islander
Latin American/Caribbean
Non-Hispanic Black
Eastern Asian
American Indian/Alaskan Native
-2
-1
0
1
2
Gestational Weight Gain Z-Score

Chapter 3. Trajectories of maternal weight from prepregnancy through postpartum and associations with childhood obesity

Introduction

Obesity affects children's physical, social, and emotional health and puts them at higher risk of obesity and its related diseases in adulthood (1). For the past 15 years, obesity (body mass index (BMI) $\geq 95^{th}$ percentile for age and sex) has affected approximately 1 in 6 American children and adolescents (2). Child obesity prevention efforts have been predominantly school-based, but many children are already obese when they begin school and a growing body of evidence suggests that gestation and early life are critical periods for child obesity development (1-7). In their recent systematic review of possible causes of child obesity occurring in the "first 1,000 days" (conception through age 2 years), Woo Baidal et al. (3) identified high prepregnancy BMI and excessive gestational weight gain, along with prenatal tobacco use, high infant birthweight, and high infant weight gain, as leading risk factors. The possible effect of postpartum weight on child obesity has also been investigated in a few recent studies. These authors (8-10) reported increased risks of child obesity with high postpartum weight retention or gain. Maternal weight and weight change are thought to affect child obesity through shared genetic predispositions, intrauterine effects (particularly of increased insulin concentrations on metabolic regulation), and environmental factors, such as shared diet quality, feeding behaviors, and obesogenic home and community environments (4-7). The interplay of these pathways, however, is complex and not yet understood (4-6).

Prepregnancy BMI, gestational weight gain, and postpartum weight retention have generally been studied as distinct causes of child health outcomes (3, 10-13). This approach, however, fails to consider the combined effects of these closely related maternal weight measures (14-16). Studying maternal weight as a trajectory from before pregnancy through the postpartum period could enable a more comprehensive understanding of maternal weight measures and how they may jointly influence the development of child obesity. This approach has provided new insights into child growth and development (8, 17, 18), but, to our knowledge, has not been applied to maternal weight across the childbearing period. The identification of high-risk maternal weight trajectories could improve the understanding of the relationship between maternal and child weight, inform targeted interventions in mothers, and help determine which children are at the highest risk of obesity.

In this study, the goals were to (1) describe longitudinal trajectories of maternal weight from before pregnancy through the postpartum period using national, longitudinal data from 1981 to 2014 and (2) assess the relationships between maternal weight trajectories and offspring obesity in childhood.

Methods

Study design and population

Data were used from the National Longitudinal Survey of Youth 1979 (NLSY79), which is an ongoing, prospective cohort study that enrolled adolescents and young adults aged 14 to 21 years old in 1979 and followed them annually until 1994 and biennially thereafter. The NLSY79 began

collecting data on weight and height in 1981. In 1986, the study began to enroll female participants' children in the Child and Young Adult sub-cohort (NLSY79-CYA), conducting biennial assessments and interviews thereafter. These studies have been described in detail elsewhere (19, 20). This study draws from the NLSY79-CYA mothers and their children through 2014 (4,932 women and 11,512 children). The study population was restricted to full-term (≥ 37 weeks' gestation) singletons born after 1981 to primiparous women (n = 3,428). By restricting the sample to full-term, singleton births, the IOM gestational weight gain recommendations (16) could be applied appropriately. By selecting for primiparity, it was possible to control for the strong influence of parity on maternal weight and weight change. Maternal weight and height were only collected after 1981. We excluded participants because of missing data for the following variables: maternal prepregnancy, delivery, or postpartum BMI (n = 825 (24%)), gestational age (n = 76 (2%)), child BMI (if missing all measurements during ages 3-16 years) (n = 316 (9%)), or covariates (n = 330 (10%)). The final sample included 1,881 mother-child pairs. Further sample selection details are shown in Supplemental Figure 1. As a sensitivity analysis, we used multiple imputation for missing covariate data. The University of California, Berkeley Committee for the Protection of Human Subjects approved the study.

Maternal weight status and characteristics

NLSY79 participants self-reported their current weight in each survey wave beginning in 1981, and prepregnancy and delivery weights were self-reported in the first survey wave of the NLSY79-CYA after delivery beginning in 1986. Maternal height was self-reported in 1981, 1982, 1985, 2006, and 2008; the first height measurement preceding the delivery year was used as prepregnancy height. The reliability of prepregnancy weight, self-reported postpartum, was previously assessed by comparing prepregnancy weight to the weight reported at the closest survey prior to that pregnancy, which were found to be similar (21). Prepregnancy BMI was calculated from prepregnancy weight and height (kg/m^2) and gestational weight gain was the difference between delivery weight and prepregnancy weight (kg). Postpartum weight was defined as women's first self-reported current weight between 6 to 36 months after delivery. If a subsequent pregnancy began during this time frame, the prepregnancy weight reported for that pregnancy was used as the postpartum weight measurement corresponding to the first pregnancy (n = 95 (5%)). Postpartum weight retention was defined as the difference between postpartum weight and prepregnancy weight (kg), which could include weight gain or loss.

We used national recommendations and prior studies (14, 16, 22) to dichotomize each woman's prepregnancy BMI (overweight or obese: ≥ 25 kg/m^2), gestational weight gain (excessive based on the IOM guidelines: ≥ 18 kg if underweight, ≥ 16 kg if normal weight, ≥ 11.5 kg if overweight, ≥ 9 kg if obese), and postpartum weight retention (high: ≥ 5 kg). Thus, each woman was classified as 'above' or 'below' the cut-off for each time point and these were combined into 1 of 8 maternal weight trajectory groups: below-below-below (reference group), below-below-above, below-above-below, below-above-above, above-below-below, above-below-above, above-above-below, and above-above-above.

To investigate whether our results were robust to different classification schemes for maternal weight across the childbearing period, we assessed three additional trajectory classifications in sensitivity analyses. For the first sensitivity analysis, we used latent class growth modeling (LCGM) to allow the data to inform the trajectory groups instead of pre-specifying

classifications. The LCGM method identifies subgroups of individuals following distinct patterns of change over time and the Bayesian information criterion can then be used to determine the number of trajectories that best fit the data (23, 24). This method also can account for varying gestational durations and postpartum follow-up times. For the second sensitivity analysis, we used three categories of gestational weight gain (inadequate, adequate, excessive) instead of two categories (not excessive, excessive) to determine if there were differences between inadequate and adequate weight gain, as defined by the IOM (16), in relation to child obesity. For the third sensitivity analysis, we used the median gestational weight gain (13.6 kg; 30.0 lb) instead of IOM recommendations to dichotomize gestational weight gain. Gestational weight gain defined using the IOM recommendations is a relative measure; less weight must be gained as prepregnancy BMI group increases to qualify as excessive weight gain. In this study, median gestational weight gain was 14.5 kg in women with prepregnancy BMI < 25 and was 12.9 kg in women with prepregnancy BMI ≥ 25.

We used causal diagrams based on prior evidence and knowledge to select covariates *a priori* from available data (25). Confounders included maternal education level at delivery (less than high school, high school completion, some college or more), employment status at delivery (unemployed, part-time, full-time), race/ethnicity (set by NLSY79 as Hispanic, non-Hispanic black, non-Hispanic non-black), marital status (married/unmarried), equivalized household income (inflation-adjusted dollars), smoking during pregnancy (yes/no), delivery year, child sex (female/male), large-for-gestational age (LGA, weight-for-gestational age > 90th percentile) (26), and ever breastfed (1-3, 12, 16, 27, 28).

Child obesity

Child weight and height data were collected in biennial surveys from age 3 to 16 years. We used the SAS program for the 2000 CDC growth charts to calculate age- and sex-specific BMI percentiles and biologically implausible values, which were then excluded (29). We grouped the age-specific BMI percentiles into two-year periods that reflected the data collection schedule. For example, one BMI value could be available for the period of age 3-4 years. If child data were collected at two consecutive ages, we averaged the BMI values. Trained study personnel measured 64% of the child weights and 66% of the child heights in the final sample; the remaining data were self-reported by the mothers or children (at older ages). Our primary outcome of interest was child obesity (BMI ≥ 95th percentile). We also used overweight (BMI ≥ 85th and < 95th percentile) as the outcome in a secondary analysis.

Statistical analysis

We tested the associations between maternal weight trajectories and child obesity using Poisson regression models with robust standard errors, which enable the estimation of risk ratios as opposed to odds ratios. The models were fit with generalized estimating equations to account for repeated BMI measurements within individual children. We adjusted the regression models for education, employment, race/ethnicity, marital status, household income, smoking, delivery year, child sex, LGA status, and ever breastfed, as detailed above. The multiple regression models were used to predict the adjusted probability of child obesity in each maternal weight trajectory group.

We used the same analytical procedure in several secondary analyses. First, child overweight was used as the outcome instead of child obesity. We then replicated the regression models with missing covariate data multiply imputed to assess bias from missing data. The multiple imputation procedure used chained equations to create 50 datasets. The percentage of missing observations for each covariate ranged from 0 to 9%, with a median of 2%. Finally, we tested associations using the alternative trajectory groups: made using 1) LCGM, 2) three categories of gestational weight gain adequacy, and 3) median gestational weight gain.

All analyses were conducted in Stata MP version 14.2 (Stata Corporation, College Station, Texas).

Results

Nearly two-thirds of women in the study sample started pregnancy overweight or obese, gained gestational weight above the IOM guidelines, and/or retained ≥ 5 kg postpartum (Table 1). Characteristics of mother-child pairs varied across the maternal weight trajectory groups. Compared to women in the reference group (ideal trajectory: below-below-below), a higher proportion of women with the least ideal trajectory (above-above-above) were not college educated, were employed full-time, were Hispanic or non-Hispanic black, and had a lower household income. The characteristics of mother-child pairs included in the final sample, eligible but excluded from the final sample, and ineligible for the study are provided in Supplemental Table 1. Within the eligible study population, there were minimal differences between included and excluded subjects.

The overall prevalence of child obesity increased from 12% at age 3-4 years to 16% at age 15-16 years and was highest among women who had a higher prepregnancy BMI and lowest in the reference maternal weight trajectory group (Figure 1). In unadjusted and adjusted regression analyses, compared to the reference group, all but one maternal weight trajectory group were associated with increased risk of child obesity (Table 2), with varying magnitude. Among women without a higher prepregnancy BMI, the adjusted risk of child obesity was 36% higher in the trajectory with excessive gestational weight gain and 63% higher in the trajectory with both excessive gestational weight gain and high postpartum weight retention. The trajectory with high postpartum weight retention was associated with an 8% increased risk of child obesity, but the 95% confidence interval included zero. Among women who were overweight or obese pregnancy, the adjusted risks of child obesity were 129-145% higher than in the reference group. Adjustment for covariates attenuated association estimates, but did not change the statistical significance of the results.

Predicted probabilities of child obesity adjusted for covariates also varied by maternal trajectory group (Figure 2). The lowest predicted probability of child obesity was 0.10 (95% CI: 0.08, 0.11) in the reference group. For excessive gestational weight gain only, the predicted probability was 0.14 (95% CI: 0.11, 0.17) and, for both excessive gestational weight gain and postpartum weight retention, was 0.18 (95% CI: 0.15, 0.22). In the trajectories with higher prepregnancy BMI, the predicted probabilities of child obesity ranged from 0.26 (95% CI: 0.21, 0.30) to 0.30 (95% CI: 0.24, 0.35), with minimal variation by gestational weight gain or postpartum weight retention.

In the LCGM analysis, which used the data to classify trajectories, prepregnancy BMI was the main measure that differentiated groups (Table 3). Correspondingly, we termed the three LCGM trajectories: normal-weight, overweight, and obese. Compared to the normal-weight LCGM trajectory, the adjusted risk of child obesity was 68% higher in the overweight trajectory and 181% higher in the obese trajectory (Table 4).

There were slight differences in results for additional analyses using child overweight instead of child obesity, in models where covariates were multiply imputed, and using different maternal weight trajectory classifications (Supplemental Tables 2-5). The overall findings, however, did not change.

DISCUSSION

In this national, longitudinal study, the trajectory of maternal weight from the beginning of pregnancy through the postpartum period was associated with the risk of obesity in childhood. Maternal weight that followed a recommended pattern was associated with the lowest absolute risk of child obesity, but was still 10%. There was also a strong relationship between prepregnancy BMI and child obesity. Beginning pregnancy at an overweight/obese BMI was associated with a two-and-half-fold increased risk of child obesity, which dwarfed the contributions of gestational weight gain and postpartum weight retention to the risk of child obesity. Among women who began pregnancy normal-weight/underweight, however, high gestational weight gain and high postpartum weight retention were influential risk factors. The novel approach used here provides new insights into the complex relationship between maternal and child weight, which may be useful in informing efforts to prevent obesity in childhood.

The ideal pattern of weight change during the childbearing period is to begin pregnancy at a healthy weight, gain moderately during pregnancy, and return to a healthy BMI within a year. There is consistent evidence that beginning pregnancy at a high BMI and, to a lesser extent, gaining excessive weight during pregnancy increase the risk of child obesity (12, 26, 27). Recently some investigators have found that weight retention and gain postpartum may also increase this risk (8-10). In a Dutch birth cohort, van Rossem et al. (9) found that BMI and risk of overweight were highest in children whose mothers gained gestational weight above the IOM recommendations and had a high rate of weight gain between 1 and 14 years postpartum, adjusting for prepregnancy BMI. Among children in our study whose mothers were normal-weight or underweight before pregnancy, the risk of obesity was highest in those whose mothers both gained excessive gestational weight and retained at least 5 kg within 3 years postpartum. Taken together, these findings suggest that high gestational weight gain and high postpartum weight retention or postpartum gain may have compounded effects on child BMI. However, the risk of obesity among all children in this study was highest in those children whose mothers were overweight or obese before pregnancy. This risk did not vary by gestational weight gain or postpartum weight retention and was higher than any risk estimates among children with mothers who were normal-weight or underweight before pregnancy. For example, even without excessive gestational weight gain or high postpartum weight retention, the predicted probability of obesity in children with overweight/obese mothers was 44% higher (0.26 vs. 0.18) than in children with normal-weight/underweight mothers who did have excessive gestational weight gain and high postpartum weight retention.

The observed importance of prepregnancy BMI is supported by biological evidence. Children born to heavier women are exposed from the earliest embryonic stages to the physiological environment created by their excess weight, which may have long-lasting effects on their metabolic regulation (4-7). This exposure is amplified by further differences associated with infant feeding and the family food environment that likely contributed to their mothers' excess weight as well as genetic and epigenetic factors (4-6). However, maternal weight interventions to date have concentrated on reducing excessive gestational weight gain after the first trimester and/or promoting postpartum weight loss in women who begin pregnancy overweight/obese (5, 30, 31). These interventions fail to influence the early intrauterine environment and have had little to no effect on offspring health outcomes, although such studies have also had only modest effects on gestational weight gain and have not been long enough to assess child obesity (5, 30, 31). Interventions that help women lose excess weight after pregnancy may, however, improve prepregnancy BMI and thus offspring health in subsequent pregnancies.

The strengths of this study included the use of data collected prospectively from 1981 to 2014 in a national sample of women and their children. The sample included various racial/ethnic groups, socioeconomic backgrounds, and geographic regions of the US. It is unusual to have data on offspring weight and height collected from birth into adolescence, which allowed us to observe sustained differences in child obesity across ages. Most child weight and height values were also measured by trained study personnel, which reduced the chance of outcome misclassification (32). Additionally, maternal weight measurements were collected prospectively after 6 months postpartum, which allowed us to study postpartum weight after most gestational weight is lost (14). Longitudinal trajectories were a novel approach to classifying maternal weight change and enabled a more comprehensive assessment of prepregnancy BMI, gestational weight gain, and postpartum weight retention than in previous studies. We assessed several trajectory classifications and did not observe any meaningful changes in the pattern of results. It is therefore unlikely that the findings resulted from differences between inadequate and adequate gestational weight gain or between the IOM recommended ranges of gestational weight gain relative to prepregnancy BMI.

There were also several limitations in this study. Maternal weights and heights were self-reported, which could have caused misclassification of the maternal BMI and weight measures and thus the maternal weight trajectories. However, a recent systematic review concluded that the misclassification of pregnancy-related weight caused by self-report does not meaningfully bias associations with perinatal health outcomes (33). We defined postpartum weight retention as the difference between weight 6-36 months postpartum and weight prepregnancy. We recognize that 6 months may not have allowed adequate time for women to lose their gestational weight gain and 3 years may have allowed women to gain weight unrelated to pregnancy. Unfortunately, the design of the cohort did not allow an adequate sample size to assess postpartum weight retention at one year, as has been suggested (34-36). Nonetheless, the time frame we used is consistent with the "intermediate postpartum weight retention" definition (3 months to 3 years) used by the Agency for Health Quality Research and the IOM (16, 37). Future studies that measure weight prospectively from before pregnancy through 1 year postpartum and then follow their children for obesity are needed. Missing data were an additional limitation of our study, causing the exclusion of one-third of eligible subjects; however, analyses with multiply imputed covariate data and comparison of the included and excluded samples did not indicate differences

that would meaningfully bias results. Although many covariates were available in the dataset to adjust statistical analyses, we were unable to assess several covariates, particularly dietary intake, physical activity, body composition, paternal weight, and detailed infant feeding practices, which should be addressed in future studies.

The generalizability of these results to other populations is unknown. Women in the study sample delivered between 1981 and 2006, 28% of women were overweight/obese before pregnancy, 44% gained excessive weight in pregnancy, and 28% retained ≥ 5 kg postpartum. The most recent national estimates for prepregnancy overweight/obesity, excessive gestational weight gain, and postpartum weight retention ≥ 5 kg are higher than in our study, approximately 50% for each indicator (16, 38, 39). Women in the sample were also primiparous and delivered full-term singletons. Additional research in contemporary birth cohorts, on maternal weight change across multiple pregnancies, and in preterm and twin births would be natural next steps to expand the findings of this study.

Maternal weight trajectories from before pregnancy through the postpartum period were identified and associated with offspring obesity risk in childhood in this national cohort study. The results suggest that studying prepregnancy BMI, gestational weight gain, and postpartum weight retention in combination may further our understanding of the connection between maternal and child weight. Additionally, high maternal weight across the childbearing period may compound the risk of child obesity, but we found that a high prepregnancy BMI has the strongest influence.

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Tables and Figures

Table 1. Distribution of characteristics within each maternal weight trajectory group in the study sample (n = 1881)

Prepregnancy BMI-Gestational weight gain-Postpartum weight retention n (%)	Below-Below-Below n = 710 (38%)	Below-Below-Above n = 163 (9%)	Below-Above-Below n = 314 (17%)	Below-Above-Above n = 178 (9%)	Above-Below-Below n = 145 (8%)	Above-Below-Above n = 35 (2%)	Above-Above-Below n = 196 (10%)	Above-Above-Above n = 140 (7%)
Characteristics								
Prepregnancy BMI (kg/m^2), mean (SD)	21.1 (2.0)	21.6 (2.2)	21.4 (1.9)	21.6 (2.2)	30.9 (6.5)	29.5 (3.9)	29.5 (4.4)	29.8 (4.3)
Gestational weight gain (kg), mean (SD)	11.7 (3.2)	11.5 (3.6)	20.8 (4.0)	22.1 (4.2)	5.6 (4.9)	7.0 (3.9)	16.4 (5.1)	18.3 (6.9)
Postpartum weight retention (kg), mean (SD)	0.2 (3.2)	9.7 (4.8)	0.7 (3.3)	10.9 (5.1)	-4.1 (7.9)	14.8 (13.6)	-1.7 (5.8)	11.5 (5.6)
Education at birth, %								
Less than high school	13.8	19.6	25.2	19.1	20.7	20.0	13.8	11.4
High school	66.5	63.8	29.6	68.0	67.6	71.4	68.9	73.6
College	19.7	16.6	45.2	12.9	11.7	8.6	17.4	15.0
Employment at birth, %								
Unemployed	26.1	29.5	25.2	21.9	36.6	34.3	25.0	25.0
Part-time	33.8	31.9	29.6	34.3	22.1	37.1	29.1	23.6
Full-time	40.1	38.7	45.2	43.8	41.4	28.6	45.9	51.4
Race/ethnicity, %								
Non-Hispanic non-black	65.1	54.0	70.4	56.7	55.2	37.1	62.8	44.3
Non-Hispanic black	20.0	27.0	18.5	26.4	29.7	37.1	23.0	39.3
Hispanic	14.9	19.0	11.2	16.9	15.2	25.7	14.3	16.4
Married at birth, %	76.3	57.1	73.3	60.1	73.8	62.9	78.1	56.4
Equivalized household income at birth, %								
Lowest tertile	31.6	44.2	32.5	42.7	31.7	51.4	25.5	37.9
Middle tertile	31.7	30.1	28.3	28.7	44.1	37.1	40.8	42.9
Highest tertile	36.8	25.8	39.2	28.7	24.1	11.4	33.7	19.3
Age at birth, %								
< 20 y	4.9	6.8	7.0	9.6	5.5	2.9	1.5	0.7
20-30 y	71.6	71.2	72.6	64.0	64.8	62.9	66.8	69.3

≥ 30 y	23.5	22.1	20.4	26.4	29.7	34.3	31.6	30.0
Smoked during pregnancy, %	24.5	23.3	29.6	33.7	25.5	17.1	16.3	22.9
Child birth year, %								
Before 1985	33.4	31.9	32.8	35.4	31.0	17.1	19.4	22.1
1985 until 1995	56.1	57.7	58.9	53.9	52.4	62.9	62.8	65.0
During or after 1995	10.6	10.4	8.3	10.7	16.6	20.0	17.9	12.9
Child sex, %								
Female	52.5	50.9	44.9	48.9	48.3	34.3	41.3	48.6
Male	47.5	49.1	55.1	51.1	51.7	65.7	58.7	51.4
Child large-for-gestational age, %	6.8	11.7	15.3	13.5	10.3	8.6	15.8	15.7
Child ever breastfed, %	57.2	47.9	54.1	51.7	42.1	48.6	51.0	47.9

Table 2. Associations between maternal weight trajectory group and child obesity (n = 1881)

Maternal Weight Trajectory	Unadjusted Risk Ratio (95% CI)	Adjusted Risk Ratio (95% CI)[1]
Below-Below-Below	Reference	Reference
Below-Below-Above	1.23 (0.89, 1.71)	1.08 (0.78, 1.48)
Below-Above-Below	1.42 (1.09, 1.86)	1.36 (1.05, 1.77)
Below-Above-Above	1.92 (1.47, 2.51)	1.63 (1.25, 2.13)
Above-Below-Below	2.76 (2.14, 3.55)	2.38 (1.84, 3.07)
Above-Below-Above	2.92 (1.91, 4.48)	2.29 (1.52, 3.46)
Above-Above-Below	2.67 (2.10, 3.39)	2.36 (1.86, 3.00)
Above-Above-Above	3.07 (2.40, 3.93)	2.45 (1.90, 3.15)

[1] Modified Poisson regression models adjusted for maternal education, employment, race/ethnicity, marital status, equivalized household income, smoking during pregnancy, delivery year, child sex, large-for-gestational age status, and ever breastfed.

Table 3. Maternal weight characteristics of latent class growth modeling groups of maternal weight (n = 1881)

	Normal weight prepregnancy trajectory n = 1208 (64%)	Overweight prepregnancy trajectory n = 532 (28%)	Obese prepregnancy trajectory n = 141 (8%)
Maternal Weight Characteristics	Mean (SD)	Mean (SD)	Mean (SD)
Prepregnancy BMI (kg/m^2)	21.0 (2.1)	26.3 (2.7)	36.4 (4.9)
Gestational weight gain (kg)	14.2 (5.4)	16.2 (7.4)	11.6 (9.3)
Postpartum weight retention (kg)	1.8 (5.0)	4.4 (8.2)	4.2 (14.1)

Table 4. Associations between latent class growth modeling groups of maternal weight and child obesity (n = 1881)

Maternal Weight Trajectories	Unadjusted Risk Ratio (95% CI)	Adjusted Risk Ratio (95% CI) [1]
Normal weight prepregnancy trajectory	Reference	Reference
Overweight prepregnancy trajectory	1.89 (1.60, 2.23)	1.68 (1.42, 1.98)
Obese prepregnancy trajectory	3.34 (2.77, 4.03)	2.81 (2.31, 3.42)

[1] Modified Poisson regression models adjusted for maternal education, employment, race/ethnicity, marital status, equivalized household income, smoking during pregnancy, delivery year, child sex, large-for-gestational age status, and ever breastfed.

Figure 1. Prevalence of child obesity across ages and stratified by maternal weight trajectories. Legend indicates below (B) or above (A) at each maternal weight time point (prepregnancy, delivery, and postpartum). Above status prepregnancy is BMI ≥ 25 kg/m^2; above status at delivery is gestational weight gain above the IOM recommendations; above status postpartum is weight retention ≥ 5 kg.

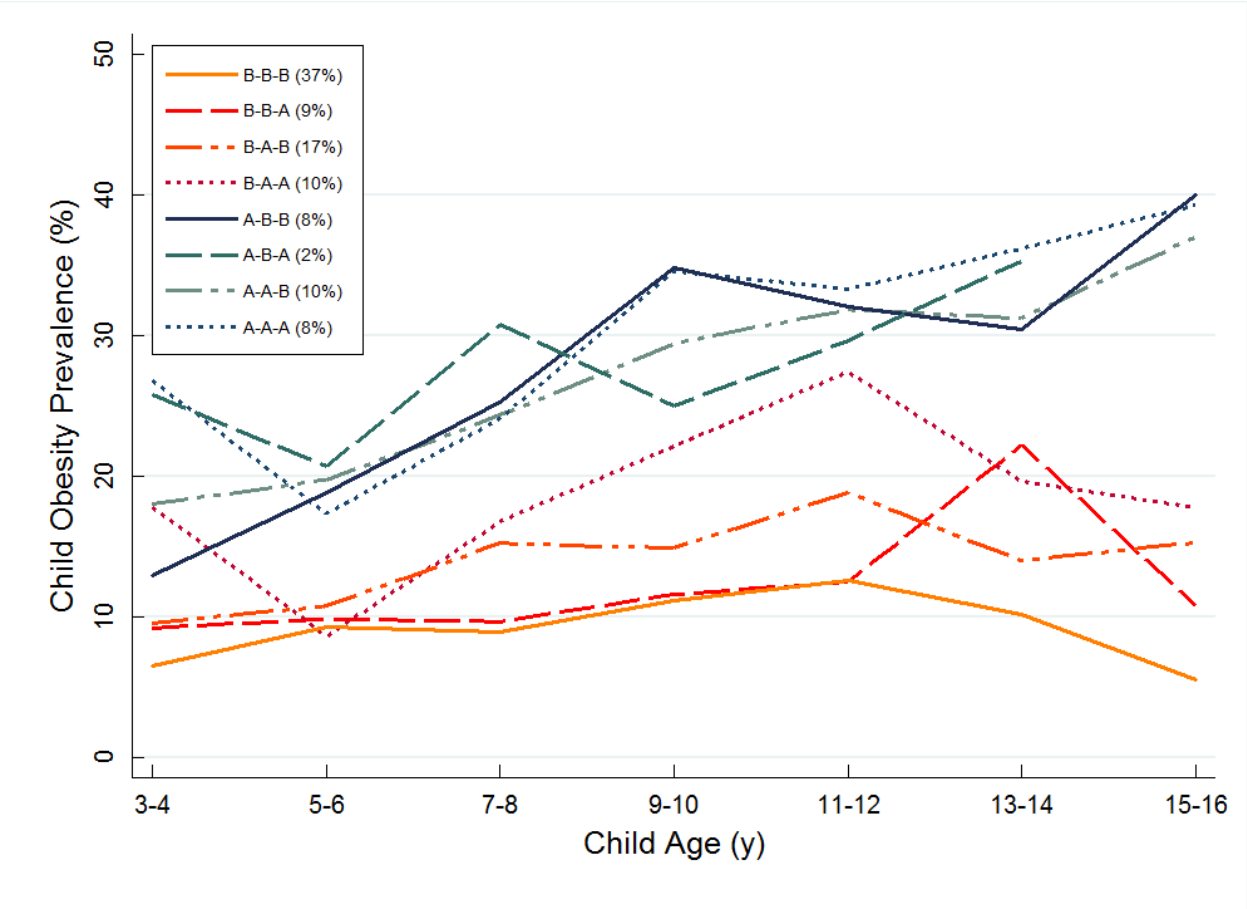
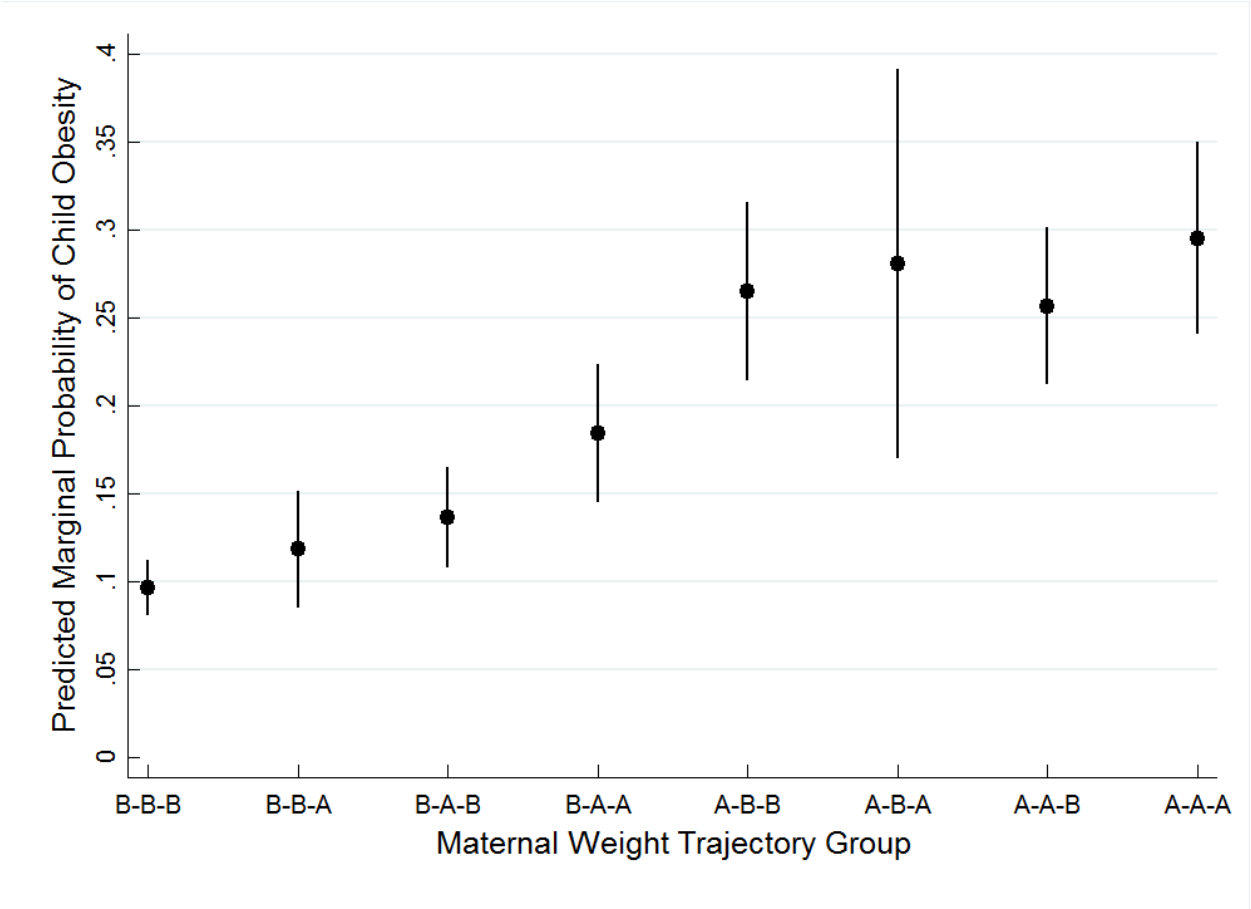


Figure 2. Adjusted predicted marginal probabilities of child obesity across maternal weight trajectories. Points indicate predicted marginal probabilities of child obesity and lines indicate 95% confidence intervals, adjusted for covariates. Trajectories are defined by below (B) or above (A) at each maternal weight time point (prepregnancy, delivery, and postpartum). Above status prepregnancy is BMI ≥ 25 kg/m^2; above status at delivery is gestational weight gain above the IOM recommendations; above status postpartum is weight retention ≥ 5 kg.



Supplemental Table 1. Characteristics of mother-child pairs included in the final sample, ineligible for the study, and eligible but excluded from the final sample

Characteristics	Final Sample (n = 1881) column %	Excluded Sample (n = 1547) column %	Ineligible Sample (n = 8078) column %
Prepregnancy BMI (kg/m^2)			
Underweight (<18.5)	6.5	7.4	10.2
Normal weight (18.5-24.9)	66.0	65.9	66.9
Overweight (25-29.9)	17.3	16.9	16.0
Obese (≥30)	10.2	9.7	6.9
Gestational weight gain			
Inadequate	25.9	27.1	35.0
Adequate	30.0	28.2	27.3
Excessive	44.0	44.7	37.7
Postpartum weight retention			
<5 kg	72.6	70.6	70.2
≥5 kg	27.4	29.4	29.8
Education at birth			
Less than high school	15.3	18.2	26.5
High school	68.1	63.7	61.1
College	16.6	18.2	12.4
Employment at birth			
Unemployed	26.6	46.1	46.7
Part-time	30.9	23.2	25.9
Full-time	42.5	30.7	27.4
Race/ethnicity			
Non-Hispanic non-black	61.1	63.0	54.3
Non-Hispanic black	23.8	22.4	28.7
Hispanic	15.1	14.6	17.1
Married at birth	70.9	69.0	65.1
Equivalized household income			
Lowest tertile	34.1	34.7	43.9
Middle tertile	33.6	34.1	31.8
Highest tertile	32.4	31.2	24.4
Smoked during pregnancy	25.1	30.0	30.1
Child birth year			
Before 1985	30.6	30.2	50.8
1985 until 1995	57.7	53.3	39.3
During or after 1995	11.8	16.5	9.9
Child sex			
Female	48.6	48.6	49.1
Male	51.4	51.4	50.9
Child large-for-gestational age	11.2	9.7	9.6
Child ever breastfed	52.7	52.0	42.7

Supplemental Table 2. Associations between maternal weight trajectory group and child overweight (85th-95th BMI percentile) status (n = 1881)

Weight Change Trajectory	Unadjusted RR (95% CI)	Adjusted RR (95% CI)[1]
Below-Below-Below	Reference	Reference
Below-Below-Above	1.04 (0.81, 1.34)	1.03 (0.80, 1.33)
Below-Above-Below	1.12 (0.92, 1.35)	1.09 (0.90, 1.33)
Below-Above-Above	1.10 (0.87, 1.38)	1.09 (0.87, 1.37)
Above-Below-Below	1.31 (1.05, 1.64)	1.27 (1.02, 1.59)
Above-Below-Above	1.42 (1.00, 2.00)	1.43 (1.01, 2.03)
Above-Above-Below	1.31 (1.07, 1.60)	1.31 (1.07, 1.60)
Above-Above-Above	1.44 (1.16, 1.79)	1.43 (1.14, 1.79)

[1] Modified Poisson regression models adjusted for maternal education, employment, race/ethnicity, marital status, equivalized household income, smoking during pregnancy, delivery year, child sex, large-for-gestational age status, and ever breastfed.

Supplemental Table 3. Associations between maternal weight trajectory groups and child obesity in analyses using multiple imputation for missing covariates (n = 2211)

Maternal Weight Trajectory	Unadjusted Risk Ratio (95% CI)	Adjusted Risk Ratio (95% CI)[1]
Pre-specified Groups		
Below-Below-Below	Reference	Reference
Below-Below-Above	1.23 (0.91, 1.66)	1.09 (0.82, 1.46)
Below-Above-Below	1.38 (1.08, 1.77)	1.33 (1.04, 1.70)
Below-Above-Above	1.95 (1.52, 2.49)	1.69 (1.32, 2.15)
Above-Below-Below	2.74 (2.17, 3.45)	2.41 (1.91, 3.04)
Above-Below-Above	3.11 (2.12, 4.58)	2.43 (1.67, 3.54)
Above-Above-Below	2.70 (2.16, 3.37)	2.36 (1.89, 2.95)
Above-Above-Above	3.17 (2.53, 3.97)	2.53 (2.01, 3.20)
LCGM Groups		
Normal weight prepregnancy trajectory	Reference	Reference
Overweight prepregnancy trajectory	1.97 (1.70, 2.29)	1.74 (1.50, 2.02)
Obese prepregnancy trajectory	3.42 (2.86, 4.09)	2.94 (2.45, 3.53)

[1] Modified Poisson regression models adjusted for maternal education, employment, race/ethnicity, marital status, equivalized household income, smoking during pregnancy, delivery year, child sex, large-for-gestational age status, and ever breastfed.

Supplemental Table 4. Associations between maternal weight trajectory groups and child obesity in analyses using trajectory groups with 3 levels gestational weight gain following IOM guidelines (n = 1881)

Weight Change Trajectory	Unadjusted RR (95% CI)	Adjusted RR (95% CI)[1]
Below-Below-Below	1.32 (0.95, 1.83)	1.19 (0.87, 1.64)
Below-Below-Above	1.62 (1.04, 2.52)	1.23 (0.80, 1.89)
Below-Within-Below	Reference	Reference
Below-Within-Above	1.23 (0.77, 1.96)	1.12 (0.70, 1.79)
Below-Above-Below	1.63 (1.20, 2.22)	1.49 (1.10, 2.02)
Below-Above-Above	2.20 (1.61, 3.00)	1.79 (1.31, 2.44)
Above-Below-Below	3.59 (2.53, 5.08)	2.87 (2.02, 4.08)
Above-Below-Above	4.01 (2.11, 7.60)	2.79 (1.47, 5.30)
Above-Within-Below	2.78 (1.95, 3.96)	2.35 (1.65, 3.34)
Above-Within-Above	2.96 (1.68, 5.21)	2.33 (1.37, 3.96)
Above-Above-Below	3.06 (2.30, 4.07)	2.58 (1.95, 3.43)
Above-Above-Above	3.52 (2.63, 4.72)	2.69 (2.00, 3.61)

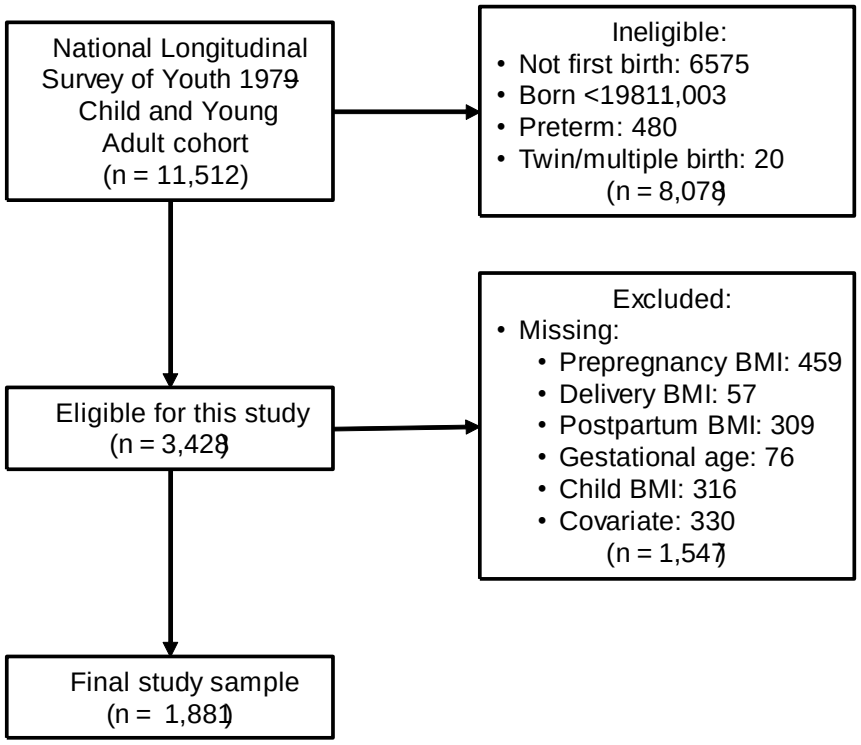
[1] Modified Poisson regression models adjusted for maternal education, employment, race/ethnicity, marital status, equivalized household income, smoking during pregnancy, delivery year, child sex, large-for-gestational age status, and ever breastfed.

Supplemental Table 5. Associations between maternal weight trajectory groups based on median BMI and weight values with child obesity outcomes (n = 1881)

	Trajectory Groups Using Median BMI and BMI Change		Trajectory Groups Using Absolute Weight and Weight Change	
Weight Change Trajectory	Unadjusted RR (95% CI)	Adjusted RR[1] (95% CI)	Unadjusted RR (95% CI)	Adjusted RR[1] (95% CI)
Below-Below-Below	Reference	Reference	Reference	Reference
Below-Below-Above	1.12 (0.72, 1.75)	1.03 (0.66, 1.58)	1.07 (0.64, 1.78)	0.98 (0.60, 1.60)
Below-Above-Below	1.50 (0.98, 2.32)	1.44 (0.94, 2.20)	1.19 (0.75, 1.90)	1.21 (0.77, 1.91)
Below-Above-Above	1.73 (1.15, 2.61)	1.60 (1.07, 2.40)	1.35 (0.88, 2.07)	1.29 (0.85, 1.96)
Above-Below-Below	3.21 (2.22, 4.65)	2.74 (1.89, 3.97)	2.65 (1.77, 3.98)	2.40 (1.61, 3.59)
Above-Below-Above	3.27 (2.26, 4.74)	2.61 (1.80, 3.81)	2.75 (1.83, 4.12)	2.28 (1.52, 3.41)
Above-Above-Below	3.02 (2.08, 4.38)	2.65 (1.83, 3.84)	1.98 (1.32, 2.98)	1.91 (1.28, 2.85)
Above-Above-Above	3.56 (2.47, 5.13)	2.71 (1.87, 3.92)	2.60 (1.75, 3.86)	2.14 (1.45, 3.17)

[1] Modified Poisson regression models adjusted for maternal education, employment, race/ethnicity, marital status, equivalized household income, smoking during pregnancy, delivery year, child sex, large-for-gestational age status, and ever breastfed.

Supplemental Figure 1. Selection of final study sample.



Chapter 4. Maternal history of child abuse and obesity risk in offspring: mediation by weight in pregnancy

Introduction

The prevalence of obesity in American children and adolescents has not improved over the past decade, affecting approximately one in six (1). Public health efforts to prevent child obesity have largely targeted exposures in childhood, but knowledge on how to prevent obesity in early childhood is limited (2). Evidence increasingly suggests that there are intergenerational causes of child obesity (3). Pre-pregnancy obesity and excessive gestational weight gain, in particular, have been consistently linked with obesity in children (4, 5). In numerous additional studies, researchers have also found adverse childhood experiences (ACE) to be associated with obesity in adulthood (6-9). Most recently, adversity in childhood has been associated with high pre-pregnancy body mass index (BMI) and excessive weight gain during pregnancy (10-12) as well as offspring obesity (13).

We sought to bridge the bodies of evidence connecting childhood adversity with maternal obesity and maternal obesity with child obesity (4, 5, 9). Findings suggest that childhood adversity may cause long-term emotional dysregulation and depression that can lead to unhealthy eating behaviors and obesity in adulthood (14-16). In turn, obesity and excessive weight gain in pregnant women may contribute to obesity in their children (4, 5). If maternal adversity in childhood does contribute to offspring obesity by causing high maternal weight and weight gain, prevention of abuse, neglect, or adversity in children and screening for ACE with treatment of its psychological consequences in women could potentially help efforts to prevent child obesity. We used 33 years of follow-up data from a diverse, national cohort study to investigate whether women's experience of childhood adversity is associated with their children's risk of obesity, and, if so, whether pre-pregnancy BMI and gestational weight gain partially mediate the association.

Methods

Study population

The National Longitudinal Survey of Youth 1979 (NLSY79) is an ongoing, national, prospective cohort study designed to represent the U.S. population of youths aged 14-21 years old in 1979. The Bureau of Labor Statistics enrolled 12,686 youths in the study in 1979 and began enrolling the biological children of female participants into the NLSY Child and Young Adult study in 1986. Participants were visited in person and/or received questionnaires annually until 1994 and every two years thereafter. As shown in Figure 1, 11,512 mother-child pairs (4932 individual mothers) have participated in the studies as of 2012. A total of 3191 mothers with 7894 children participated in the 2012 survey wave (69% of the original sample), which is not an uncommon participation proportion for prospective cohort studies (17, 18). Custom sampling weights created by the Bureau of Labor Statistics are used to weight the sample to match the demographics of the original target population despite differential loss to follow-up. We included mother-child pairs in the final study sample if the child was delivered as a singleton during or

after 1979 and data were available on ACE and child BMI (n = 6718). The University of California, Berkeley Committee for the Protection of Human Subjects approved the study.

Maternal Measures

In the 2012 wave of data collection, the survey administered three ACE questions, which were selected from the 11-item US Behavioral Risk Factor Surveillance System (BRFSS) questionnaire based on prioritization by a panel of child development specialists (19). We were unable to use the full set of BRFSS ACE questions because of questionnaire length limitations. Participants were asked to recall their experience of physical abuse, household alcohol abuse, and household mental illness before age 18 years with the following questions:

1. How often did a parent or adult in your home ever hit, beat, kick, or physically harm you in any way? Do not include spanking. Would you say never, once, or more than once?
2. Did you live with anyone who was a problem drinker or alcoholic?
3. Did you live with anyone who was depressed, mentally ill, or suicidal?

Ninety-nine percent of the respondents in 2012 answered the ACE questions. We dichotomized the history of physical abuse responses as 'yes' if abuse was reported as two or more times and 'no' otherwise to capture recurrent physical abuse.

The NLSY79 collected data on weight and height at each wave beginning in 1981. Pre-pregnancy weight and delivery weight were self-reported in the first survey postpartum starting in 1986. Specifically, within 2 years of delivery, women reported their weight "just before [they] became pregnant" and "just before [they] delivered." We regression-calibrated height data using error data from the National Health and Nutrition Examination Survey. The reliability of recalled pre-pregnancy weight and the weight reported at the closest survey prior to that pregnancy was 0.9.(10) Pre-pregnancy body mass index (BMI) was calculated from pre-pregnancy weight and height (kg/m^2). Gestational weight gain was defined as the difference between delivery weight and pre-pregnancy weight. We converted gestational weight gain into weight gain-for-gestational age z-scores using pre-pregnancy BMI-specific z-score charts previously created by our team using serial prenatal weight measurements from women in Pennsylvania with healthy, term, singleton births (20, 21). Use of the z-scores accounts for the inherent link between duration of pregnancy and weight gain during pregnancy (22, 23). Pre-pregnancy BMI and gestational weight gain were tested as mediators of any associations between maternal ACE and child obesity (4, 10, 11, 13).

Confounding maternal characteristics were selected using theory-based causal diagrams based on prior evidence (Supplemental Figure 1) (24). Confounding variables included early life characteristics (race/ethnicity, born in the U.S., born in the U.S. South, urban/non-urban childhood home at age 14, and maternal grandmother's education level) (3, 13) and prenatal characteristics (age, education level, employment status, household income in year 2000 dollars and equivalized for household size, race/ethnicity, marital status, parity, and smoked cigarettes during pregnancy) (4, 25).

Child Measures

Child BMI values were calculated using weight and height measurements that were either made in person by trained study interviewers (74% of weight and 82% of height measurements) or

reported by the mother. We used the CDC growth chart SAS program to calculate age- and sex-specific BMI percentiles and identify biologically implausible values for exclusion (26). We assessed if a child was ever obese (BMI $\geq 95^{th}$ percentile) in early, middle, or late childhood (ages 2-5 years, 6-11 years, and 12-19 years, respectively), in accord with the age groups used by national child BMI surveillance methods (1).

Statistical Analysis

All statistical analyses accounted for the complex sampling design ('survey' package in R) (27) of the NLSY studies and family-level clustering. We first characterized the study sample and compared all variables between included, ineligible, and excluded mother-child pairs. The distributions of covariates were also compared across outcome groups to detect any patterns in the missingness of child BMI information. Multiple imputation with chained equations ('mice' package in R) (28) was used for missing covariate data (29). The percentage of missing observations for each covariate ranged from 0 to 15%, with a median of 3%.

To test our hypothesis, we first estimated the total effect of each maternal ACE exposure (physical abuse, household alcohol abuse, and household mental illness) on child obesity in each age group (2-5 y, 6-11 y, and 12-19 y) using log-binomial regression models, unadjusted and then adjusted for maternal early life characteristics. Because there was an overall association observed between maternal history of physical abuse and early childhood obesity in 2-5 year olds only, we limited further assessment of mediation by pre-pregnancy BMI and gestational weight gain to this age group. We followed the methods of Petersen et al. (30) to assess mediation, which we describe step-by-step in Appendix A. In short, we applied the parametric g-formula to estimate the effect of childhood physical abuse in mothers on early childhood obesity in offspring if pre-pregnancy BMI and/or gestational weight gain were unrelated to childhood physical abuse. This estimate, the natural direct effect, assumes the maternal weight values to be those mothers would have attained in the absence of physical abuse. We adjusted these analyses for the covariates described previously. Statistical analyses were conducted in R version 3.1.1 (31).

Sensitivity Analyses

We pre-specified several sensitivity analyses to determine the robustness of the main results to methodological changes. (1) We added interaction terms between physical abuse and each mediator to models to detect effect modification. (2) We tested joint mediation by pre-pregnancy BMI and gestational weight gain. (3) We changed the outcome to childhood overweight or obesity (BMI $\geq 85^{th}$ percentile for age and sex). (4) We evaluated mediation by estimating controlled direct effects instead of natural direct effects. Natural direct effects provide estimates of the effect of maternal physical abuse on early childhood obesity if one were to intervene to prevent maternal physical abuse, and thereby change pre-pregnancy BMI or gestational weight gain. In contrast, controlled direct effects estimate the effect of maternal physical abuse on early childhood obesity if one were to intervene directly on pre-pregnancy BMI or gestational weight gain, setting them to pre-specified values.

Results

The mothers of 17.3% of children in the study reported physical abuse in childhood, 11.0% reported living with someone in their childhood home who was mentally ill, and 22.2% reported living with someone who was a problem drinker or alcoholic. Overall, mothers were mostly non-Hispanic white, born in the U.S., and had at least a high school education (Table 1). Compared to other mothers in the sample, a higher proportion of those who reported physical abuse as children were born to a mother who did not complete high school, did not complete high school themselves, had a low household income, and smoked during pregnancy. Consistent with previous findings in this sample (10), pre-pregnancy obesity and high gestational weight gain were more prevalent in women who experienced physical abuse, alcohol abuse in the household, and mental illness in the household, with the strongest association being between physical abuse and pre-pregnancy obesity. Compared to mother-child pairs in the final sample, those ineligible for the study (non-singleton birth, delivery before 1979, or not included in the 2012 survey) and those excluded for missing exposure or outcome data delivered in earlier years at younger ages and had lower prevalences of pre-pregnancy obesity and child obesity (Supplemental Table 1). Ineligible mother-child pairs reported a higher prevalence of physical abuse (21.3%) and alcohol abuse (25.7%), but a lower prevalence of household mental illness (7.8%) than those included in the final sample. There were no patterns detected in the missingness of child BMI information among the age groups.

Physical abuse in a woman's childhood was associated with a higher risk of her child being obese 2-5 years old (Figure 2, panels A and B). After adjusting for maternal early life characteristics, children 2-5 years old with mothers who reported childhood physical abuse were 21% more likely to be obese. Among every 100 mothers who were physically abused, there were 3.7 excess cases of early childhood obesity compared with mothers who were not physically abused. The predicted probability of early childhood obesity was 0.21 (95% CI: 0.18, 0.25) if women experienced physical abuse and 0.17 (95% CI: 0.16, 0.19) if women did not experience physical abuse.

After accounting for mediation by pre-pregnancy BMI, the association between maternal physical abuse and early childhood obesity was attenuated (Figure 2, panel C). Differences in pre-pregnancy BMI between physically abused and not physically abused mothers accounted for 25.7% of the excess cases of early childhood obesity that occurred among mothers who reported physical abuse. Accounting for mediation by gestational weight gain, without changing pre-pregnancy BMI, minimally attenuated the association between maternal physical abuse and early childhood obesity (Figure 2, panel D). Differences in gestational weight gain between mothers who reported physical abuse and those who did not were estimated to account for 5.7% of the excess cases of child obesity among mothers who reported physical abuse.

In the sensitivity analyses, adding multiplicative interaction terms between physical abuse and the mediators to the models did not change the results (Supplemental Table 2). Additionally, joint mediation by pre-pregnancy BMI and gestational weight gain resulted in slightly smaller effect estimates as for mediation by pre-pregnancy BMI alone (Supplemental Table 2). Using child overweight or obesity (BMI percentile $\geq 85^{th}$ percentile) as the outcome instead of obesity (BMI percentile $\geq 95^{th}$ percentile) yielded attenuated effect estimates (Supplemental Table 2).

Finally, controlled direct effects estimates were nearly identical to the natural direct effect estimates (Supplemental Table 3).

Physical abuse was not associated with obesity in 6- to 11 or 12- to 19-year-olds. Mental illness and alcohol abuse in a mother's childhood home were not associated with child obesity in any age group.

Discussion

We found in a diverse, national sample that maternal history of physical abuse in childhood was related to obesity in the next generation of preschool-age children. Specifically, reporting one or more episodes of physical harm from a parent or adult in the mother's childhood home was associated with 3.7 excess cases of early childhood obesity per 100 mother-child pairs—a 21% relative increase in risk. This relationship was partially mediated by maternal pre-pregnancy BMI, but not gestational weight gain. Although we found no evidence of a similar relationship for older children, or for two other ACE markers, our results shed light on a possible intergenerational pathway contributing to obesity in childhood.

Abuse in childhood may lead to obesity prior to pregnancy through a constellation of factors, including emotional eating used to cope with anxiety and depression (14-16), dysregulated cortisol response and chronic inflammation (15, 16), and obesogenic behaviors and environments related to socioeconomic disadvantages (6, 16). In turn, obesity in pregnancy may contribute to obesity in childhood through shared genetic predispositions, epigenetic effects on offspring metabolic regulation, and shared lifestyle factors (4, 5). This hypothesis is supported by recent findings in a large, national study of female nurses and their children, in which researchers reported a total association between a composite measure of physical, emotional, and sexual abuse in childhood and self-reported high BMI in adolescent offspring (13). This association was largely attenuated by adjusting for mother's concurrent BMI but unaffected by adjustment for the child's own exposure to abuse. Our study expands previous findings to include an overall association between physical abuse and early childhood obesity and a mediating role of maternal weight before conception in a diverse study population with mostly measured child weights and heights.

The results of this study may be informative for future interventions and research.
Trials that aim to promote healthy weight gain during pregnancy have been conducted in part to hopefully reduce risk for child obesity (32, 33). Such interventions, however, have been met with limited success in preventing excessive gestational weight gain and large-for-gestational age births, and have not demonstrated an effect on child obesity (2, 32-34). For this reason, it has recently been suggested that interventions should target maternal weight before conception, although no such randomized trials have been conducted (35). Our results underscore the need for preconception interventions for women who are overweight or obese and suggest that incorporation of childhood abuse screening and management could bolster effectiveness in reducing maternal and child obesity.

It is unknown why our findings are limited to physical abuse and early childhood obesity. However, our results are consistent with other findings of only physical abuse being associated with adult obesity and that other ACE exposures may confer different effects than physical abuse (6-8, 12). The prevalence of physical abuse in this study was similar to that among women in the BRFSS, but the prevalences of household mental illness and alcoholism were lower by 8.1 and 4.6 percentage points, suggesting that our study group may have underreported these exposures (36); therefore, we cannot confidently rule out their importance. We were also unable to assess other types of abuse and neglect, which could confound the association between physical abuse and early childhood obesity or be independent risk factors. Future studies that comprehensively assess abuse and neglect are needed. Additionally, an association of maternal physical abuse with offspring obesity limited to preschool-age children may be due to their younger age and closer proximity to pregnancy. Exposure to both positive and negative lifestyle factors at preschool ages may overshadow the effects of prenatal risk factors in school-age children and adolescents, although we did not study this possibility (37).

Several factors limit the results of this study. Mothers self-reported all their characteristics, which may have led to some misclassification. We regression-calibrated maternal height, but lacked calibration data for maternal weight. Although self-reported weight can be prone to error, a recent systematic review concluded that self-reported pre-pregnancy and delivery weight does not bias associations with perinatal outcomes in most studies (38). Adverse childhood experiences were recalled much later in life, although validation studies on retrospective ACE measurement suggest our measures would likely result in false negatives and weaker associations than if ACE measures were collected earlier in life (39). We were also only able to study three ACE exposures because of questionnaire length limitations. We were therefore unable to use the full set of 11 ACE questions and could not assess the severity of ACE or other ACE exposures, which would better inform the relationships between ACE, maternal obesity, and child obesity. The validity of our approach could not be tested, but shortened ACE assessment has been shown to be appropriate (40). Additionally, the available data lacked information on several factors likely to confound the associations studied, including psychological measures, family history of obesity, paternal characteristics, pregnancy complications, and the child's exposure to ACE. The prevalences of pre-pregnancy obesity and preschool-age obesity were lower in NLSY mother-child pairs ineligible for this study, which could have inflated effect sizes in the included sample. The NLSY also only collected child weight and height measurements from 1986 to 2012, resulting in measurements not being recorded at certain ages if a child was born close to the beginning or the end of the study period.

A number of strengths counterbalance this study's limitations. The NLSY79 was designed to be nationally representative of youths and adolescents in 1979 and prospectively followed participants for 33 years, including 26 years of measuring the weights and heights of female participants' children. Additionally, trained study staff made 74% of weight and 82% of height measurements in person. These attributes strengthen both the internal and external validity of our results. Our mediation findings are strengthened by clear temporality, z-scores that standardized gestational weight gain for gestational duration (20), and mediation analysis methods that improve upon the conventional adjustment approach, which is often severely biased (30).

In conclusion, maternal physical abuse in childhood was associated with a modest increase in children's risk of obesity at pre-school ages. Pre-pregnancy BMI explained approximately a quarter of this association. In contrast, weight gain during pregnancy explained a very small portion of the association. No associations were found with later childhood obesity or with maternal experience of mental illness or alcohol abuse in the childhood household. This study's results expand our limited knowledge of intergenerational contributors to obesity in young children and the importance of efforts to prevent childhood abuse. Additionally, they suggest that interventions to promote healthy weight prior to pregnancy and prevent childhood obesity should consider evaluating the impact of screening and management of maternal adverse childhood experiences, particularly physical abuse.

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Tables and Figures

Table 1. Maternal and child characteristics in total sample and by maternal ACE[a]

	Total	Physical abuse	Alcohol abuse in household	Mental illness in household
	(n = 6718) %	(n = 1181) %	(n = 1414) %	(n = 636) %
Child obesity status				
Age 2-5 years[b]	17.2	20.3	16.5	18.7
Age 6-11 years	25.3	24.5	21.6	21.2
Age 12-19 years	22.5	23.0	20.5	22.6
Early life characteristics of mother				
Maternal grandmother completed high school	62.9	59.0	61.3	69.8
Race/ethnicity				
Non-Hispanic white or other	74.4	76.3	79.6	85.4
Non-Hispanic black	17.1	13.3	13.1	10.0
Hispanic	7.6	9.2	6.8	4.6
Asian	1.0	1.2	0.5	0.0
Born in the U.S.	95.3	91.9	95.3	93.7
Born in southern U.S.	31.7	25.0	26.4	28.5
Urban childhood home	78.3	79.3	76.7	78.2
Prenatal characteristics[c]				
Pre-pregnancy BMI (kg/m^2)				
Underweight (< 18.5)	7.3	8.6	8.0	8.6
Normal weight (18.5 to < 25)	64.3	60.4	63.0	64.2
Overweight (25 to < 30)	17.7	15.6	16.2	14.3
Obese (≥ 30)	10.7	15.4	12.0	12.9
Gestational weight gain[d]				
Inadequate	29.2	25.7	25.5	29.2
Adequate	29.4	26.0	29.3	26.6
Excessive	41.5	48.3	45.2	44.2
Age				
< 20 years	7.0	8.9	7.7	5.7
20-30 years	55.9	57.3	56.7	56.7
≥ 30 years	37.0	33.8	35.6	37.6
Education				
Less than high school completion	15.7	24.5	18.3	13.0
High school graduate	63.3	62.5	65.1	65.2
College graduate	20.9	13.0	16.6	21.8
Employment				
Unemployed	34.2	40.3	36.2	36.5
Part-time	28.3	27.7	29.3	28.7
Full-time	37.5	32.0	34.5	34.8

Equivalized household income				
Lowest quartile	24.9	31.7	25.5	22.4
Second quartile	25.1	28.6	29.9	30.7
Third quartile	25.1	20.0	22.7	27.0
Highest quartile	25.8	19.6	21.9	19.8
Married	74.9	68.4	74.7	74.5
Smoked cigarettes in pregnancy	25.9	33.6	30.0	26.9
Primiparous	43.0	41.8	43.6	44.9
Child birthyear				
<1980	7.7	7.6	8.6	5.9
1980-1990	54.1	57.0	53.9	56.3
>1990	38.2	35.3	37.5	37.8

ACE, adverse childhood experience; BMI, body mass index

[a] Percentages are weighted for the survey sampling design. Sample sizes are not weighted and refer to number of mother-child pairs.

[b] Child obesity percentages includes children who had an obese BMI at least once during the specified age range.

[c] Pre-pregnancy BMI and gestational weight gain were assessed as mediators. All other maternal characteristics in pregnancy were treated as confounding variables.

[d] Based on Institute of Medicine 2009 recommendations.

Figure 1. Selection flowchart of mother-child pairs for the study. Participants not included in the 2012 survey wave either were intentionally dropped from the original cohort due to funding constraints, lost to follow-up, or died.

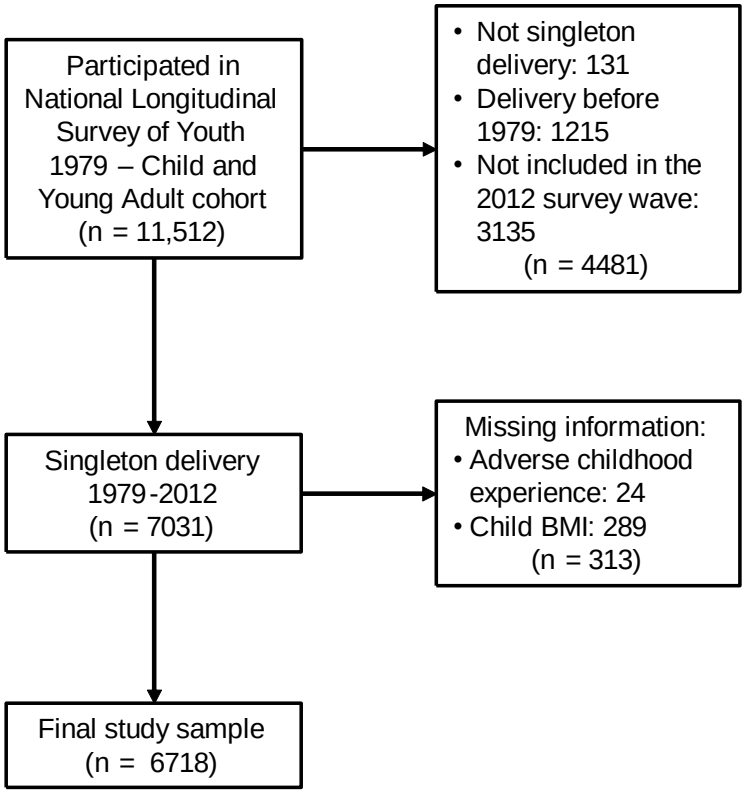
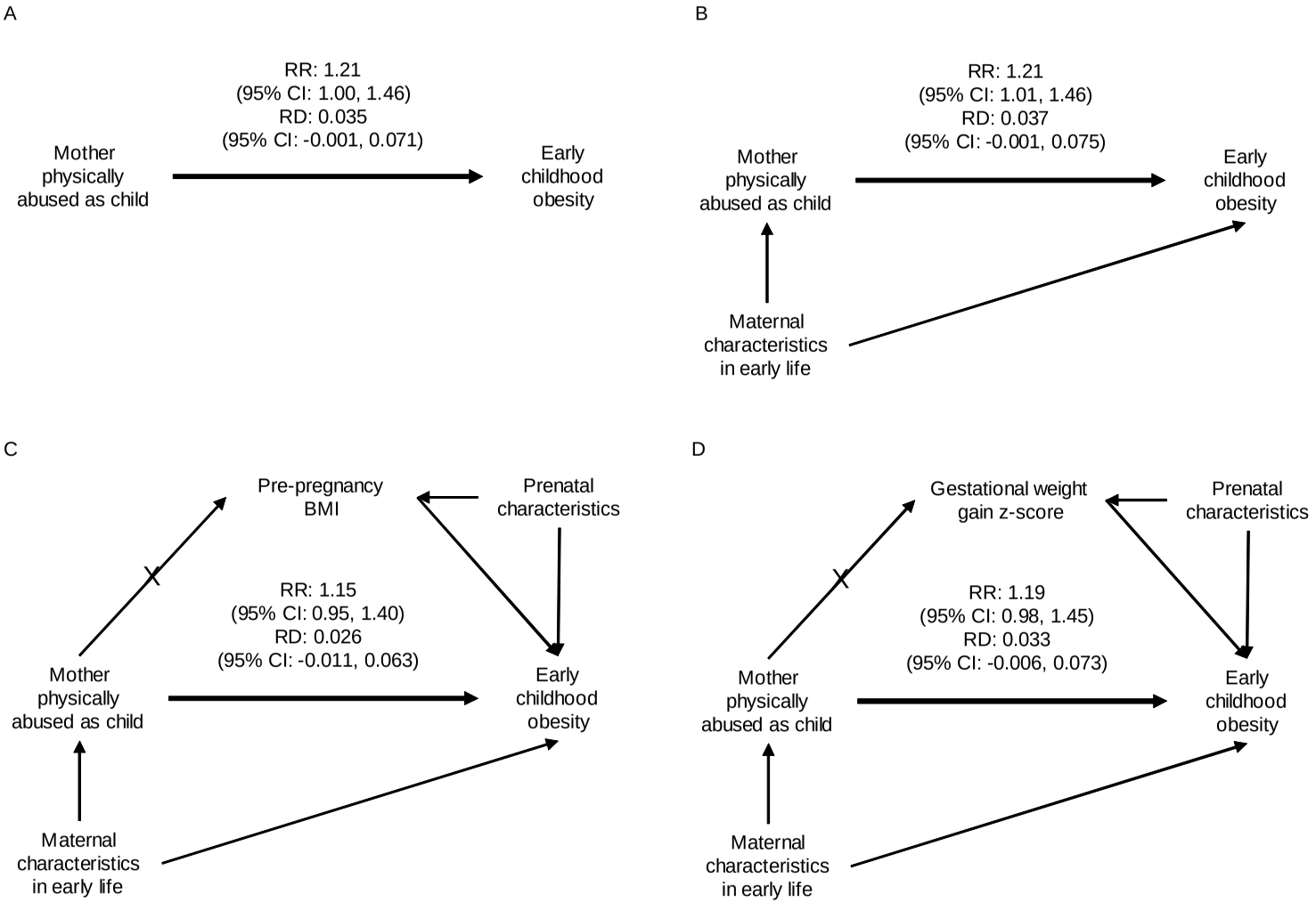


Figure 2. Diagrams of estimates of unadjusted (A) and adjusted (B) total effects of maternal history of physical abuse in childhood on risk of obesity in children ages 2-5 years, and natural direct effect estimates for mediation by pre-pregnancy BMI (C) and gestational weight gain (D). Risk ratios (RR) and risk differences (RD) with 95% confidence intervals (CI) shown correspond to each emboldened pathway.



Appendix A. Detailed methods to estimate natural direct effects and controlled direct effects.

Below, we outline the steps of our analysis using, as an example, pre-pregnancy BMI as the mediator. We repeated these steps for gestational weight gain z-score as the mediator, gestational weight gain adjusted for pre-pregnancy BMI, and with childhood overweight/obesity as the outcome.

1. We applied log-binomial regression to estimate the total effect of physical abuse on early childhood obesity.
2. We updated the log-binomial regression model to adjust for pre-pregnancy BMI and all confounders.
3. We replicated the data into a second dataset and set all physical abuse observations to 'no' (0) in one dataset (all unexposed) and to 'yes' (1) in the second dataset (all exposed).
4. In each dataset, we predicted all confounding maternal characteristics at pregnancy using regression models with physical abuse, pre-pregnancy BMI, and all confounding maternal characteristics in early life as predictors.
5. We applied linear regression to estimate the association between physical abuse and pre-pregnancy BMI, adjusting for all covariates. In the unexposed dataset, we predicted pre-pregnancy BMI using the regression model. We set pre-pregnancy BMI in both the unexposed and exposed datasets to this expected value if unexposed to physical abuse ("the natural value").
6. In each dataset, we predicted the expected probabilities of early childhood obesity using the total effect log-binomial regression model from Step 2.
7. We calculated the risk ratio for the natural direct effect (NDE) by dividing the mean of the expected probabilities of obesity in the exposed dataset by the mean of the expected probabilities of obesity in the unexposed dataset. The risk difference for the NDE was calculated as the difference of these two quantities.
8. We bootstrapped the analyses 1000 times for statistical inference.
9. The steps above were repeated with the addition of an interaction term between physical abuse and pre-pregnancy BMI.
10. To estimate the controlled direct effect (CDE), we repeated the same steps; however, in Step 4 we set pre-pregnancy BMI for all women in each dataset to 25 kg/m^2 and we did not predict the natural value of pre-pregnancy BMI (Step 6).
11. We repeated the CDE estimation for values of 22 and 20 kg/m^2 for a range of estimates.
12. For gestational weight gain z-score mediation analysis, we set z-score to 0 (the standard mean) for CDE estimation. When using the Institute of Medicine gestational weight gain recommendation categories as the mediator in sensitivity analyses, we also adjusted for gestational duration.

Supplemental Table 1. Characteristics of mother-child pairs included in the final sample, ineligible for the study, and eligible but excluded from the final sample[a]

	Final sample	Ineligible sample	Excluded sample
	(n = 6718) %	(n = 4477) %	(n = 317) %
Adverse childhood experiences			
Physical abuse of child	17.3	21.3	0
Alcohol abuse in household	22.2	25.7	11.1
Mental illness in household	11.0	7.8	2.8
Child obesity status			
Age 2-5 years[b]	17.2	14.3	14.4
Age 6-11 years	25.3	16.0	17.0
Age 12-19 years	22.5	20.8	19.0
Early life characteristics of mother			
Maternal grandmother completed high school	62.9	60.3	65.7
Race/ethnicity			
Non-Hispanic white or other	74.4	75.0	81.3
Non-Hispanic black	17.1	17.2	11.9
Hispanic	7.6	7.2	6.3
Asian	1.0	0.6	0.5
Born in the U.S.	95.3	95.0	94.6
Born in southern U.S.	31.7	34.7	31.2
Urban childhood home	78.3	78.6	79.1
Prenatal characteristics[c]			
Pre-pregnancy BMI (kg/m^2)			
Underweight (< 18.5)	7.3	11.3	9.7
Normal weight (18.5 to < 25)	64.3	71.1	71.0
Overweight (25 to < 30)	17.7	13.0	13.7
Obese (≥ 30)	10.7	4.6	5.5
Gestational weight gain[d]			
Inadequate	29.2	31.7	29.8
Adequate	29.4	29.1	30.8
Excessive	41.5	39.3	39.3
Age			
< 20 years	7.0	26.9	12.9
20-30 years	55.9	47.3	55.9
≥ 30 years	37.0	25.7	31.2
Education			
Less than high school completion	15.7	16.7	16.8
High school graduate	63.3	60.6	61.4
College graduate	20.9	22.7	21.8
Employment			
Unemployed	34.2	39.4	39.5
Part-time	28.3	25.3	25.6

Full-time	37.5	35.3	34.9
Equivalized household income			
Lowest quartile	24.9	25.0	24.9
Second quartile	25.1	23.4	23.9
Third quartile	25.1	24.4	24.5
Highest quartile	25.8	27.3	26.7
Married	74.9	77.7	77.9
Smoked cigarettes in pregnancy	25.9	32.8	31.6
Primiparous	43.0	43.8	45.8
Child birthyear			
<1980	7.7	31.4	14.8
1980-1990	54.1	42.4	53.5
>1990	38.2	26.2	31.8

BMI, body mass index

[a] Percentages are weighted for the survey sampling design. Sample sizes are not weighted and refer to number of mother-child pairs.

[b] Child obesity percentages includes children who had an obese BMI at least once during the specified age range.

[c] Pre-pregnancy BMI and gestational weight gain were assessed as mediators. All other maternal characteristics in pregnancy were treated as confounding variables.

[d] Based on Institute of Medicine 2009 recommendations.

Supplemental Table 2. Results of total effect and additional natural direct effect estimates for the association between history of physical abuse in childhood and children's overweight/obesity status age 2-5 years.

	Obese	Overweight/Obese
Unadjusted total effect		
RR (95% CI)	1.21 (1.00, 1.46)	1.10 (0.97, 1.24)
RD (95% CI)	0.035 (-0.001, 0.071)	0.030 (-0.010, 0.072)
Adjusted total effect		
RR (95% CI)	1.21 (1.01, 1.46)	1.10 (0.97, 1.24)
RD (95% CI)	0.037 (-0.001, 0.075)	0.032 (-0.010, 0.074)
NDE: pre-pregnancy BMI		
RR (95% CI)	1.15 (0.95, 1.40)	1.07 (0.94, 1.21)
RD (95% CI)	0.026 (-0.011, 0.063)	0.022 (-0.019, 0.063)
NDE: gestational weight gain		
RR (95% CI)	1.19 (0.98, 1.45)	1.09 (0.96, 1.24)
RD (95% CI)	0.033 (-0.006, 0.073)	0.028 (-0.015, 0.070)
NDE: pre-pregnancy BMI and physical abuse interaction		
RR (95% CI)	1.18 (0.97, 1.44)	1.09 (0.96, 1.23)
RD (95% CI)	0.031 (-0.008, 0.070)	0.027 (-0.015, 0.069)
NDE: gestational weight gain and physical abuse interaction		
RR (95% CI)	1.19 (0.98, 1.46)	1.09 (0.95, 1.24)
RD (95% CI)	0.034 (-0.006, 0.074)	0.028 (-0.017, 0.073)
NDE: joint mediation by pre-pregnancy BMI and gestational weight gain		
RR (95% CI)	1.14 (0.94, 1.38)	1.06 (0.93, 1.20)
RD (95% CI)	0.024 (-0.013, 0.060)	0.019 (-0.022, 0.060)

RR, risk ratio; RD, risk difference; CI, confidence interval; NDE, natural direct effect; BMI, body mass index

Total effects adjusted for maternal grandmother's education, maternal race/ethnicity, born in U.S., born in southern U.S., urban childhood home. Natural direct effects additionally adjusted for age, education, employment status, equivalized household income, marital status, parity, smoking, and child birth year.

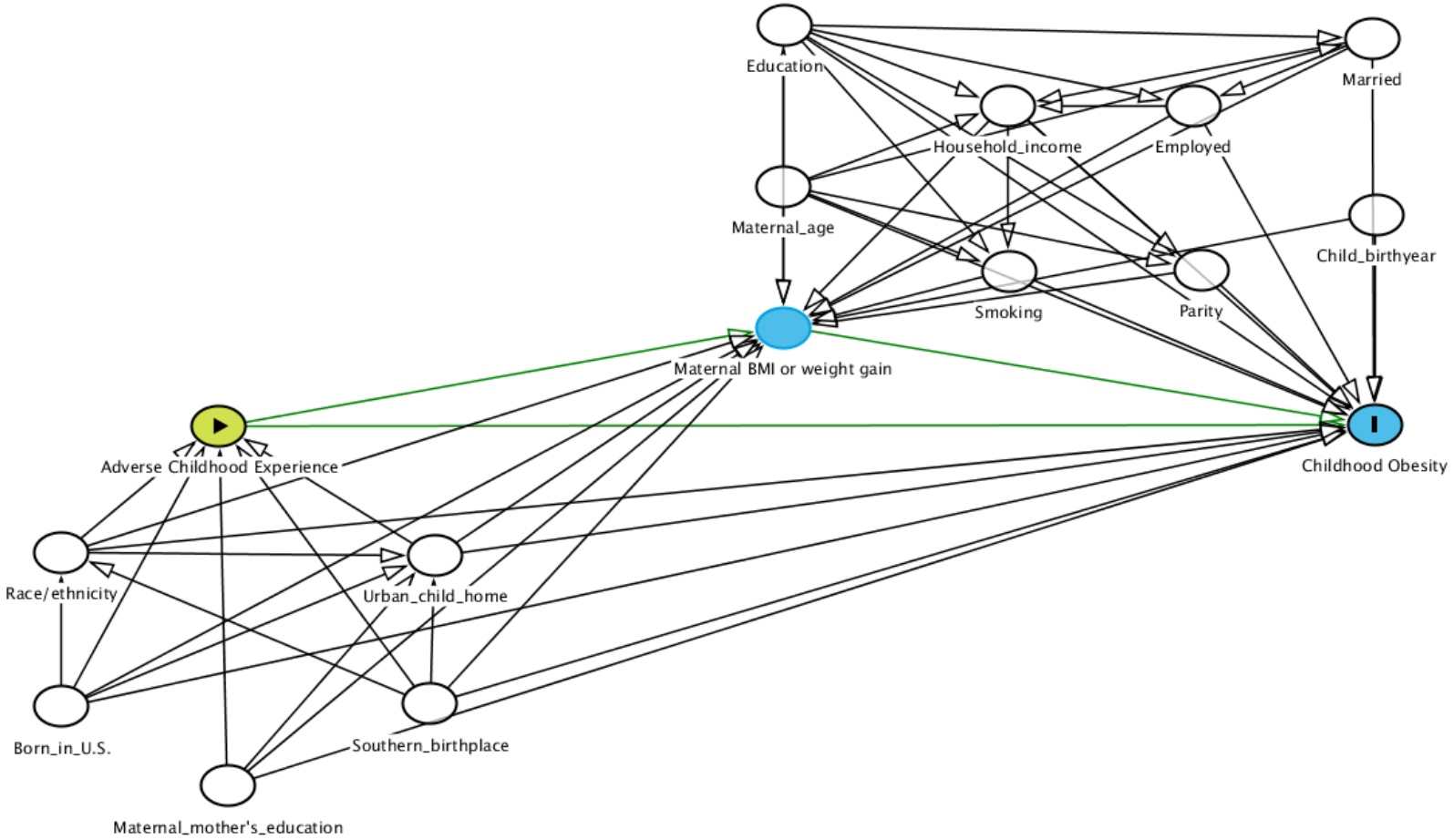
Supplemental Table 3. Results of controlled direct effect (CDE) estimates for the association between history of physical abuse in childhood and children's overweight/obesity status age 2-5 years.

	Obese	Overweight/Obese
CDE: pre-pregnancy BMI set to normal weight		
RR (95% CI)	1.17 (0.96, 1.43)	1.08 (0.95, 1.22)
RD (95% CI)	0.027 (-0.008, 0.062)	0.023 (-0.017, 0.062)
CDE: gestational weight gain set to within IOM recommendation		
RR (95% CI)	1.19 (0.98, 1.45)	1.09 (0.96, 1.23)
RD (95% CI)	0.033 (-0.006, 0.072)	0.028 (-0.015, 0.070)

RR, risk ratio; RD, risk difference; CI, confidence interval; CDE, controlled direct effect; BMI, body mass index; IOM, Institute of Medicine

Adjusted for maternal grandmother's education, maternal race/ethnicity, born in U.S., born in southern U.S., urban childhood home, maternal age at pregnancy, education, employment status, equivalized household income, marital status, parity, smoking, and child birth year. CDE for IOM recommendations additionally adjusted for gestational duration.

Supplemental Figure 1. Directed acyclic graph to determine confounding variables. The covariates on the lower, left-hand side are maternal characteristics in early life and were used in modeling the associations between maternal adverse childhood experiences and childhood obesity. The covariates on the upper, right-hand side are prenatal characteristics and were used in modeling the associations between maternal pre-pregnancy BMI and childhood obesity. The same set of covariates were used in testing both pre-pregnancy BMI and gestational weight gain z-score as mediators. Green lines indicate direct pathways and black lines indicate confounding pathways.



Chapter 5. Conclusion

Advancing infant and child health will require prevention efforts that consider exposures that occur *in utero*. This dissertation demonstrates that helping women begin their pregnancies at healthy weights and gain moderate amounts of weight during pregnancy could be an effective approach to reducing the large burdens of preterm birth, child obesity, and their related outcomes. Additionally, unconventional research methods may be useful tools for continuing to understand the relationship between maternal weight and child health.

As described in Chapter 2, valid, quantitative approaches are available to estimate associations between gestational weight gain and gestational age-dependent outcomes as well as to determine optimal ranges of gestational weight gain. These methods help address challenges that have plagued gestational weight gain research and policy for decades, and may be useful for studying outcomes in addition to preterm birth. Gestational weight gain z-scores were also found to be generalizable to diverse populations in the U.S. Furthermore, there was no evidence that gestational weight gain guidelines should be tailored to maternal racial/ethnic groups; however, future guidelines should consider separate recommendations for grades of prepregnancy obesity.

A unique approach to studying maternal weight and weight change across the childbearing period was demonstrated in Chapter 3. Trajectories of maternal weight were described and it was found that high maternal weight from prepregnancy through the postpartum period compounded the risk of offspring obesity in childhood. However, in comparison to excessive gestational weight gain and high postpartum weight retention, high prepregnancy BMI had the strongest influence on child obesity. Finally, findings presented in Chapter 4 showed that an association observed between maternal obesity and child obesity was due in part to women's experience of physical abuse in childhood. Women who reported childhood physical abuse were at increased risk of prepregnancy obesity and their children were at increased risk of obesity in early childhood. However, gestational weight gain was not identified as a mediator.

Overall, this dissertation deepens the understanding of the relationships between pregnancy weight, weight change, and health outcomes in infants and children. Although gestational weight gain and postpartum weight retention are important factors for infant and child health, the findings presented here emphasize the overwhelmingly strong role of prepregnancy obesity. Additionally, the observed role of maternal abuse in childhood sheds on a novel risk factor for maternal and child obesity. These dissertation results underscore the importance of life-course exposures in the etiology of preterm birth and child obesity as well as the need for interventions that help women address sequalae of childhood abuse and achieve a healthy weight status before becoming pregnant.