DETERMINANTS OF LOW BIRTH WEIGHT, UNITED STATES, 2014-2023

by

CHLOE BURJAK

(Under the Direction of José F Cordero)

ABSTRACT

Low birth weight has significant etiological heterogeneity. Risk factors that impact gestational age and fetal growth patterns among LBW infants are not well understood. Using the National Vital Statistics System birth data (2014–2023), we developed log-binomial regression models to estimate the adjusted risk ratios for determinants of LBW for the subgroups preterm birth and small for gestational age. LBW was associated with multiple factors, but they varied by the underlying leading factors PTB and SGA. Significant associations for preterm infants with LBW were biological conditions like eclampsia (RR = 1.2, 95%CI = 1.18-1.22) and plurality (RR = 1.5, 95%CI = 1.47 -1.48). Among SGA infants with LBW, pre-pregnancy risk factors such as previous PTB (RR = 1.6, 95%CI = 1.61-1.66) and pre-pregnancy BMI (RR = 1.2, 95%CI = 1.14-1.18) were significant. Distinct determinants influence LBW among different birth pathways, such as PTB and SGA varying in their risk factors.

INDEX WORDS: Low birth weight, Small for gestational age, Adequate for gestational age, Large for gestational age, Preterm birth, Early term, Full Term, Late Term, NVSS

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DEDICATION

Thank you to my brother Mohammad Burjak. I am grateful for your patience with me all these years, driving me to and from class so I can purse my education. I also extend my gratitude to my mother, Jamile Natour, and my father, Khudr Burjak, for creating a nurturing home environment that has enabled me to pursue higher education and personal independence.

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CHAPTER 1

INTRODUCTION

Purpose of the Study

This study has two objectives. The first objective was to examine the main determinants of low birth weight in the U.S and by preterm birth (PTB) and small for gestational age (SGA). This means that after examining general LBW determinants, I then analyzed which determinants were associated with the various low birth weight types. The second objective was to examine time trends of low birth weight determinants in the U.S.

How This Study is Original

This study is original because it examines the determinants of diverse LBW types. The current research around this topic is underdeveloped with most studies only looking at determinants of LBW compared to normal birth weight (NBW) infants or the general population. By analyzing what are the determinants of different LBW types, we get a clearer picture of how pathways to LBW vary by gestational age and fetal growth patterns. This introduces the key concept that distinct determinants may influence LBW across different birth groups, such as preterm, full term, or small, adequate, or large for gestational age, with varying determinants impacting each pathway.

Expected Results

Since preterm birth is the most common type of LBW, we expect to see that there are more determinants or pathways linked to LBW compared to infants SGA which makes up less LBW cases.

Paper Structure and Organization

The following thesis is divided into three chapter. Chapter 1 explains the thesis's purpose, originality, hypothesis, and provides the layout of thesis's parts. Chapter 2 is a review of the literature about low birth weight. Chapter 3 is the manuscript titled "Determinants of Low Birth Weight, United States, 2014-2023". This includes the section's: Introduction, methods, results, discussion, and conclusion.

CHAPTER 2

LITERATURE REVIEW

What is Low Birth Weight?

The World Health Organization (WHO) defines low birth weight (LBW) as a birth weight of less than 2,500 g regardless of gestational age (1). Categories of LBW include moderately low birth weight (MLBW, 1500 – 2499g), very low birth weight (VLBW, < 1500 g) and extremely low birth weight (ELBW, <1000 g) (1). Low birth weight can arise from two pathways: preterm birth (PTB) and small for gestational age (SGA), or both (2). Preterm birth is defined as gestational age less than 37 weeks (3). Preterm birth is further categorized into very preterm (28-31 weeks), and late term (31-36 weeks) (3). Gestational age is determined by the length of the pregnancy in weeks. It is measured from the date of the last menstrual period (LMP) to the date of birth, or by obstetric estimation through clinical assessment(s). Infants with a birth weight less than the 10^{th} percentile for gestational age are considered small for gestational age (SGA) (4). This review aims to examine the existing knowledge on low birth weight determinants in the U.S.

Why is Low Birth Weight a Public Health Concern?

Low birth weight is an important indicator of maternal and neonatal health. Infants with LBW face greater health complications throughout life compared to normal birth weight (NBW) infants. LBW infants have a higher risk of mortality and morbidity compared to NBW infants. LBW is the second leading cause of infant mortality in the U.S. (5) Because LBW infants are more likely to experience developmental disabilities such as cerebral palsy and autism spectrum

disorders, compared to NBW infants, they must carry this burden into childhood and unfortunately the rest of their lives (6). The effects of being born with LBW may also persist into adulthood. Due to fetal programming, LBW infants have a higher risk of developing chronic diseases such as type II diabetes and cardiovascular disease later into adulthood (7-8).

How Common is Low Birth Weight?

Examining low birth weight prevalence helps to determine the effectiveness of interventions aimed at supporting mothers and their infants in the U.S and whether the measures of such interventions are beneficial or neutral. Being aware of trends in low birth weight also enables the public to recognize disparities among specific populations who are more likely to be insufficiently supported during preconception and antenatal stages. The concern over LBW is justifiable as rates in the U.S have shown a gradual increase when comparing years 2012 to 2022 (9,10). Over the span of these 11 years, LBW rates have increased by more than 7% in the U.S (9,10).

Low birth weight rates differ across the various states and regions of the U.S with the southeast region having among the highest rates of LBW compared to all other regions (11). The reason for this uneven distribution is two key factors. The first is that there are higher rates of chronic diseases and poorer health in the south compared to all other U.S regions (12). The second reason for this is that more African Americans live in the south (13). African American women are almost two times more likely to give birth to a low birth weight infant compared to white women (14). They also have the highest rates for LBW compared to all other race groups (14). This disproportioned distribution of LBW emphasizes the racial and socioeconomic disparities within the south.

Premature Birth and Small for Gestational Age

LBW can result from preterm birth (PTB), small for gestational age (SGA), or both. Preterm birth is formally defined as any birth before 37 gestational weeks from the 1st day of the last menstrual period (15). Preterm infants spend less time growing and developing in utero, often resulting in lower weight at birth (15). In 2022, preterm births accounted for 10.4% of all births (14). Small for gestational age (SGA) is defined as an infant whose weight is less than the 10th percentile for their gestational age at birth (16). LBW is the product of many underlying factors, but the literature identifies 3 main types. A LBW infant can be preterm, SGA, or both SGA and preterm (6).

Determinants of Low Birth Weight

Low birth weight determinants can be categorized into 3 groups: Maternal factors, placental factors, and fetal factors (6). This sub-section will review what current research observe for the LBW determinants.

Maternal Factors

Some maternal determinants of low birth weight include smoking and alcohol consumption, body mass index (BMI), access to quality prenatal care, medical assisted reproduction (MAR), and chronic/acute disease and or conditions.

Toxins found in cigarettes and alcohol are harmful to a developing fetus (17,18). Alcohol consumption and cigarette smoking interfere with normal fetal development and are linked to LBW (17,18). Women who smoke during pregnancy are estimated to have almost twice the risk of delivering a LBW infant compared to non-smokers (19). This risk is similar among pregnant women who consume alcohol during pregnancy versus those who don't (20).

Maternal weight and BMI are other important LBW determinants. There are three weight-related measures that are important to maternal and fetal health. They include maternal

weight gain, body mass index (BMI), and current weight at delivery. Weight and weight gain can be affected by many factors such as smoking status, metabolic conditions, genetics, lack of access and financial stability to have enough food, and time to prepare meals (21,22). In 2009, the Institute of Medicine (IOM) updated their guidelines for weight gain for pregnancies that would reflect the 21st-century landscape of the U.S. This meant accounting for higher rates of women having children at later ages, women dealing with more chronic conditions, and births with multiple gestations (23). Pregnant women who do not meet the IOM recommendations had a higher risk of SGA (OR 1.53 [95% CI 1.44-1.64]) and preterm birth (OR 1.70 [95% CI 1.32-2.20]) infants (23).

In the U.S, disparities in access to quality prenatal care persists, contributing to the ongoing challenges in reducing rates of LBW. Over 35% of counties in the U.S have no access to birthing hospitals, birth centers offering obstetric care, or obstetric providers (24). In 2022, this affected over 2.3 million women of reproductive age (24). Compared to mothers who do not receive prenatal care, mothers who receive prenatal care have a 38% lower risk of delivering a baby with LBW (RR 0.62, 95% CI 0.47–0.81) (25).

Medically assisted reproductions (MAR) include infertility treatments, fertility enhancing drugs, and artificial reproductive technologies (ART). Infertility treatments encompasses all medical interventions or procedures that help couples having difficulty reproducing. Fertility-enhancing drugs are medications given to stimulate or regulate ovulation to increase the chances of conception (27). These are typically first line treatments (27). ART are medical procedures that involve handling eggs, sperm, or embryos outside the body to achieve pregnancy (27). ART singletons have a 2 to 3 fold increased risk of adverse perinatal outcomes (28).

Placental and Fetal Factors

Some placental factors include issues related to the placement and function. An example of abnormal placenta placement is placenta previa. Placenta previa is characterized by a low lying placenta that can partial or totally cover the cervix (29). This can restrict blood flow and compromise fetal growth (29). An example of abnormal placental function is placenta insufficiency which impairs the placenta's ability to support the fetus's needs (30). A prime example of a fetal factor is plurality. Having to share uterine space and resources can create a high risk environment for the fetuses (31).

REFERENCES

1. Organization WH. International statistical classification of diseases and related health problems, tenth revision, 2nd ed. World Health Organization; 2004.
2. Cutland CL, Lackritz EM, Mallett-Moore T, Bardají A, Chandrasekaran R, Lahariya C, Nisar MI, Tapia MD, Pathirana J, Kochhar S, Muñoz FM; Brighton Collaboration Low Birth Weight Working Group. Low birth weight: Case definition & guidelines for data collection, analysis, and presentation of maternal immunization safety data. Vaccine. 2017 Dec 4;35(48 Pt A):6492-6500. doi: 10.1016/j.vaccine.2017.01.049. PMID: 29150054; PMCID: PMC5710991.
3. Howson C.P., Kinney M.V., Lawn J. March of Dimes, PMNCH, Save the Children, WHO; 2012. Born Too Soon: the global action report on preterm birth.
4. de Onis M., Habicht J.P. Anthropometric reference data for international use: recommendations from a World Health Organization Expert Committee. *Am J Clin Nutr.* 1996;**64**:650–658
5. Murphy SL, Kochanek KD, Xu JQ, Arias E. Mortality in the United States, 2020. NCHS Data Brief, no 427. Hyattsville, MD: National Center for Health Statistics. 2021. DOI: https://dx.doi.org/10.15620/cdc:112079.
6. National Academies of Sciences, Engineering, and Medicine. 2024. Low Birth Weight Babies and Disability. Washington, DC: The National Academies Press. https://doi.org/10.17226/27375.

7. Kwon EJ, Kim YJ. What is fetal programming?: a lifetime health is under the control of in utero health. Obstet Gynecol Sci. 2017 Nov;60(6):506-519. doi: 10.5468/ogs.2017.60.6.506. Epub 2017 Oct 26. PMID: 29184858; PMCID: PMC5694724.
8. Godfrey KM, Barker DJ. Fetal programming and adult health. Public Health Nutr. 2001 Apr;4(2B):611-24. doi: 10.1079/phn2001145. PMID: 11683554.
9. Martin JA, Hamilton BE, Osterman MJK, et al. Births: Final data for 2012. National vital statistics reports; vol 62 no Hyattsville, MD: National Center for Health Statistics. 2013.
10. Hamilton BE, Martin JA, Osterman MJK. Births: Provisional data for 2020. Vital Statistics Rapid Release; no 12. Hyattsville, MD: National Center for Health Statistics. May 2021. DOI: https:// doi.org/10.15620/cdc:104993.
11. Brown CC, Moore JE, Felix HC, Stewart MK, Tilford JM. Geographic Hotspots for Low Birthweight: An Analysis of Counties With Persistently High Rates. Inquiry. 2020 Jan-Dec;57:46958020950999. doi: 10.1177/0046958020950999. PMID: 33043787; PMCID: PMC7550956.
12. Benavidez GA, Zahnd WE, Hung P, Eberth JM. Chronic Disease Prevalence in the US: Sociodemographic and Geographic Variations by Zip Code Tabulation Area. Prev Chronic Dis 2024;21:230267. DOI: http://dx.doi.org/10.5888/pcd21.230267
13. Majority of African Americans live in 10 states; New York City and Chicago are cities with largest black populations. *M2 Presswire*. August 13, 2001. Accessed November 19, 2024. https://research.ebsco.com/linkprocessor/plink?id=d297898f-dd86-349c-b26f-83548116923f
14. Osterman MJK, Hamilton BE, Martin JA, Driscoll AK, Valenzuela CP. Births: Final Data for 2022. Natl Vital Stat Rep. 2024 Apr;73(2):1-56. PMID: 38625869.

15. Quinn JA, Munoz FM, Gonik B, Frau L, Cutland C, Mallett-Moore T, Kissou A, Wittke F, Das M, Nunes T, Pye S, Watson W, Ramos AA, Cordero JF, Huang WT, Kochhar S, Buttery J; Brighton Collaboration Preterm Birth Working Group. Preterm birth: Case definition & guidelines for data collection, analysis, and presentation of immunisation safety data. Vaccine. 2016 Dec 1;34(49):6047-6056. doi: 10.1016/j.vaccine.2016.03.045. Epub 2016 Oct 13. PMID: 27743648; PMCID: PMC5139808.
16. Schlaudecker EP, Munoz FM, Bardají A, Boghossian NS, Khalil A, Mousa H, Nesin M, Nisar MI, Pool V, Spiegel HML, Tapia MD, Kochhar S, Black S; Brighton Collaboration Small for Gestational Age Working Group. Small for gestational age: Case definition & guidelines for data collection, analysis, and presentation of maternal immunisation safety data. Vaccine. 2017 Dec 4;35(48 Pt A):6518-6528. doi: 10.1016/j.vaccine.2017.01.040. PMID: 29150057; PMCID: PMC5710996.
17. Odendaal HJ, Kruger M, Botha MH. Dangers of smoking cigarettes and drinking alcohol during pregnancy. S Afr Med J. 2020 Oct 28;110(11):1066-1067. doi: 10.7196/SAMJ.2020.v110i11.14738. PMID: 33403977; PMCID: PMC8011951.
18. Cornelius MD, Day NL. The effects of tobacco use during and after pregnancy on exposed children. Alcohol Res Health. 2000;24(4):242-9. PMID: 15986719; PMCID: PMC6709748.
19. Gayle C. Windham, Barbara Hopkins, Laura Fenster and Shanna H. Swan Source: Epidemiology, Jul., 2000, Vol. 11, No. 4 (Jul., 2000), pp. 427-433 Published by: Lippincott Williams & Wilkins
20. Sbrana M, Grandi C, Brazan M, Junquera N, Nascimento MS, Barbieri MA, Bettiol H, Cardoso VC. Alcohol consumption during pregnancy and perinatal results: a cohort study.

Sao Paulo Med J. 2016 Apr;134(2):146-52. doi: 10.1590/1516-3180.2015.02040211. Epub 2016 Mar 18. PMID: 27007799; PMCID: PMC10496540.

21. Goldstein RF, Abell SK, Ranasinha S, Misso M, Boyle JA, Black MH, Li N, Hu G, Corrado F, Rode L, Kim YJ, Haugen M, Song WO, Kim MH, Bogaerts A, Devlieger R, Chung JH, Teede HJ. Association of Gestational Weight Gain With Maternal and Infant Outcomes: A Systematic Review and Meta-analysis. JAMA. 2017 Jun 6;317(21):2207-2225. doi: 10.1001/jama.2017.3635. PMID: 28586887; PMCID: PMC5815056.
22. Ludwig DS, Currie J. The association between pregnancy weight gain and birthweight: a within-family comparison. Lancet. 2010 Sep 18;376(9745):984-90. doi: 10.1016/S0140-6736(10)60751-9. Epub 2010 Aug 4. PMID: 20691469; PMCID: PMC2974327.
23. Rasmussen KM, Catalano PM, Yaktine AL. New guidelines for weight gain during pregnancy: what obstetrician/gynecologists should know. Curr Opin Obstet Gynecol. 2009 Dec;21(6):521-6. doi: 10.1097/GCO.0b013e328332d24e. PMID: 19809317; PMCID: PMC2847829.
24. Brigance, C., Lucas R., Jones, E., Davis, A., Oinuma, M., Mishkin, K. and Henderson, Z. (2022). Nowhere to Go: Maternity Care Deserts Across the U.S. (Report No. 3). March of Dimes. https://www.marchofdimes.org/research/maternity-care-deserts-report.aspx
25. **Group Prenatal Care Reduces Risk of Preterm Birth and Low Birth Weight: A Matched Cohort Study** *Shayna D. Cunningham, Jessica B. Lewis, Fatma M. Shebl, Lisa M. Boyd, Marc A. Robinson, Stephanie A. Grilo, Susan M. Lewis, Anne L. Pruett, and Jeannette R. Ickovics*

26. Jain M, Singh M. Assisted Reproductive Technology (ART) Techniques. [Updated 2023 Jun 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK576409/
27. Jain M, Singh M. Assisted Reproductive Technology (ART) Techniques. [Updated 2023 Jun 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK576409/
28. Mertens, J., Belva, F., van Montfoort, A.P.A. *et al.* Children born after assisted reproduction more commonly carry a mitochondrial genotype associating with low birthweight. *Nat Commun* **15**, 1232 (2024). https://doi.org/10.1038/s41467-024-45446-1
29. Anderson-Bagga FM, Sze A. Placenta Previa. [Updated 2023 Jun 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539818/
30. Wardinger JE, Ambati S. Placental Insufficiency. [Updated 2022 Oct 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK563171/
31. Kinare A. Fetal environment. Indian J Radiol Imaging. 2008 Nov;18(4):326-44. doi: 10.4103/0971-3026.43848. PMID: 19774194; PMCID: PMC2747450.

CHAPTER 3

MANUSCRIPT

DETERMINANTS OF LOW BIRTH WEIGHT, UNITED STATES, 2014-2023

INTRODUCTION

Low birth weight (LBW) is the second leading cause of infant mortality and a major contributor to infant morbidity in the United States (1, 2). LBW is defined as a birth weight of less than 2,500 grams regardless of gestational age (3). It is categorized into moderately low birth weight (MLBW, 1500 – 2499g), very low birth weight (VLBW, < 1500 g) and extremely low birth weight (ELBW, <1000 g) (3).

The determinants of low birth weight are well-studied; however, the literature remains limited in examining how these determinants vary across different types of LBW. There are three main types of LBW. This includes LBW infants that are preterm, small for gestational age (SGA), or both. This research examines five distinct types of low birth weight infants: those born preterm, those who are both preterm and small for gestational age (SGA), those who are exclusively SGA, those who are neither preterm nor SGA, and those classified as appropriate for gestational age (AGA) or large for gestational age (LGA). By understanding which different determinants are linked to specific LBW types, we may identify certain pathways and trends in infants with LBW. The aims of this study were (1) To examine the main determinants of low birth weight in the U.S and by various categories of gestational age and fetal growth patterns, and (2) To examine the time trends of important LBW determinants from 2014-2023.

METHODS

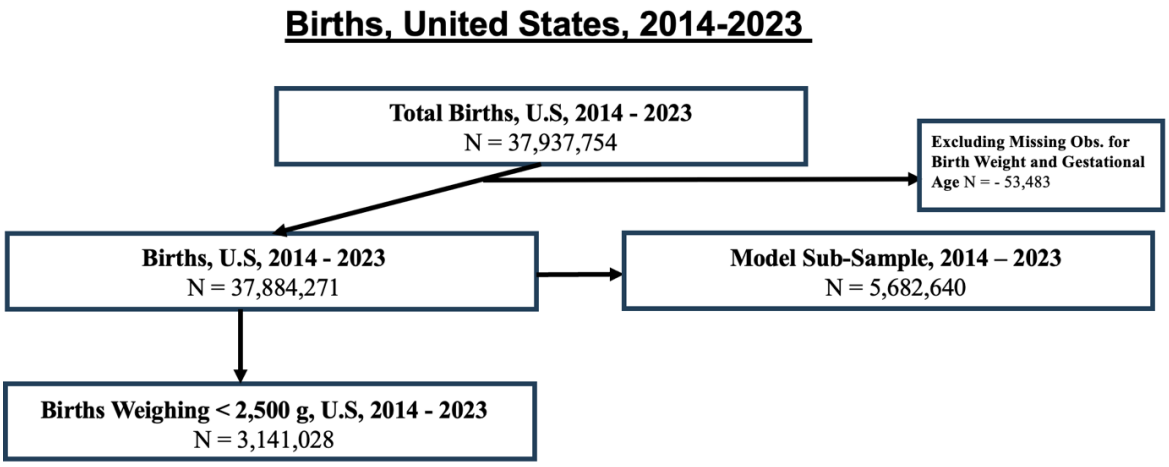
Data Source

The National Vital Statistics System (NVSS) birth data documents 100% of birth certificates registered in all U.S states and D.C. These documented births account for more than 99.9% of all births in the U.S. The NVSS birth data captures maternal and neonatal health characteristics during the prenatal, delivery, and postnatal stages.

Analytic Population

The source population were the total births from 2014-2023, N = 37,937,754. N = 53,483 were excluded from the study as observations had missingness for variables birth weight (main outcome), and gestational age (main exposure). This left N = 37,884,271 observations left that were used to analyze any type of descriptive data such as rates or frequencies. We then randomly sampled 15% of births each year leaving 5,683,640 births that was used to model the relationships. Due to resource constraints, the computational system used for analysis lacked the capacity to process and model the dataset when observations were over 37 million, hence, a random sample was utilized for modeling. A chi-square test was conducted to test whether there were significant differences between the distribution of the sample and the distribution of the complete dataset. All p-values were statistically insignificant reflecting that there were no significant differences in the distributions. Refer to **Figure 1**.

Figure 1: *Births, United States, 2014-2023*



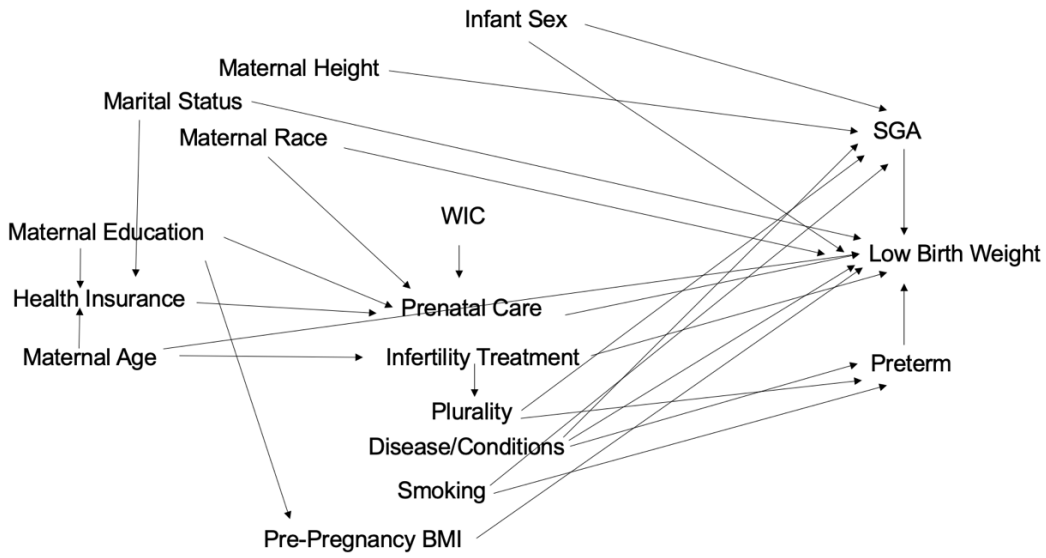
Statistical Analysis

We began by conducting descriptive which included calculating simple frequencies and rates. Then we analyzed what were the potential risk factors and mediators of low birth weight. This was done by calculating unadjusted risk ratios for all variable and by constructing a directed acyclic graph (DAG). After examining the unadjusted risk ratios, we then did the same analysis but stratified by preterm birth (PTB) and small for gestational age (SGA) as they appeared to be effect modifiers in the early stages of the analysis. Time trends describing relevant LBW risk factors were analyzed using simple rates over the 2014-2023 time span.

Direct Acyclic Graph

The DAG included potential determinants and the main outcome (low birth weight). The DAG was the first step at analyzing potential relationship as it offers a visual approach to understand the relationship between variables. The variables STIs, gestational hypertension, and eclampsia were all grouped together into the category diseases/conditions, but only for the purpose of not overburdening the DAG. These variables were not merged in the analysis. Refer to **Figure 2**.

Figure 2: *Direct Acyclic Graph*



Variable Selection

Unadjusted risk ratios were calculated for all potential determinants of LBW (reference: normal birth weight, NBW). Refer to **Figure 3**. We considered an unadjusted risk ratio of 1.2 or greater to be a strong risk factors, and anything less than 1.1, but greater than 1.0 to be weaker risk factors. We also hypothesized that SGA and preterm birth were effect modifiers since their risk ratios were very large. We tested this by stratifying by preterm birth and SGA. If the unadjusted risk ratios in the stratum were significantly different from the overall adjusted risk ratio, we considered them to be effect modifiers. Refer to **Table 1** of an example of stratifying by preterm birth. The DAG and the calculated unadjusted risk ratios for both the overall and the stratum specific, were used to direct which variables to select and how they would be used in the modeling analysis.

Figure 3: *Forest Plot of Unadjusted Risk Ratios*

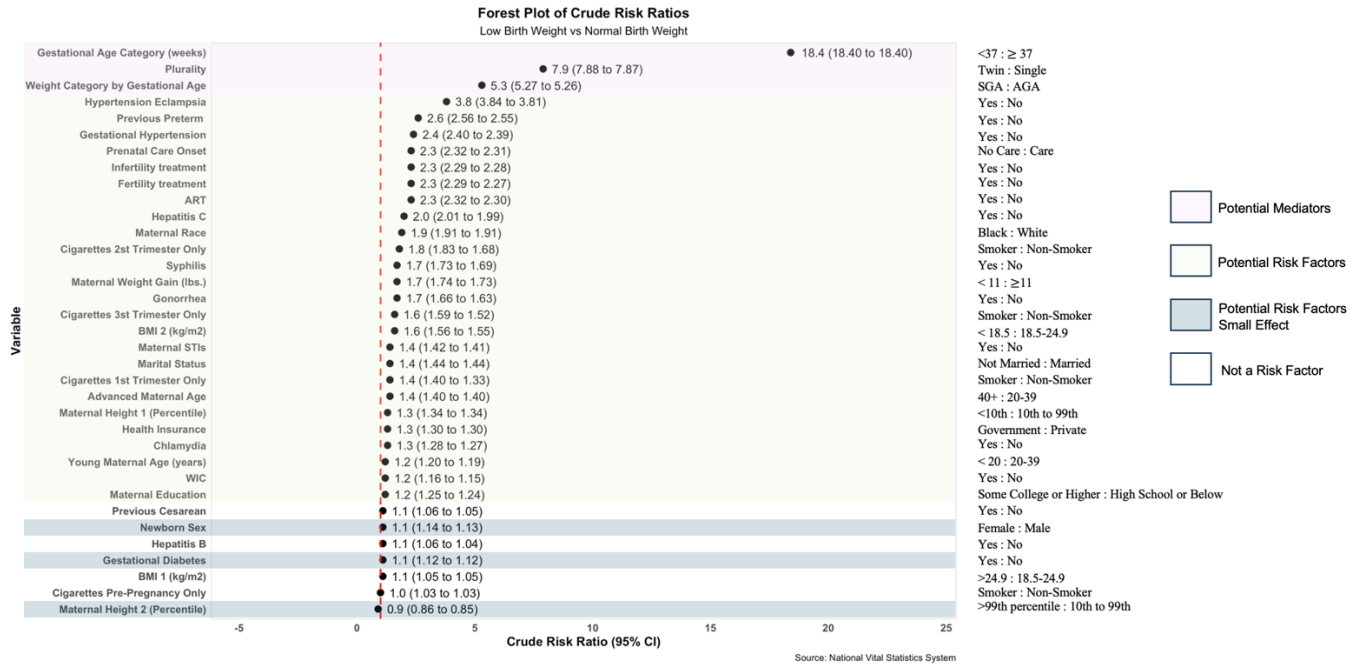


Table 1: Example of Stratum Specific Risk Ratios

Overall RR = 3.8 95%CL(3.81, 3.86)		
	Low Birth Weight	**Normal Birth Weight**
Eclampsia: Yes	32,453	62,568
Eclampsia: No	3,086,598	31,624,570
Preterm = Yes; RR = 2.7 95%CL (2.67, 2.82)		
	Low Birth Weight	**Normal Birth Weight**
Eclampsia: Yes	4,763	51,079
Eclampsia: No	963,776	30,044,471
Preterm = No ; RR = 1.2 95%CL (1.22, 1.24)		
	Low Birth Weight	**Normal Birth Weight**
Eclampsia: Yes	4,763	51,079
Eclampsia: No	963,776	30,044,471

Variables

Final variables selected were categorized into maternal and fetal factors, and pregnancy outcomes. Refer to **Figure 4**. Some variables were recategorized for the model to reduce convergence. Maternal race and ethnicity were recategorized into non-Hispanic White, non-Hispanic Black, and other races. Other race included multiple races, non-Hispanic AIAN, non-Hispanic Asian, non-Hispanic NHOPI, and Hispanic. Maternal height was made into percentiles with short stature being considered anything below the 10^{th} percentile, anything above the 99^{th} percentile being tall stature, and anything between being average. Pre-pregnancy BMI was recategorized as a BMI > 24.9 kg/m^2 being overweight or greater and underweight being BMI < 18.5 kg/m^2. Educational attainment was recategorized into the level's attainment of a high school degree or anything less and the second level which was attainment of some college, a college degree, or anything higher. Health insurance was recategorized into government insurance which included Medicaid and other types of government insurances like Indian Health Service and CHAMPUS/TRICARE, private health insurance, and self-pay. All STIs types were grouped together as a binary (yes or no). Infertility treatment which was an umbrella term to include treatments like fertility enhancing drugs and assisted reproductive technology. Gestational hypertension included pregnancy induced hypertension (PIH) and pre-eclampsia. Prenatal care and cigarette smoking were binary variables (either yes or no). Weight gain was a binary variable with mother either gaining 11 pounds or more during her pregnancy or less than 11 pounds.

Figure 4: *Variables*

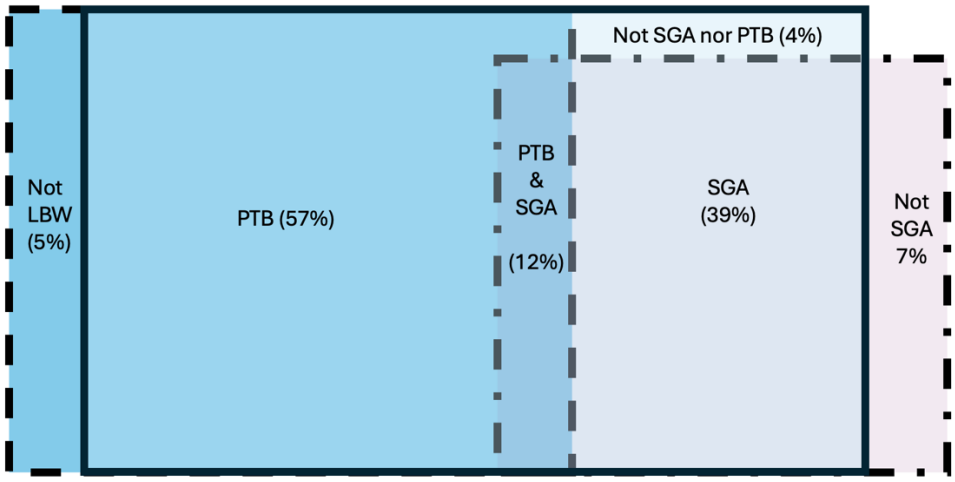
Maternal Factors	Fetal Factors	Pregnancy Outcomes

• **Pre-Pregnancy**
  • Marital status
  • Maternal age (years)
  • Race and ethnicity
  • Height (inches)
  • Previous preterm
  • BMI (kg/m2)
  • Infertility treatment
• **Socioeconomic**
  • Educational Attainment
  • Health insurance
  • WIC recipience
• **During Pregnancy**
  • Sexually transmitted diseases
  • Eclampsia
  • Gestational hypertension
  • Prenatal care
  • Cigarette smoking
  • Weight Gain
	• Sex
	• Multiple gestations
		• Obstetrics estimates gestational age (weeks) at birth
		• Birth weight (grams)
		• Birth weight for gestational age

Outcome Variables

The main outcome variable was low birth weight (< 2,500 g), and low birth weight types This means that LBW was analyzed among those who were preterm, non-preterm, SGA, AGA/LGA, and those neither preterm nor SGA. Refer to **Figure 5**.

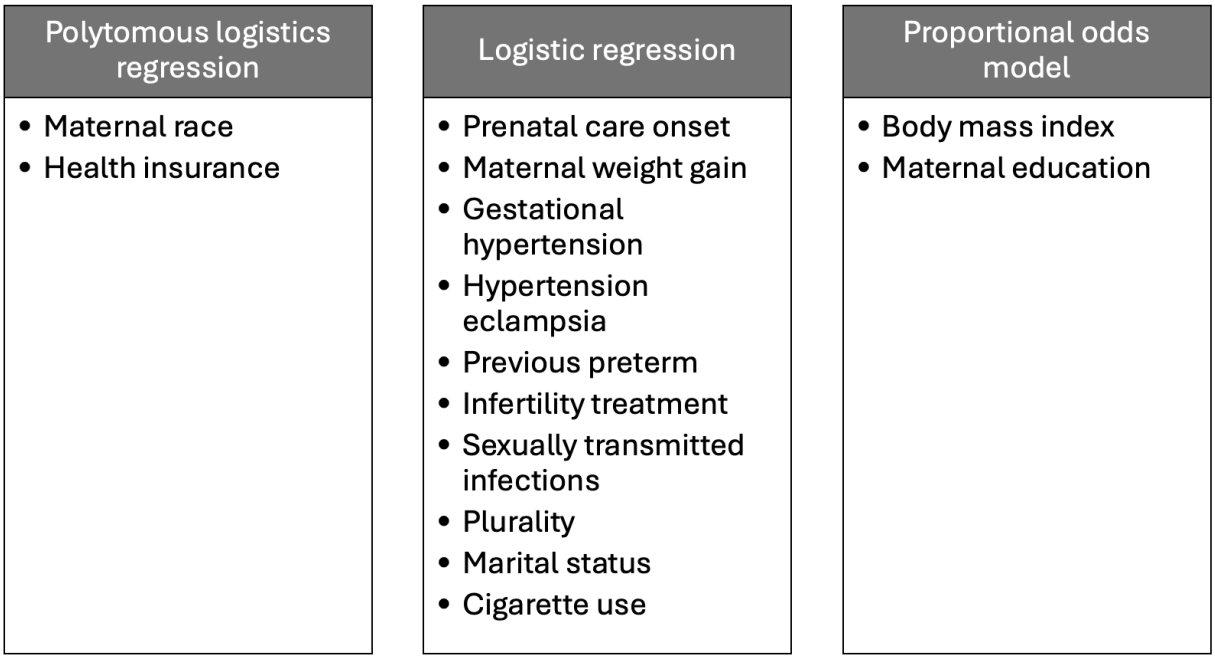
Figure 5: *Etiologic Diversity of Low Birth Weight*



Models

For the last part of the analysis, log binomial regression (link = log) was employed to obtain the adjusted risk ratios. Before the models were build, multivariate imputation by chained equations (MICE) in R were used. No variable in the subsample had more than 8% missingness. Each variable type had a different method of imputation. Refer to **Figure 6**. Five datasets were imputed (m = 5) with a maximum of five iterations (maxit = 5). The imputed datasets were combined using Rubin's rule to produce the final pooled dataset used for modeling.

Figure 6. *Multivariate Imputation by Chained Equations*



The following models were built to find the adjusted risk ratio for each subgroup taking in consideration not to overfit and to work around convergence. The Wald test was used to compare nested models and to aid in building models with better fit. An adjusted risk ratio with its respective 95%CL were considered clinically significant if ≥ 1.2. Statistical insignificance was based on if the 95% confidence intervals included 1.0. This includes adjusted risk ratios of 1.1 that had a confidence interval with values below 1.1. All determinants were based on

clinically significant findings. Note that variables not included in the following models were analyzed in separate models to understand their adjusted risk ratios.

Model 1: Comparing Low Birth Weight vs Normal Birth Weight

Y = 1 low birth weight, and 0 for normal birth weight

$$P(Y = 1|X) = e\text{^}(\beta_0 + \beta_1(\text{MaternalAge}) + \beta_2(\text{InfantSex}) + \beta_3(\text{PrenatalCare}) + \beta_4(\text{MaternalRace}) + \beta_5(\text{HealthInsurance}) + \beta_6(\text{MaternalEducation}) + \beta_7(\text{MaritalStatus}) + \beta_8(\text{WIC}) + \beta_9(\text{STIs}))$$

Model 2: Comparing Low Birth Weight Among PTB vs Normal Birth Weight Among PTB

Y = 1 low birth weight among preterm birth, and 0 for normal birth weight among preterm birth

$$P(Y = 1|X) = e\text{^}(\beta_0 + \beta_1(\text{MaternalAge}) + \beta_2(\text{InfantSex}) + \beta_3(\text{PrenatalCare}) + \beta_4(\text{MaternalRace}) + \beta_5(\text{MaternalEducation}) + \beta_6(\text{MaritalStatus}) + \beta_7(\text{WIC}))$$

Model 3: Comparing Low Birth Weight Among Not PTB vs Normal Birth Weight Among Not PTB

Y = 1 low birth weight among non-preterm birth, and 0 for normal birth weight among non-preterm birth

$$P(Y = 1|X) = e\text{^}(\beta_0 + \beta_1(\text{Gestational Hypertension}) + \beta_2(\text{InfertilityTreatment}) + \beta_3(\text{MaternalAge}) + \beta_4(\text{InfantSex}) + \beta_5(\text{PrenatalCare}) + \beta_6(\text{MaternalRace}) + \beta_7(\text{MaternalEducation}) + \beta_8(\text{WIC}) + \beta_9(\text{BMI}) + \beta_{10}(\text{HealthInsurance}) + \beta_{11}(\text{MaritalStatus}) + \beta_{12}(\text{STIs}) + \beta_{13}(\text{Smoking}) + \beta_{14}(\text{WeightGain}))$$

Model 4: Comparing Low Birth Weight Among SGA vs Normal Birth Weight Among SGA

Y = 1 low birth weight among SGA and 0 for normal birth weight among SGA

$$P(Y = 1|X) = e\text{^}(\beta_0 + \beta_1(\text{MaternalAge}) + \beta_2(\text{InfantSex}) + \beta_3(\text{PrenatalCare}) + \beta_4(\text{HealthInsurance}) + \beta_5(\text{STIs}) + \beta_6(\text{MaternalEducation}) + \beta_7(\text{WIC}) + \beta_8(\text{BMI}) + \beta_9(\text{Unmarried}))$$

Model 5: Comparing Low Birth Weight Among AGA/LGA vs Normal Birth Weight Among AGA/LGA

Y = 1 low birth weight among AGA/LGA and 0 for normal birth weight among AGA/LGA

$$P(Y = 1|X) = e\text{^}(\beta_0 + \beta_1(\text{InfertilityTreatment}) + \beta_2(\text{MaternalAge}) + \beta_3(\text{InfantSex}) + \beta_4(\text{PrenatalCare}) + \beta_5(\text{MaternalRace}) + \beta_6(\text{WIC}) + \beta_7(\text{MaternalEducation}) + \beta_8(\text{MaritalStatus}) + \beta_9(\text{STIs}) + \beta_{10}(\text{Smoking}) + \beta_{11}(\text{HealthInsurance}))$$

Model 6: Comparing Low Birth Weight Among Not PTB No SGA vs Normal Birth Weight Among Not PTB No SGA

Y = 1 low birth weight among non-preterm birth and not SGA and 0 for normal birth weight among non-preterm birth and not SGA

$$P(Y = 1|X) = e\text{^}(\beta_0 + \beta_1(\text{WeightGain}) + \beta_2(\text{MaternalAge}) + \beta_3(\text{InfantSex}) + \beta_4(\text{PrenatalCare}) + \beta_5(\text{MaternalRace}) + \beta_6(\text{WIC}) + \beta_7(\text{MaternalEducation}) + \beta_8(\text{MaritalStatus}) + \beta_9(\text{STIs}) + \beta_{10}(\text{Smoking}) + \beta_{11}(\text{HealthInsurance}) + + \beta_{12}(\text{GestationalHypertension}) + \beta_{13}(\text{Plurality}) + \beta_{14}(\text{PreviousPreterm}) + \beta_{15}(\text{InfertilityTreatment}) + \beta_{16}(\text{MaternalHeight}) + \beta_{17}(\text{BMI}))$$

RESULTS

8.3% (N = 3,141,028) of births were low birth weight. The average birth weight among LBW infants was 2,310 g. The average birth weight of an infant who was born preterm and low birth weight was 1,838 g, and 2,081 g if the infant was SGA and LBW. Infants with LBW had an average gestational age of 34.2, with 1.84 standard deviations lower than the mean gestational age in the overall population (Cohen's d= 1.84). Preterm birth rates in the U.S have slightly increased in 2023 compared to 2014 (10% vs 9.5%) but have slightly decreased among infants born with LBW (58% to 56%). This relationship is reversed for SGA births. SGA births have slightly decreased in the overall population (10% to 9.6%) but have increased among LBW infants (38% vs 42%). 57% of LBW infants were classified as preterm, 39% were classified as SGA, 12% were classified as both SGA and PTB, and 4% were classified as neither SGA nor preterm. Refer to **Figure 5**.

The overall findings are summarized in **Table 2** and **Table 3**. All columns labeled as "subset" in both tables are the LBW types tested for. In general term, all LBW determinants were statistically significant except for maternal age < 20 years (adjusted RR = .99, 95%CI = .98-1.00) and government health insurance (adjusted RR = 1.0, 95%CI = 1.03-1.05). Infertility treatment and female infant sex were considered non-clinically meaningful variables for LBW infants compared to NBW infants.

The overall trend was that there were more defined trends among LBW infants born preterm and among infants born SGA. The links to LBW among preterm infants are biologically related through variables such as eclampsia, maternal race, and plurality, whereas the links to

LBW infants that are SGA are factors related to pre-pregnancy conditions that were not important in LBW infants born before 37 gestational weeks.

Table 2. *Summary Adjusted Risk Ratio (95%CL) for Variables by LBW and LBW Types*

Variables	LBW : NBW	Preterm subset	Not Preterm subset	SGA subset	AGA/LGA subset	Not Preterm Not SGA subset
Maternal Age 40 + years	1.5 (1.45, 1.49)	1.0 (1.02, 1.04)	1.2 (1.19, 1.25)	1.3 (1.32, 1.36)	1.34 (1.32,1.36)	1.3 (1.19, 1.36)
Maternal Age <20 years	0.99 (0.98, 1.00))	1.1 (1.05, 1.07)	1.07 (1.05, 1.09)	0.91 (0.90, 0.93)	0.97 (0.97, 1.02)	1.1 (1.07, 1.21)
Race Black: White	1.7 (1.66, 1.69)	1.2 (1.23, 1.24)	2.1 (2.03, 2.09)	1.1 (1.11, 1.13)	1.7 (1.72, 1.76)	1.9 (1.86, 2.02)
WIC	0.93 (0.92, 0.93)	.97 (0.96, 0.97)	1.0 (1.00, 1.01)	0.97 (0.96, 0.97)	0.93 (0.90, 0.96)	0.93 (0.90, 0.97)
No Prenatal Care	1.8 (1.73, 1.82)	1.0 (1.02, 1.04)	1.2 (1.16, 1.24)	1.1 (1.11, 1.16)	2.0 (1.95, 2.01)	1.2 (1.08, 1.30)
BMI <18.5 kg/m2	1.5 (1.48, 1.52)	1.1 (1.05, 1.07)	1.7 (1.69, 1.76)	1.2 (1.14, 1.18)	1.4 (1.40, 1.45)	1.8 (1.66, 1.89)
Pre-Pregnancy BMI > 24.9 kg/m2	0.9 (0.90, 0.91)	1.1 (1.06, 1.07)	0.70 (0.69, 0.70)	1.1 (1.10, 1.12)	1.0 (0.94, 0.96)	0.69 (0.66, 0.71)
Weight Gain < 11 lbs.	1.6 (1.61, 1.63)	1.2 (1.16, 1.17)	1.6 (1.56, 1.61)	1.1 (1.13, 1.16)	1.9 (1.83, 1.87)	1.7 (1.60, 1.76)
Gestational Hypertension	2.3 (2.32, 2.34)	1.1 (1.11, 1.12)	2.2 (2.14, 2.21)	2.2 (2.14, 2.21)	2.0 (1.97, 2.00)	2.8 (2.69, 2.90)
Eclampsia	3.6 (3.56, 3.72)	1.2 (1.18, 1.22)	2.6 (2.38, 2.75)	2.3 (2.21, 2.33)	4.0 (3.90, 4.14)	2.6 (2.18, 3.14)
Previous Preterm	2.4 (2.33, 2.38)	1.0 (1.00, 1.01)	1.5 (1.51, 1.58)	1.6 (1.61, 1.66)	2.9 (2.88, 2.94)	1.8 (1.71, 1.94)
Infertility Treatment	1.1 (1.13, 1.13)	1.0 (1.00, 1.01)	1.1 (1.06, 1.12)	1.6 (1.55, 1.60)	1.1 (1.06, 1.09)	1.1(1.00, 1.18)
STIs	1.2 (1.16, 1.19)	1.05 (1.06, 1.07)	1.1 (1.07, 1.12)	1.0 (1.02, 1.06)	1.1 (1.12, 1.17)	1.2 (1.13, 1.30)
Infant Sex	1.1 (1.13, 1.14)	1.1 (1.12, 1.25)	1.5 (1.48, 1.51)	0.93 (0.92, 0.94)	1.0 (1.02, 1.03)	1.4 (1.41, 1.49)
Maternal Education	1.2 (1.16, 1.18)	1.0 (0.99, 1.00)	1.1 (1.00, 1.14)	1.1 (1.02, 1.06)	1.2 (1.22, 1.25)	1.1 (1.08, 1.17)
Plurality	7.9 (7.86, 7.94)	1.5 (1.47, 1.48)	8.5 (8.41, 8.65)	2.9 (2.90, 2.94)	10.7 (10.63, 10.77)	15.6 (15.04, 16.27)
Marital Status	1.2 (1.17, 1.19)	1.0 (1.05, 1.07)	1.2 (1.15, 1.18)	1.0 (1.03, 1.05)	1.2 (1.18, 1.21)	1.2 (1.12, 1.21)
Cigarette Smoking	1.7 (1.72, 1.75)	1.1 (1.12, 1.13)	2.1 (2.09, 2.16)	1.2 (1.15, 1.18)	1.4 (1.43, 1.46)	1.9 (1.77, 1.95)
Maternal Height (<10th percentile)	1.2 (1.24, 1.26)	1.1 (1.07, 1.08)	1.6 (1.60, 1.65)	1.0 (1.04, 1.06)	1.6 (1.53, 1.66)	1.6 (1.53, 1.66)
Maternal Height: (>99th percentile)	0.89 (0.85, 0.92)	0.91 (0.89, 0.94)	0.62 (0.57, 0.68)	1.02 (0.96, 1.08)	0.55 (0.44, 0.68)	0.54 (0.44, 0.68)
Government: Private Insurance	1.0 (1.03, 1.05)	1.00 (0.99, 1.00)	1.0 (1.06, 1.07)	1.0 (1.00, 1.02)	1.0 (1.02, 1.04)	1.0 (1.01,1.09)
Self Pay : Private Insurance	0.76 (0.710, 0.818)	0.95 (0.94, 0.97)	0.85 (0.80, 0.91	0.82 (0.79, 0.96)	0.84 (0.80, 0.88)	0.75 (0.68, 0.82)

Table 3. *Summary Clinically Significant Risk Factors of LBW and LBW Types*

Variables	LBW : NBW	Preterm subset	Not Preterm subset	SGA subset	AGA/LGA subset	Not Preterm Not SGA subset
Maternal Age 40 + years	X		X	X	X	X
Race Black: White	X	X	X		X	X
No Prenatal Care	X		X		X	
BMI <18.5 kg/m2	X		X	X	X	X
Pregnancy Weight Gain < 11 lbs.	X		X		X	X
Gestational Hypertension	X		X	X	X	X
Eclampsia	X	X	X	X	X	X
Previous Preterm	X		X	X	X	X
STIs	X					X
Infant Sex			X			X
Maternal Education	X				X	
Plurality	X	X	X	X	X	X
Marital Status	X		X		X	X
Cigarette Smoking	X		X	X	X	X
Maternal Height (<10th percentile)	X		X		X	X

"X" denotes a risk factor with an adjusted risk ratios ≥ 1.2

Low Birth Weight Determinants Among Preterm Infants

Pathways to LBW among preterm infants are more specific and are biologically related. This groups of infants had only 3 clinically significant risk factors: Eclampsia (adjusted RR = 1.2, 95%CI = 1.18-1.22), plurality (adjusted RR =1.5, 95%CI = 1.47- 1.48), and non-Hispanic African American maternal race (adjusted RR =1.2, 95%CI = 1.23- 1.24). Variables such as maternal weight gain, gestational hypertension, infant sex, and cigarette smoking were significant but with low risks.

All factors relating to socioeconomic status and pre-pregnancy conditions such as previous preterm and pre-pregnancy BMI were not associated with LBW infants born before 37 gestational weeks. Non-modifiable factors such as maternal height and maternal age were insignificant, yet maternal race which was also non-modifiable was significant. Pregnant non-Hispanic African American women were 1.2 times as likely to deliver a LBW infant that was born before 37 weeks compared to pregnant non-Hispanic White women, controlling for all other factors.

Female infants have higher rates of LBW compared to male infants (Female:9% vs Male:7.6%). They also have higher rates of LBW among preterm births (Female: 61% vs Male: 54%). However, males have higher rates of preterm birth compared to females (Female:9.6% vs Male:10.4%). Males also have higher rates of preterm birth among low birth weight infant (Female: 64.8% vs Male: 73.6%). When comparing between LBW types, the non-preterm group and the non-preterm and non-SGA group had higher rates for LBW among female infants compared to the preterm group. Lastly, we found that preterm birth was the most common type

of LBW (57%), yet out of all the LBW types it had the fewest determinants, and the most specific trends.

Low Birth Weight Determinants Among Non-Preterm Infants

Low birth weight infants that were born 37 weeks or later had many determinants and broader pathways. LBW was associated with eclampsia (adjusted RR = 2.6, 95%CI 2.38 - 2.75)) and gestational hypertension (adjusted RR = 2.2, 95%CI 2.14- 2.21) in the non-preterm group. It was also associated with pre-pregnancy conditions like having a pre-pregnancy BMI that was underweight (adjusted RR = 1.7, 95%CI 1.69-1.76) and with previous preterm (adjusted RR = 1.5, 95%CI 1.51-1.58. LBW was also linked to non-preterm birth through maternal weight and height. For example, pregnant women that gained less than 11 lbs. during their pregnancy were 1.6 times as likely to give birth to a LBW infant at 37 weeks or after compared to women that gain 11 pounds or more, controlling for all other factors (adjusted RR = 1.6, 95%CI 1.56-1.61).

We calculated the adjusted risk ratios for the interaction effect between preterm birth, LBW, and the variables. This allowed a between group comparison of preterm and non-preterm birth. However, looking at the determinants of each LBW type separately was a within group comparison. Refer to **Table 4**. Most adjusted risk ratios were less than 1 indicating that the risk of LBW was associated with covariates greater among non-preterm births. The association of such LBW determinants were stronger or had a greater effect in the non-preterm birth infants than in the preterm infants. The within and between group analyses justifies that there are more determinants and broader pathways to LBW among non-preterm infants compared to preterm infants.

Table 4. *Adjusted Risk Ratios for Interaction Effects of Preterm Birth on Low Birth Weight and Variables*

Variables	Preterm Adjust Risk Ratios 95%CI
Preterm : Maternal Age 40 + years	0.80 (0.78, 0.82)
Preterm : Maternal Age <19 years	0.94 (0.92, 0.96)
Preterm : Maternal Race Black	0.68 (0.67, 0.68)
Preterm: No Prenatal Care	0.82 (0.80, 0.85)
Preterm: WIC	0.95 (0.93, 0.96)
Preterm : BMI > 24.9	1.2 (1.15, 1.18)
Preterm: Weight Gain < 11 lbs.	0.81 (0.80, 0.82)
Preterm: Gestational Hypertension	0.56 (0.55, 0.56)
Preterm: Eclampsia	0.48 (0.45, 0.52)
Preterm: Previous Preterm Birth	0.63 (0.62, 0.65)
Preterm: Infertility Treatment	1.03 (1.00, 1.07)
Preterm : STIs	0.81 (0.79, 0.83)
Preterm : Health Insurance GOV	0.87 (0.85, 0.88)
Preterm : Infant Sex	0.75 (0.74, 0.76)
Preterm : Maternal Education	0.81 (0.80, 0.82)
Preterm : Plurality	0.17 (0.17, 0.18)
Preterm : Marital Status	0.84 (0.82, 0.84)
Preterm : Cigarette Smoking	0.56 (0.55, 0.57)

Low Birth Weight Determinants Among Infants with AGA/LGA Growth

Similarly to the non-preterm LBW group, AGA/LGA infants born with low birth weight had many associated determinants. The trends were also less defined, and the pathways were broader. This group however seems to have the highest associated risk for LBW in the absence of prenatal care (adjusted RR = 2.0, 95%CL 1.95-2.01). Receiving no prenatal care was the highest among non-Hispanic NHOPI (5.4%) and non-Hispanic AIAN (3.5%) pregnant women. Rates were also relatively high among non-Hispanic Black pregnant women (3.1%). The lowest

rates of not receiving any prenatal care were among Non-Hispanic Asians (0.88%). More pregnant women did not receive any prenatal care in 2023 compared to 2014 (2.2% vs 1.4%).

Low Birth Weight Determinants Among Small for Gestational Age Infants

Unlike LBW infants that were born before 37 gestational weeks, LBW infants that were classified as SGA were affected by pre-pregnancy factors such as previous preterm (adjusted RR = 1.6, 95%CI 1.61-1.66) and pre-pregnancy BMI < 18.5 kg/m^2 (adjusted RR = 1.2, 95%CI 1.14-1.20). Mothers who previously gave birth to a preterm infant were 1.6 times as likely to give birth to a LBW infant that was SGA in their later pregnancy compared to women who did not have a previous preterm birth (controlling for all other factors).

Based on the results, non-Hispanic Black women have a higher rate of delivering a LBW infant compared to white women overall and in all LBW group. However, their risk for LBW among SGA growth (adjusted RR= 1.1, 95%CL (1.11, 1.13), controlling for all factors) was lower compared to all other LBW types. Refer to **Table 5** to see differences in SGA rates by maternal race and birth weight.

Table 5. *Rates of SGA by Maternal Race and Birth Weight*

	Non-Hispanic White Mothers	Non-Hispanic Black Mothers
Rate of SGA among NBW Infants	6.4%	11.9%
Rate of SGA among LBW Infants	37.1%	41.2%

Low Birth Weight Determinants Among Infants Neither SGA nor Preterm

Low birth weight infants that are neither SGA nor preterm are the rarest type of LBW infants. These infants made up 4% of LBW births. All infants within this group were born early term at 37 weeks with a mean birth weight of 2,464 g. The minimum birth weight was 2,430 g

and the maximum was 2,499 g. Although this is a rare type of LBW, it has many determinants linked to it. Like non-preterm LBW infants, and AGA/LGA LBW infants, the pathways to LBW among infants that are neither SGA nor preterm are less defined and broad. This group however does have the highest risk for gestational hypertension (adjusted RR= 2.8, 95%CL (2.69, 2.90) compared to all other LBW types. Rates of gestational hypertension in the U.S have increased by 2 fold from 2014 to 2023 (4.95% to 10.1%). The highest rates of gestational hypertension were among pregnant non-Hispanic Black women (9%) and pregnant non-Hispanic-AIAN women (9.2%).

Specific Trends

In 2023, more pregnant women used an infertility treatment compared to rate in 2014 (1.5% vs 2.5%). After adjusting for by plurality, infertility treatment showed no significant association with any type of LBW, except for the general LBW group and the SGA subset. However, due to convergence issue, infertility treatment could not be adjusted for by plurality for the SGA subset. Although we were unable to adjust for it, this estimate might decrease or become insignificant after adjustment. The groups with the highest use of infertility treatment(s) are non-Hispanic Asians (3.6%) and non-Hispanic White (2.7%)

The Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) was slightly protective in reducing LBW (adjusted RR= 0.93, 95%CL (0.92, 0.93). WIC as a protective factor against LBW was most pronounced when analyzed by maternal race. It was protective in reducing LBW across all racial groups except for non-Hispanic White women. It provided the greatest protection for non-Hispanic AIAN and non-Hispanic NHOPI women. Refer to **Table 6.** Although WIC provides protection against LBW, there are less pregnant women receiving WIC in 2023 compared to 2014 (31% vs 41%).

Table 6. *Adjust Risk Ratios and Rates of WIC Recipients by Maternal Race*

Maternal Race	Adjusted Risk Ratio	WIC Rate: Overall vs LBW
non-Hispanic AIAN	0.88 (0.86, 0.91)	52.5 vs 50.0
non-Hispanic Black	0.91 (0.91, 0.91)	53.0 vs 51.9
non-Hispanic Asian	0.92 (0.90, 0.93)	19.9 vs 19.3
non-Hispanic NHOPI	0.92 (0.87, 0.97)	39.2 vs 36.1
non-Hispanic White	0.99 (0.98, 0.99)	23.2 vs 28.1
Hispanic	0.92 (0.91, 0.92)	53.9 vs 52.0

DISCUSSION

The most defined pathways to LBW are among infants born preterm and infants born SGA. The link between preterm birth and LBW is related to biological factors like eclampsia and plurality but were independent of pre-pregnancy conditions and SES factors. The non-PTB group and the SGA group were linked to pre-pregnancy conditions like previous preterm and pre-pregnancy BMI. Non-preterm births were linked to LBW through non-modifiable risk factors like advanced maternal age, maternal race, infant sex, and maternal height.

In the paper by Villar et al. (2012), preterm birth is described as a syndrome influenced by various determinants. The authors emphasize that preterm birth is associated with significant maternal, fetal, and placental conditions. While maternal factors are acknowledged as critical, Villar et al. appears to highlight a greater number of fetal and placental determinants that contribute to preterm birth. Maternal factors he highlights are biological conditions like pre-eclampsia, eclampsia, and extrauterine infections (4). Similarly, this study identified biological pathways linking preterm birth to LBW, specifically through the same conditions - eclampsia and plurality. Since few fetal and placental factors were included in this study, it could be that these factors are the missing link as to why preterm birth pathways are very specific and few even though preterm birth was the most common LBW type.

A study on SGA determinants found that some of its main risk factors included advanced maternal age and underweight pre-pregnancy BMI (5). This matches our study except we have linked it with LBW. It was unusual that previous preterm birth was not linked to LBW infants who were preterm birth but was linked to non-preterm and SGA infants. This relationship is

understudied, however there was one study that explored this relationship. It found that women with a previous preterm birth had an increased likelihood of delivering an SGA baby if their pregnancy went to full term (6).

Many studies have linked infertility treatments to LBW and various adverse pregnancy outcomes (7-8). However, this study found that infertility treatments had an overall insignificant or low association with LBW after adjusting for plurality. One reason for this low risk is that the study grouped many therapies together. It could be that some treatments are associated with a lower risk, while others are linked to a higher risk for LBW. We believe a similar issue may apply to STIs, as some STIs were associated with a greater unadjusted risk ratio for low birth weight compared to others. By combining all STI types into one category, the effect may appear to have a low or negligible risk for LBW.

This study has several limitations. First due to convergence issues, we were unable to adjust for some variables, which could lead to residual confounding. To address this, we considered a conservative estimate of clinical significance, defining an adjusted risk ratio of 1.2 or greater as significant. Second, MICE assumes data is missing at random. If this assumption is not met, it could introduce selection bias. Third, the data contained outliers, such as infants born at 17 weeks, which is extremely rare. Including these outliers in the analysis could affect the cut off points for categories like SGA, AGA, and LGA, making them slightly wider. Additionally, we had to merge some categories including STIs, race, and infertility treatments, to prevent frequent convergence issues. Finally, we lacked information on fetal and placental characteristics as well as pregnancy intervals, which could have provided a deeper explanation of trends in LBW types.

The strength of this study is that we used population based data and a large enough sample size in the model to get estimates that were generalizable to LBW in the U.S. Another strength is that because we analyzed multiple LBW groups, we were able to compare different kinds of LBW and how determinants varied by LBW type. Lastly, although we could not fully adjust for confounding we did manage to control for some.

In the future, we plan to incorporate fetal and placental factors to this analysis. Further exploration is due to preterm birth accounting for most LBW births yet its pathways were specific and few. Whereas non-SGA and non-PTB, which made up 4% of LBW births, had a broader range of pathways. This may seem contradictory, but it could reflect the predominant influence of maternal factors in our current analysis.

CONCLUSION

In conclusion, the pathways to low birth weight are heterogeneous and vary by gestational age and fetal growth patterns. This suggests that distinct determinants may influence low birth weight across different birth pathways, such as preterm, full-term, or small, adequate, or large for gestational age, with varying factors at play for each pathway.

REFERENCES

1. Ely DM, Driscoll AK. Infant mortality in the United States, 2022: Data from the period linked birth/infant death file. National Vital Statistics Reports; vol 73 no 5. Hyattsville, MD: National Center for Health Statistics. 2024. DOI: https://dx.doi.org/10.15620/cdc/157006.

2. National Academies of Sciences, Engineering, and Medicine. 2024. Low Birth Weight Babies and Disability. Washington, DC: The National Academies Press. https://doi.org/10.17226/27375.

3. Organization WH. International statistical classification of diseases and related health problems, tenth revision, 2nd ed. World Health Organization; 2004.

4. Jose Villar, Aris T. Papageorghiou, Hannah E. Knight, Michael G. Gravett, Jay Iams, Sarah A. Waller, Michael Kramer, Jennifer F. Culhane, Fernando C. Barros, Agustín Conde-Agudelo, Zulfiqar A. Bhutta, Robert L. Goldenberg, The preterm birth syndrome: a prototype phenotypic classification, American Journal of Obstetrics and Gynecology, Volume 206, Issue 2, https://doi.org/10.1016/j.ajog.2011.10.866.

5. Campbell MK, Cartier S, Xie B, Kouniakis G, Huang W, Han V. Determinants of small for gestational age birth at term. Paediatr Perinat Epidemiol. 2012 Nov;26(6):525-33. doi: 10.1111/j.1365-3016.2012.01319.x. Epub 2012 Aug 29. PMID: 23061688.

6. Chang JJ, Chien LC, Macones G. 33: Prior preterm birth in first pregnancy and risk of small-for-gestational-age birth in second pregnancy: a population-based study. *AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY*. 2012;206(1SUPP):S22. Accessed

November 21, 2024. https://research.ebsco.com/linkprocessor/plink?id=8f408b78-6276-3ee1-b9b0-dd444b9bf5a8

7. A. Pinborg, U.B. Wennerholm, L.B. Romundstad, A. Loft, K. Aittomaki, V. Söderström-Anttila, K.G. Nygren, J. Hazekamp, C. Bergh, Why do singletons conceived after assisted reproduction technology have adverse perinatal outcome? Systematic review and meta-analysis, *Human Reproduction Update*, Volume 19, Issue 2, March/April 2013, Pages 87–104, https://doi.org/10.1093/humupd/dms044

8. Shilpi Pandey, Ashalatha Shetty, Mark Hamilton, Siladitya Bhattacharya, Abha Maheshwari, Obstetric and perinatal outcomes in singleton pregnancies resulting from IVF/ICSI: a systematic review and meta-analysis, *Human Reproduction Update*, Volume 18, Issue 5, September/October 2012, Pages 485–503, https://doi.org/10.1093/humupd/dms018