Maternal Depletion, Sibship Size, and the Intergenerational Transmission of Low Birth Weight

by

Nicole Bentov Carbone

A Thesis Submitted in Partial Fulfillment of the

Requirements for the Degree of Bachelor of Science

With Honors in Evolutionary Anthropology from the

University of Michigan

2013

Advisor:

Dr. Beverly I. Strassmann

ABSTRACT

Low birth weight is a health issue associated with increased infant mortality, stunted growth, and hypertension in adulthood. Mothers that are born with low birth weight have an increased risk of giving birth to low birth weight offspring. Thus, the purpose of my thesis is to investigate the factors that cause low birth weight and the mechanisms of low birth weight transmission, and use those findings to study low birth weight in the Dogon of Mali. The literature shows that adverse maternal health conditions like depletion of micronutrients, low body mass index during pregnancy, and stunted childhood growth increase the risk of low birth weight. Environmental factors such as sibship size and resource availability not only influence birth weight, but also influence childhood nutritional status and growth. Although the exact mechanisms of birth weight transmission remain unknown, birth weight is most likely transmitted epigenetically. The analyses on Dogon data show that maternal body fat percentage impacts low birth weight prevalence. Therefore, the findings illustrate a quantity versus quality trade-off exists in relation to birth weight. Since both sibship size and maternal health influence birth weight, both components should be taken into consideration when studying this trade-off. In conclusion, despite the current relevance of low birth weight as a public health issue, low birth weight may also serve an evolutionary role through the selection against larger family sizes.

ACKNOWLEDGEMENTS

I would like to thank Dr. Beverly Strassmann for all of her support and help. I really appreciate all that Dr. Strassmann has done to help me write my thesis. I would also like to thank my parents and friends for their continual love and support.

TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

INTRODUCTION

Low birth weight is defined as an infant weighing less than 2500 grams at birth, and can result from factors such as preterm birth, nutrient deficiency, and limited space for growth in utero due to short maternal stature and low body mass index (Martorell and Zongrone, 2012; Walton and Hammond, 1938). Women who are born low birth weight have an increased chance of delivering low birth weight infants (Baird, 1985), and mothers who have low iron levels during pregnancy are more likely to have low birth weight offspring (Godfrey et al., 1991). The negative health consequences of being born low birth weight extend throughout life. A study in Stockholm found that men who were born with low birth weight were at risk for high diastolic blood pressure greater than or equal to 90 mm Hg possibly due to restricted in utero growth and placental blood flow (systolic blood pressure tended to be in a normal range below 145 mm Hg) (Gennser, Rymark, and Isberg, 1988).

Systolic blood pressure and birth weight were inversely related among children aged five to seven years in England and Wales (Whincup, Cook, and Papacosta, 1992). The average difference in systolic blood pressure was 2.7 mm Hg between the lowest (below 2950 g) and highest (3741-4880 g) birth weight classes, and this relationship remained true even after adjustments for number of siblings and parental history of blood pressure (Whincup, Cook, and Papacosta, 1992).

A study in Lancashire, England, on adults aged 46 to 54 years found that when birth weight increased from less than 5.5 pounds (2494.8 grams) to more than 7.5 pounds (3401.9 grams), mean adult systolic blood pressure decreased by 11 mm Hg. When placental weight increased from less than 1 pound (453.6 grams) to greater than 1.5 pounds (680.4 grams), mean adult systolic blood pressure increased by 15 mm Hg. (Barker et al., 1990). Overall, people who

were born low birth weight and with heavy placental weights have the highest risk of increased blood pressure as adults (Barker et al., 1990). When a mother has high blood pressure during pregnancy, the risk of delivering a low birth weight infant is increased, which can further the intergenerational transmission of low birth weight (Buchbinder et al., 2002).

Overall, these studies show that: (1) low birth weight negatively influences blood pressure and (2) the negative effects of low birth weight carry over to subsequent generations. First, through an extensive literature review, my thesis seeks to answer: (1) what are the major factors that cause low birth weight, and (2) how is low birth weight transmitted across multiple generations. Next, under the supervision of Dr. Strassmann, I analyzed data from an ongoing longitudinal study in the Dogon Country in Mali to study the maternal health conditions that influence the risk of having low birth weight offspring. Lastly, I compared the information from the literature review and the data analyses to draw conclusions, propose directions for future low birth weight research, and explain the evolutionary significance of low birth weight.

METHODS

I found and obtained all published articles through the University of Michigan library databases, Web of Knowledge and PubMed. I used keywords like low birth weight, sibship size, maternal depletion, infant mortality, and low birth weight transmission to find initial articles, which I then used to find additional papers. I conducted the data analyses under the supervision of Dr. Strassmann using the software, IBM SPSS Statistics 20, and I used data from an ongoing longitudinal study in the Dogon Country, Mali. Dr. Strassmann and her research team have followed and collected anthropometric measurements on 1,700 children since between 1998 and 2000, and currently forty-one of the females have given birth (Strassmann, 2011). I merged files containing information about the mothers and their children in order to compare maternal qualities like height and body mass index with offspring birth weight. I then did descriptive, binary logistic regression, and bivariate correlation tests. Since the data on birth weight are part of an ongoing longitudinal study, I recognize that sample sizes are small and future analyses should include a larger sample size.

MATERNAL DEPLETION

Evolutionary theory states that there is a trade-off between the number of offspring born and the amount of energy that is invested in each offspring, and therefore a quantity versus quality trade-off exists among offspring (Lack, 1947). When the supply of nutrients is limited during pregnancy, both the mother and the fetus must compete for resources, which increases the risks for both maternal and fetal health complications. Maternal depletion is an imbalance in maternal energy and micronutrient stores, which is a result of closely spaced pregnancies and maternal undernutrition (DeSweemer, 1984). Women in the United States who gave birth within two years after the start of menarche and women who conceived before eighteen months after giving birth to their previous child are at highest risk for maternal depletion and adverse health outcomes (King, 2003).

A study of Michigan women with interbirth intervals of less than eighteen months had a fifty percent increased chance of having low birth weight children in comparison to women with intervals of at least eighteen months (Zhu et al., 2001; Ventura et al., 1995). Children born within eighteen months or less of the previous sibling's birth are likely to be significantly shorter in comparison to children born after long birth intervals (Desai, 1995). Women in Latin America and the Caribbean with interbirth intervals of less than eighteen months had increased risk of death due pregnancy, third trimester bleeding, prelabor rupture of membranes, anemia, and puerperal endometritis, which is inflammation of the endometrium after childbirth (Lenders, McElrath, and Scholl, 2000; Ventura et al., 1995).

The extent of maternal depletion varies depending on resource availability. The resources the fetus receives versus those used for maternal health depend on the initial nutritional status of the mother. Women in well-nourished populations gain fat stores, and women in low

resource populations experience fat depletion with each pregnancy (King, 2003; Miller, 2010). Among rats when the mothers had food restrictions of about 25%, maternal body weight and fetal body weight decreased by about 30% and 50% respectively (Berg, 1965). Therefore, food restrictions will negatively affect both the mother and the fetus. Adolescent females who are still developing gain fat stores during pregnancy to support maternal growth at the expense of fetal growth, which is indicated by lower birth weights (Scholl, Stein, and Smith, 2000). Undernourished women in Pakistan (those who weighed less than 45 kilograms before pregnancy) had a positive weight change of about 5.1 kilograms between two subsequent pregnancies, while offspring birth weight decreased from the first to second birth (Winkvist et al., 1994).

A. ***Macronutrients and Micronutrients***

Macronutrients can be defined as, "nutrients required in the greatest amounts: carbohydrate, protein, fat or lipid, and water for the normal growth and development of an organism" (Merriam-Webster). Micronutrients can be defined as, "any dietary element essential only in minute amounts for the normal physiologic processes of the body, including vitamins and minerals or chemical elements such as zinc or iodine" (Merriam-Webster). Both types of nutrients are essential to the growth and development of the human body and are especially important during pregnancy since the mother supplies the developing fetus with the nutrients.

The influence of all macronutrients on birth outcomes was analyzed among Spanish women in the 1990s and the results show that protein was the only macronutrient that had a significant influence on offspring birth weight (Cuco et al., 2006). However, among women in southern England in the 1990s, maternal macronutrient nutrition was not related to placental growth or offspring birth weight. Conversely, there was a positive association between vitamin

C levels and birth weight, and positive associations between vitamin C, vitamin E, and folate levels with placental weight (Matthews, Yudkin, and Neil, 1999). Therefore, micronutrient levels tended to influence pregnancy outcomes in this study.

All women can experience maternal depletion in response to pregnancy despite living in a society where resources are plentiful or not initially being malnourished. Iron and folate are depleted during pregnancy and iron is further depleted during childbirth due to blood loss. With shorter intervals between pregnancies, folate will not be able to fully replete (Miller, 2010). Maternal folate concentrations decrease after the fifth month of pregnancy and continue to decrease at birth and for several months after pregnancy (Smits & Essed, 2001). Therefore, maternal folate takes time to replete even after the pregnancy is over, so with intervals between two successive births shorter than eighteen months, there is not enough time for folate to be fully restored. In mothers without sufficient levels of folate during pregnancy, offspring have higher risks of developing neural tube defects and being born preterm and low birth weight (Smits & Essed, 2001).

There is a significant relationship between maternal anemia during pregnancy (defined as hemoglobin levels lower than 11 g/dl) and anemia in newborn children (Koura et al., 2012). Low levels of iron and folate are both associated with intrauterine growth retardation, which has a direct influence on fetal growth and development (King 2003). Short birth intervals can also lead to lower birth weights and increased risk of having offspring that are small for gestational age (Eijsden et al., 2008).

A study conducted on lactating Ariaal women in Kenya found a direct relationship between hemoglobin levels and time since giving birth, which illustrates that women are able to partially replete the hemoglobin levels that decreased during pregnancy and birth (Miller, 2010).

However, there is an association between increased parity and lower hemoglobin levels, which demonstrates that after each birth, women are not able to fully replete their hemoglobin levels (Miller, 2010).

B. ***Lactation***

Breastfeeding may also contribute to the association between short interbirth intervals and low birth weight, since lactation contributes to maternal depletion (Eijsden et al., 2008). Longer duration of lactation causes decreased maternal bone mineral density. Depleted calcium stores can be restored in mothers within twelve months after giving birth through use of calcium supplements with calcium levels of about 200 mg/d, or through normal diet among mothers who had adequate pre-pregnancy nutritional status (Sowers et al., 1993).

Lactation is a high-energy process since maternal resource stores are used to produce milk. Lactation caused weight loss among urban Filipino women, especially when breastfeeding lasted longer than twelve months (Adair and Popkin, 1992). In response to chronic undernourishment, rats gained protein, fat and water during lactation, whereas well-nourished rats lost water weight (Rasmussen and Fischbeck, 1987). The exact mechanisms of weight gain are not known, but the weight gain among undernourished rats may be adaptive to protect and maintain long-term energy balance in the female rats (Rasmussen and Fischbeck, 1987).

When lactation and the next pregnancy overlap, the mother must provide energy for milk production and for the development of the fetus (Merchant, Martorell, and Haas, 1990). This overlap is stressful since lactation and gestation both contribute to depletion. When a woman is already depleted, risk for restricted fetal growth increases. Among women in rural Guatemala, birth weight decreased non-significantly due to the overlap of lactation and pregnancy (Merchant, Martorell, and Haas, 1990). Fetal growth may be protected despite the mother's

nutritional status and at the expense of the mother's own health and nutritional status (Laskey and Prentice, 1997). The mother's energy intake and mobilization of energy stores increased in response to the stress of both lactation and pregnancy (Merchant, Martorell, and Haas, 1990).

Breast milk is the main source of vitamin A for newborns and it allows for the creation of vitamin A stores in infants' livers (Fujita et al., 2011). Vitamin A levels in breast milk are highest among early postpartum mothers and then the levels decrease over the first twelve months after birth among women who are both well nourished and undernourished (Gebre-Medhin et al., 1976; Fujita et al., 2011). This decrease in vitamin A in breast milk also leads to decreases in maternal liver stores at slower rates. A mother invests and provides sufficient vitamin A levels to her current offspring, but a mother also must save vitamin A liver stores for future offspring (Fujita et al., 2011). Therefore, parity size, length of interbirth intervals and initial maternal nutritional status must also be considered when studying maternal vitamin A levels (Kjolhede et al., 1995; Fujita et al., 2011).

1. *Nutritional Deficiencies and Sibship Size*

Among large sibship sizes in rural Java in Indonesia, children had significantly lower vitamin A levels than in small sibships (Kjolhede et al., 1995). Singletons had significantly higher mean levels of vitamin A in the bloodstream than children of sibship sizes two, four, and five (Kjolhede et al., 1995). The association between larger sibship size and lower vitamin A levels may be explained by the dilution of food resources containing vitamin A among larger families (Kjolhede et al., 1995), or by prenatal conditions such as maternal depletion resulting from closely spaced pregnancies (Kjolhede et al., 1995).

Larger sibship size is also associated with vitamin D deficiency, which contributes to the increased risk of rickets (Yassin and Lubbad, 2010). Similar to vitamin A deficiency, a possible

explanation is the dilution of food resources containing vitamin D within larger families (Downey, 1995). Rickets is often present among members of the same sibship—for example, in Nigeria eighteen percent of children with rickets also had siblings with rickets (Akpede et al., 2001).

A direct relationship exists between parity and the prevalence of rickets (Yassin and Lubbad, 2010). Vitamin D deficiency may be due to maternal depletion when the mother is not able to replete her calcium and vitamin D stores due to short intervals between pregnancies. Poor nutritional status during pregnancy is associated with lower amounts of vitamin D stored in fetal livers and offspring receiving fewer nutrients from breast milk, which could in turn lead to rickets (Yassin and Lubbad, 2010).

Overall, these results indicate the probable influence of both nutritional and environmental factors (Akpede et al., 2001; Yassin and Lubbad, 2010). Since children are at higher risk for rickets when both they and their mothers were insufficiently exposed to sunlight, it is possible that this deficiency is, in part, passed down from mother to child (Yassin and Lubbad, 2010). Serum vitamin D levels in mothers were similar to the levels observed in their children who had rickets (Majid et al., 2000). Therefore, future studies are necessary to investigate if there is transmission of vitamin D deficiency across multiple generations.

C. *Low birth weight*

Data from Dutch women in early 2000 found that low maternal vitamin D levels (mean level of 60.09 nmol/L) during the first trimester had a negative impact on offspring birth weight (van den Berg et al., 2013). Among women and their children in Amsterdam born between 2003 and 2004 low folate levels were associated with low birth weight (van Eijsden et al., 2008). Maternal calcium levels in India also influence birth weight with correlation coefficients between

calcium intake and birth weight equal to 0.276, 0.355, and 0.421 for the first, second, and third trimesters, respectively (Durrani and Rani, 2011).

Various studies have examined the complex association between maternal anemia and offspring low birth weight. A non-significant relationship exists between maternal anemia during pregnancy and risk that offspring are born low birth weight among women and their children in Benin born between 2006 and 2007 (Koura et al., 2012). The timing of maternal anemia may the influence prevalence of low birth weight, which was evident in Finland between 1990 and 2000 with how maternal anemia in the first trimester increased the risk of low birth weight (Hämäläinen, Hakkarainen, and Heinonen, 2003). This study indicates a possible critical period when low maternal hemoglobin levels influence offspring birth weight. Anemia later in pregnancy may have negative influences more on the mother and less on offspring birth weight.

D. *Placental Growth*

In response to low iron levels during pregnancy, compensatory placental growth was noted with a larger placental weight and higher placental weight to birth weight ratio (Godfrey et al., 1991). The highest placental weights were observed among women who had the lowest levels of hemoglobin during pregnancy and the largest decreases in mean cell volume (Godfrey et al., 1991). Another study found a significant ($p=0.021$) inverse association between protein intake and placental weight (Chan, Ho, and Lao, 2003). Increased placental weight is most likely a compensatory mechanism for insufficient iron and hemoglobin levels during pregnancy (Godfrey et al., 1991). Similarly, placental weight increased in response to the Dutch famine (see p. 28) (Lumey, 1998).

Studies on the influence of fasting during Ramadan found that the placenta compensates for restricted maternal caloric intake and protects against changes in birth weight (Alwasel et al.,

2010). Placental growth slowed in response to second and third trimester exposure to fasting, which allowed the placenta to increase efficiency and to provide the fetus with necessary nutrients and resources to maintain growth (Alwasel et al., 2010). The placenta has a reduced reserve capacity and further research is required to investigate whether the lower reserve capacities influence pregnancy outcomes (Alwasel et al., 2010).

SIBSHIP SIZE

A. *Perinatal Mortality*

The medical records of births in Norway between 1967 and 1973 demonstrated that perinatal mortality risk decreased among the first three births within a family from 55.3 to 36.1 to 15.1 per 1000 births for the first, second, and third offspring, respectively (Bakketeig and Hoffman, 1979). There may be an association with low birth weight because the risk of low birth weight decreased among the first three births from 7.4% of first-born to 5.1% of second-born to 3.4% of third-born offspring (Bakketeig and Hoffman, 1979). The risk of perinatal mortality also increased when mothers had three or four children within the seven-year study period, which is most likely due to inadequate maternal repletion of nutrients after closely spaced pregnancies (Bakketeig and Hoffman, 1979). Moreover, mothers often become pregnant again soon after the loss of an infant, which can further increase the risk of perinatal mortality. Mothers are most likely nutritionally depleted after previously gestating and lactating and then not having enough time to recover (Cain and Cain, 1964; Bakketeig and Hoffman, 1979).

In Niger the risk of perinatal mortality significantly increased with parity (Ozumba and Igwegbe, 1992). The rate of mortality for grand multiparae (mothers who gave birth to at least five children) was 71 per 1000 births and the rate for non-grand multiparae was 34 per 1000 births. The higher perinatal mortality risk among grand multiparae mothers may be caused by low birth weight, which was more prevalent among offspring of grand multiparae mothers (Ozumba and Igwegbe, 1992).

B. *Infant and Childhood Mortality*

Multiple studies have indicated that infant mortality (mortality before one year) increases in a curvilinear pattern with family size (Charbonneau, 1970; Henry, 1956; Knodel and

Hermalin, 1984; Ronsmans, 1995; Nault, Desjardins, Legare, 1990). For example, among German villagers in the eighteenth and nineteenth centuries, infant mortality decreased from the first to second birth and then increased after the third birth with an even larger increase in mortality after the sixth birth (Knodel and Hermalin, 1984). After controlling for maternal age, region, previous pregnancy interval, and other infants deaths, infant mortality was 0.185 for sibship sizes of five to seven (the smallest sibship size category in the study), 0.205 for sibship sizes of eight to nine, and 0.241 for sibship sizes greater than ten (Knodel and Hermalin, 1984). Thus, infant mortality increased in a curvilinear pattern with birth order and directly increased with sibship size (Knodel and Hermalin, 1984).

Among French-Canadians in the seventeenth and eighteenth centuries, infant mortality rates decreased with birth order until the fifth birth and then increased. Infant mortality rates also decreased within increasing sibship sizes up to size seven and then mortality rates increased (Nault, Desjardins, and Legare, 1990). The relationship between family size and infant mortality can most likely be explained by dilution of resources with larger family sizes and maternal age, since after mothers in the study reached age thirty, infant mortality rates increased (Nault, Desjardins, and Legare, 1990; Downey, 1995).

There is also a direct negative correlation between average birth intervals and infant mortality (Gray, 1981). Short intervals between pregnancies imply less repletion of maternal resources and lower health status at the beginning of the pregnancy (Ronsmans, 1995). High parity is also associated with short interbirth intervals and short breastfeeding duration, which may explain the increased infant mortality rates with higher birth orders and larger sibship sizes (Gray, 1984; Nault, Desjardins, and Legare, 1990; Knodel and Hermalin, 1984).

Data from the sixteenth century in Tourouvre-au-Perche in France demonstrates increasing infant mortality rates with larger family sizes (see Table 1) and decreasing infant mortality rates with birth order: the rates are 0.276, 0.259, and 0.214 for the first-born, second-born and later-born (those with birth order three or high) categories, respectively (Charbonneau, 1970; Cohen, 1975). However, the differences between the rates of mortality are not statistically significant (Charbonneau, 1970). Data given in Tables 2 and 3 demonstrate how infant and child mortality increases with increasing family size (Henry, 1956; Ronsmans, 1995).

Sibship size and birth order influence infant mortality rates differently, which may be explained by how when birth order data from Germany in the eighteenth and nineteenth centuries was controlled for sibship size, there was not a significant impact on infant mortality rates. However, sibship size after controlling for birth order did significantly influence infant mortality (Knodel and Hermalin, 1984). This result may be explained by shorter birth intervals in order for women to have more children within their reproductive lifetimes (Gray, 1981; Knodel and Hermalin, 1984). With large family sizes there is also often shorter duration of breastfeeding due to the mother becoming pregnant again and stopping breastfeeding of the previous child (Knodel and Hermalin, 1984). Infants that are breastfed have higher survival chances since breastfeeding can protect against malnourishment and decrease susceptibility to infectious diseases (Knodel and Hermalin, 1984; Gray, 1984). Further dilution of resources and parental care may also contribute to the increased infant mortality rates when family sizes are larger (Knodel and Hermalin, 1984; Downey, 1995).

Another contributing factor is increased infant and child mortality with the death of other siblings (Knodel and Hermalin, 1984; Omariba, Rajulton, and Beaujot, 2008). In Kenya an infant's risk of death is increased by 1.8 when a previous sibling died. The death of a previous

sibling accounts for forty percent of the clustering in childhood deaths (Omariba, Rajulton, and Beaujot, 2008). Siblings born near each other have the strongest influence on each other's mortality and survival, which can most likely be explained by mothers becoming pregnant soon after the loss of an infant and mothers shortening breastfeeding duration due to conceiving soon after the birth of the previous child (Cain and Cain, 1964; Gray, 1981; Knodel and Hermalin, 1984; Omariba, Rajulton, and Beaujout, 2008).

C. *Height*

Height reflects genetics, nutrition, and environmental factors (Lawson and Mace, 2008). A study on British children born between 1991 and 1992 found an association between sibship size and height (Lawson and Mace, 2008). Children of larger sibship sizes have lower initial health status. In comparison to only children, birth length decreases directly with increased number of siblings. The rate of growth per year is also negatively impacted by the presence of siblings, which is illustrated in Table 4 (Lawson and Mace, 2008). The negative association between growth and sibship size may be explained by resource dilution within larger families (Lawson and Mace, 2008).

A study looking at data on young children from England and Scotland in the 1970s found an inverse relationship between height and sibship size (Rona, Swan, and Altman, 1978). In England the negative influence of increased number of siblings on height was most evident among children whose families belonged to the manual social class. In the non-manual social class, the negative correlation between height and number of siblings was observed only for sibship sizes of five or larger. In Scotland, however, sibship size and height were negatively correlated in both social classes (Rona, Swan, and Altman, 1978). Height was found to improve in smaller sibship sizes and higher socioeconomic status in a sample from Italy in the year 2000

(Sanna and Danubio, 2009). Overall, both sibship size and socioeconomic status influence height most likely due to resource availability (Rona, Swan, and Altman, 1978; Sanna and Danubio, 2009).

Deficits in height were most evident within the first decade of life and the costs were highest to later-born offspring (Lawson and Mace, 2008). A reduced height can be costly, since taller height is usually associated with better health and increased longevity (Smith et al., 2000). These costs demonstrate a trade-off between offspring quality versus quantity, since the amount of parental resource allocation and investment can influence offspring and height and, in turn, health (Lawson and Mace, 2008).

The relationship between height and sibship size may also relate to maternal nutrition and the extent to which the mother is maternally depleted after many closely spaced pregnancies. The mother's height must also be taken into consideration, since there tends to be a strong correlation between the mother's height and offspring height (Lawson and Mace, 2008).

D. *Low Birth Weight*

Within a sibship, the firstborn child tends to have lower birth weight than later-born children. The catch-up growth of first-born children within the first year of life is also greater than that of later-born children, and this pattern of catch-up growth is associated with higher systolic blood pressure among firstborn offspring (Wells et al., 2011). Increased birth weight among later-born children can most likely be explained by permanent structural changes in the uterine spiral arteries after a woman's first pregnancy (Wells et al., 2011). The amount of non-muscular tissue increases with parity, which allows for increased blood flow and therefore increased fetal growth (Wells et al., 2011; Khong, Adema & Erwich, 2003). Overall, birth weight difference between first-born children and later-born children can most likely be

associated with limited access to the maternal supply of nutrients during a woman's first pregnancy (Wells et al., 2011).

However, the association between low birth weight and sibship size is variable (Seidman et al., 1991; Ozumba and Igwegbe, 1992). A study on grand multiparae mothers in Jerusalem, who gave birth to at least seven children found that for socioeconomically stable women about 4.1% of children were born low birth weight and that for women with low socioeconomic status about 8.4% of children were born low birth weight (Seidman et al., 1991). Therefore, parity has a greater influence when socioeconomic status is also considered (Seidman et al., 1991).

A study on two birth cohorts in northern Finland compared mothers of low (six or fewer children) and high parity (six or more children) (Sipilä, von Wendt and Hartikainen-Sorri, 1990). In the birth cohort of 1966, 4.7% offspring born to high parity mothers were low birth weight and 5.2% of offspring born to low parity mothers were low birth weight, which was a statistically significant difference. In the birth cohort of 1985-1986, 2.7% of offspring born to high mothers were born with low birth weight and 4.1% of offspring born to low parity mothers were born with low birth weight, and the difference between the parity groups was statistically significant (Sipilä, von Wendt and Hartikainen-Sorri, 1990).

A cross-sectional study of women and their children in west Jerusalem found that first-born offspring were at highest risk for low birth weight, since 7.2% of first-born children in the study were born with low birth weight (Seidman et al., 1987). In the longitudinal study, 6.1% of children with birth order between one and six were born low birth weight and 4.3% of children with birth order higher than seven were born low birth weight (Seidman et al., 1987). Obstetric data on women living in Kauai, Hawaii found that birth weight increases with birth order until the fifth birth (James, 1968).

In Oulu, Finland, birth order and birth weight were positively correlated (Juntunen, Läärä, and KauppilaKaisa, 1997). Children of birth order ten to twelve were on average 120 grams heavier than children of birth order six to nine. These children were on average 70 grams heavier than children of birth order two to five, who were on average 160 grams heavier than first-born children (Juntunen, Läärä, and Kauppila, 1997). Overall, this study was limited to ninety-six mothers, but it demonstrates the relationship between birth weight and birth order (Juntunen, Läärä, and Kauppila, 1997). There was a similar pattern among Saudi Arabian children where birth weight significantly increased with birth order, and therefore the prevalence of low birth weight decreased (Wong, 1990).

A study on obstetrical data from Enugu, Nigeria, defined grand multiparae as women who gave birth to at least five children (Ozumba and Igwegbe, 1992). Nearly 10% of babies born to grand multiparae mothers were low birth weight and 4% of babies born to non-grand multiparae mothers were low birth weight, and the difference between the two parity classes was statistically significant (Ozumba and Igwegbe, 1992). Most of the mothers in the study belonged to the lowest socioeconomic class in Nigeria, which may impact how parity influences low birth weight risk (Ozumba and Igwegbe, 1992).

In the North Carolina birth record database, birth weight increased from the first to second child and subsequently by 115, 114, and 115 grams for the second, third, and fourth children, respectively (Swamy et al., 2010). Across different ethnic groups in North Carolina, increases of 120, 101, and 103 grams were observed for non-Hispanic white, non-Hispanic black, and Hispanic individuals, respectively (Swamy et al., 2010). Overall, the pattern of increased birth weight with increasing parity was evident among the different ethnic groups, but the increase was lowest among non-Hispanic black women (Swamy et al., 2010). This finding

may be due to other factors discussed below such as socioeconomic status and genetic programming (Drake and Liu, 2010; Barker, 2004**)**.

INTERGENERATIONAL TRANSMISSION OF BIRTH WEIGHT

Both maternal and paternal genetic factors influence offspring birth weight, but since the mother provides the gestational environment, there is greater maternal influence on fetal growth (Fowden et al., 2011). A mother's own gestational experience affects the uterine environment she provides for her offspring, and in utero experiences most likely cause permanent maternal physiological changes that affect growth and development in the following generations (Drake and Liu, 2009; De Stavola, Leon, and Koupil, 2011). A maternal intergenerational link exists that allows for transmission of birth weight and birth size across multiple generations (Price, Hyde, and Coe, 1999; Hypponen and Power, 2004). A study conducted on rhesus monkeys demonstrated that mothers who were born small for gestational age have a higher chance of also having offspring that are born small for gestational age (Price, Hyde, and Coe, 1999). Additionally, the maternal influence on birth weight lasted across five generations of rhesus monkeys, which suggests the need to study the association across more generations in humans (Martorell and Zongrone, 2012).

Studies of humans found that maternal birth weight influences offspring birth weight. Women who were born low birth weight in Seattle and Tacoma, Washington, had a 1.54-fold increased risk of having offspring born preterm, which is correlated with low birth weight (De et al., 2007). An extensive review of literature on the transmission of low birth weight around the world found that the risk of having low birth weight infants was 11.76% when the mother was low birth weight and 5.30% when the mother was born normal weight (Shah and Shah, 2009).

In Swedish mothers born in the 1970s and their children born before 2000, there were an intergenerational small for gestational age correlation after controlling for socioeconomic status, smoking, body mass index, age and educational level (Selling et al., 2006). A mother that was

born small for gestational age had a 17% increased risk of her first-born child being born small for gestational age (Selling et al., 2006; Farina et al., 2010). This correlation may be the result of a genetic mechanism or an unknown factor that caused the mother to be born small for gestational age and then predisposed the offspring to be born small for gestational age (Magnus, Bakketeig, and Skjaerven, 1993; Selling et al., 2006).

For every one hundred gram increase in maternal birth weight, offspring birth weight increased by about ten to twenty grams (Ramakrishnan, 1999; Martorell and Zongrone, 2012). For every centimeter increase in the mother's birth length, there was an increase in offspring birth weight by about fifty-three grams (Ramakrishnan et al., 1999). A study of singleton children found that for every unit increase in body mass index (kg/m^2) of the mother, the weight of the placenta increased by 3.6 grams and by 49 grams for every kilogram increase in maternal birth weight (L'Abée et al., 2011).

One study of mothers and children in rural Guatemala found that maternal birth length and birth weight are both significant predictors of offspring birth size after controlling for gestational age, sex, and other confounding variables (Ramakrishnan et al., 1999). Offspring birth weight increased significantly by 29 grams for every 100-gram increase in maternal birth weight and offspring birth length increased significantly by 0.2 centimeters for every one-centimeter increase in maternal birth length. Offspring birth weight also increased significantly by 53 grams for every one-centimeter increase in maternal birth length (Ramakrishnan et al., 1999).

Although maternal factors are considered to exert a greater influence, paternal factors also impact birth weight and placental weight. A study of singleton children born in Drenthe in the Netherlands between 2006 and 2007, found that both paternal body weight and body mass

index (kg/m^2) significantly predicted the child's birth weight and placental weight (L'Abée et al., 2011).

Although both maternal and paternal heights influence offspring size at birth, maternal height exerts a stronger influence (Hypponen, Power, and Smith, 2004). Paternal height influences skeletal growth measured at birth and maternal height influences the amount of soft tissue covering at birth, which is measured as the ponderal index (body mass/$height^3$) (Veena et al. 2004). Overall, since both paternal and maternal factors influence birth size of the infant, both genetic and environmental factors most likely influence birth size (Veena et al., 2004).

A. ***Maternal Childhood Conditions***

A mother's early life experiences including her own fetal and infant nutrition and growth rate most likely influence her physiology and metabolism later in life, which in turn affects her infant's nutrition (Kuzawa and Quinn, 2007). Mothers, who were breastfed as infants, tend to give birth to larger babies only if their mother had a favorable energy status while lactating, which indicates the influence of early life nutrition on offspring birth weight (Kuzawa and Quinn, 2007).

Maternal growth during childhood influences offspring birth weight independent of the influences of maternal birth weight and maternal adult height (Martin et al., 2004; Hypponen, Power, and Smith, 2004). For example, maternal childhood height and offspring birth weight were positively correlated among women and their children from Pre-War Britain (Martin et al., 2004). Childhood height is an indicator of nutrition and resource availability, which may have an influence later in life on vascularization of the placenta and therefore efficiency of nutrient transport across the placenta (Martin et al., 2004; Barker, 1998). The exact mechanisms of how early life health conditions influence a woman's reproductive outcomes are not known.

However, low socioeconomic status and psychological stress in response to decreased amounts of available resources could factor into the correlation between maternal childhood height and offspring birth weight (Gavin et al., 2011; Gavin et al., 2012).

Women that experience poor growth in childhood also have a higher risk of stunting and giving birth to low birth weight babies (Ramakrishnan et al., 1999). On the other hand, mothers who were taller during their childhood tend to give birth to heavier babies (Martin et al., 2004). There is also a stronger influence of the mother's childhood height than her adult height on offspring birth weight (Veena et al., 2004). This result may be explained by how early growth and nutrition of the mother may influence future placenta vascularization and the nutrient transport capacity that allows for fetal growth and development (Martin et al., 2004; Urbina et al., 2002). However, the exact mechanisms are unknown.

These results suggest that childhood is an important period in determining a woman's reproductive health and possibly that nutrition during pregnancy has less of an influence on offspring growth and birth weight than previously expected (Hypponen, Power, and Smith, 2004). Therefore, it is possible that the mother's capacity to deliver nutrients to her offspring was set earlier in life and even possibly while she was in utero through programming mechanisms (Martin et al., 2004).

B. *Grandmaternal Transmission*

A study of families in Pre-War England (1937-1939) found an association between grand maternal height and birth weight within female members of the family, but found no association with grand paternal height (Martin et al., 2004). Offspring birth weight increased by 88 grams when the maternal standardized average of grand maternal and grand paternal height increased by one standard deviation (Martin et al., 2004).

After controlling for sex, energy intake, socioeconomic variables, and height in childhood and adulthood, the standardized height of maternal grandmothers was associated with offspring birth weight (Martin et al., 2004). Data from England in the 1950s demonstrated that grand maternal height significantly influenced the birth weight of grandchildren, since 10 centimeter increases in grand maternal height were associated with 53 gram increases in birth weight (Emanuel, et al., 1992). Grand maternal height is most likely influenced by both the grandmother's intrauterine environment and childhood environmental conditions such as socioeconomic status and resource availability (Alberman et al., 1991; Wedge, Alberman, and Goldstein, 1970). These factors most likely contribute to the intergenerational birth weight influence found among maternal relatives (Emanuel et al., 1992).

Similarly, a study of three generations of people born in the 1900s in Uppsala, Sweden, found that there is a significantly stronger maternal influence on offspring birth weight than on birth length (De Stavola, Leon, and Koupil, 2011). The intergenerational correlation of birth weight between the grandmother, mother, and the grandchildren can most likely be explained by how all were exposed to similar maternal uterine environments and how maternal genetic components that determine birth weight have a stronger influence than paternal genetics due to how the mother provides the uterine environment during pregnancy (De Stavola, Leon, and Koupil, 2011; Fowden et al., 2011).

LOW BIRTH WEIGHT AND THE INFLUENCE OF SLAVERY

The average birth weight of African Americans is currently lower than that of European Americans (Jasienska 2009; Masho and Archer, 2011). Thirteen percent of African American infants are born with low birth weight and eighteen percent are born premature (Masho and Archer, 2011). In 2009 the low birth weight rate was 13.61% for African Americans and 7.19% for Caucasians (Kochanek et al., 2012). Low socioeconomic status may be associated with a greater prevalence of low birth weight among African Americans (Pearl, Braveman, and Abrams, 2001).

One study examined Caucasian and African American women who lived in poor households as children and then experienced upward economic mobility as adults. The rate of preterm birth was 18.7% in impoverished areas and then decreased steadily to 16%, 15.2%, and 12.4% with low, moderate, and high economic upward mobility, respectively (Colen et al., 2006). Despite the economic improvements among these women and the decreased risk of preterm birth, the rates of low birth weight among African Americans did not significantly decrease (Colen et al., 2006). Among those classified as chronically poor, 11.82% of Caucasian infants and 14.62% of African American infants were born low birth weight. Among the upwardly mobile category, 4.5% of Caucasian infants and 9.99% of African American infants were born low birth weight (Colen et al., 2006). This suggests that birth weight is influenced by programming and epigenetic mechanisms like DNA methylation that cannot be easily reversed in response to improved environmental conditions (Colen et al., 2006).

Similar results were observed among women living in Chicago (Collins et al., 2009). A group of grandmothers were exposed to poverty while pregnant. Despite upward economic mobility among the mothers and more favorable pregnancy conditions, grandchildren had a 20-

30% increased risk of being born low birth weight independent of other maternal risk factors (Collins et al., 2009). These results can possibly also be explained by fetal programming due to undernutrition during the grandmother's pregnancy (Barker, 1990; Godfrey and Robinson, 1998).

Genetic differences and socioeconomic factors can only partially explain the difference in low birth weight prevalence between African Americans and Caucasians. When socioeconomic factors and differential risks of low birth weight are controlled for, the differences in low birth weight still persist (Jasienska, 2009). One possible explanation is that not enough time has passed since the abolition of slavery to erase its negative health impacts (Jasienska, 2009). These negative effects may continue to influence the current biological and health conditions of members of the African American population, which indicates the possibility of fetal programming (Jasienska, 2009).

During slavery people most likely ate an inadequate diet and there was an imbalance between energy intake and energy expenditure due to their poor working and living conditions. Children born to slaves were most likely born with low birth weight since physical labor during pregnancy along with not getting enough nutrients restricts uterine blood flow and therefore reduces the rate of intrauterine growth. This usually results in decreased carbohydrate intake by the fetus and low birth weight (Jasienska, 2009). The negative influence of maternal diet on offspring birth weight was most likely not limited to transmission between two generations, since low birth weight is known to be transmitted maternally across multiple generations (De et al., 2007; Shah and Shah, 2009).

A low birth weight domino effect may exist among slaves and their relatives born in the subsequent generations due to how low birth weight and poor nutrition tend to stunt growth.

Women who are shorter due to genetic factors or stunted growth are more likely to give birth to low birth weight children and if those children are females, the risk of giving birth to low birth weight infants is increased (Drake and Liu, 2010). Therefore, stunted growth that occurred among female slaves may contribute to the intergenerational transmission of low birth weight among African Americans (Drake and Liu, 2010). Although the direct mechanism of how low birth weight is transmitted across multiple generations is unknown, epigenetic mechanisms and changes in the conformation of chromatin have been proposed (Jablonka and Lamb, 2005).

Other factors such as the continued disparities and disadvantages that many African Americans face, genetic influences, and long-term environmental stressors may contribute to the persistence of low birth weight among African Americans (Masho and Archer, 2011; Jasienska, 2009). Furthermore, another study demonstrated that when women from Southern Asia moved to England, the birth weights of their children did not greatly change in response to the improved environmental conditions (Leon and Moser, 2010). Therefore, fetal programming and environmental conditions may influence the continued transmission of birth weight (Jasienska, 2009).

LOW BIRTH WEIGHT AND FAMINE

Not getting enough nutrients and calories during pregnancy has varying influences on offspring birth weight. During the Dutch famine of 1944, placental enlargement occurred in response to famine exposure during the first trimester of pregnancy. The placental index (the ratio of placental weight to birth weight) increased and birth weight remained the same after first trimester famine exposure (Lumey 1998). Birth weight, placental weight, and placental index decreased in response to third trimester exposure to famine (Lumey, 1998). Therefore, placental enlargement may be a compensatory mechanism to protect fetal growth and development when maternal nutrition is restricted during the first trimester of pregnancy (Lumey, 1998).

Another study of the Dutch famine found that first trimester exposure to the famine caused mean birth weight to increase significantly by 154 grams and third trimester exposure caused mean birth weight to decrease significantly by 251 grams when compared to the mean birth weight of those not exposed to famine. When women who were exposed to famine in utero gave birth, first-born offspring to mothers with first trimester famine exposure had average birth weights that were increased non-significantly by 72 grams. First-born offspring to mothers with third trimester exposure had average birth weights that were decreased non-significantly by 43 grams when compared to women who were not exposed to the famine (Stein and Lumey, 2000). Although the changes in birth weight in the next generation were not statistically significant, the trend was in the expected direction. This finding illustrates an intergenerational influence on birth weight even after nutritional conditions improved (Stein and Lumey, 2000).

The influence of famine exposure also varied by birth order. The first trimester is an essential time of organ development and cell division that is dependent on available nutrients (Stein and Lumey, 2000). When mothers were exposed to the famine during their first trimester,

the birth weight of first-born children increased by 72 grams, whereas the birth weight of second-born children decreased by 43 grams (Stein and Lumey, 2000; Lumey and Stein, 1997). For first-born offspring when maternal birth weight increased by 100 grams, offspring birth weight increased by 23 grams. For second-born and third-born offspring, maternal birth weight increases of 100 grams were associated with increases in offspring birth weight of 14 grams and 11 grams, respectively (Stein and Lumey, 2000). This difference associated with parity suggests that the negative effects of famine exposure during the first trimester may only be evident after the mother's first pregnancy, but further research is necessary to evaluate this possibility (Lumey and Stein, 2000). Overall, the influence of restricted maternal nutrition during pregnancy on offspring birth weight may depend on parity and the extent to which there is maternal depletion of essential micronutrients (Lumey and Stein, 1997).

PROPOSED MECHANISMS OF BIRTH WEIGHT TRANSMISSION

Transmission of low birth weight across multiple human generations is evident (Price, Hyde, and Coe, 1999; De et al., 2007). Low birth weight transmission may be attributed to programmed effects (Barker, 2004). Exposure to adverse environmental conditions in utero such as low socioeconomic status, maternal depletion, or maternal undernutrition may program maternal tissue function and therefore alter growth and development in the subsequent generations (Drake and Liu, 2010). Programming most likely contributes to the greater prevalence of birth weight in African Americans compared to Caucasians even after multiple generations have passed and living conditions have improved since the abolition of slavery (Jasienska, 2009).

In utero negative experiences such as restricted caloric and protein intake may permanently affect growth and development by causing changes in maternal physiology that influence subsequent generations (Drake and Liu, 2010; Stein and Lumey, 2000; Lumey, 1998). For example, women born with low birth weight have an increased risk of developing hypertension as adults. Moreover, women who are hypertensive during pregnancy are at risk for giving birth to low birth weight children (Klebanoff et al., 1999; Buchbinder et al., 2002). Programmed changes and establishment of a phenotype may transmit low birth weight to each successive generation (Drake and Liu, 2010).

Various imprinted genes may contribute to fetal programming and the intergenerational transmission of birth weight. For example, the maternal *PHLDA2* gene influences placental and fetal growth in mice, since increased expression of *PHLDA2* was associated with lower birth weight infants (Apostolidou et al., 2007; Lim et al., 2012). When the *PHLDA2* promoter region was sequenced, a 15 basepair repeat sequence (RS1) was found to decrease *PHLDA2* promoter

efficiency and cause significant increases in birth weight (Ishida et al., 2012). Inheritance of a SNP of the maternally imprinted *H19* gene was also significantly associated with increased birth weight (Adkins et al., 2010; Petry et al., 2011).

The imprinted genes *IGF2R* and *IGF2* also influence birth weight (Adkins et al., 2010). Genetic analysis of human placentas showed that DNA methylation of the fetal *IGF2* gene influenced birth weight, and DNA methylation of the maternal *IGF2/H19* locus regulated the fetal *IGF2* gene and fetal birth weight (St-Pierre et al., 2012). One study found significant associations between SNPs at the insulin-*IGF2* locus and the risk that offspring are born small for gestational age (Adkins et al., 2008). Similarly, the concentration of *IGF2* in the umbilical cord had a significant positive relationship with birth weight and length, and *IGFBP2* had a significant negative relationship with birth weight and birth length (Smerieri et al., 2011). One study found differences in DNA methylation at the *IGF2/H19* region in response to Dutch famine exposure, which demonstrates how famine exposure can genetically influence subsequent generations (Tobi et al., 2012). Additionally, in children that were born low birth weight, there was significant down-regulation of the paternal gene, *PEG10* when compared to children born normal birth weight (Lim et al., 2012).

LOW BIRTH WEIGHT IN THE DOGON OF MALI

Previous studies on the Dogon of Mali examined factors such as maternal depletion, sibship size, and childhood health, and the results demonstrate an offspring quality versus quantity trade-off (Strassmann and Gillespie, 2002; Strassmann, 2000; Strassmann, 2011). Dogon women who had seven births had a reproductive success of 3.9 with a confidence interval of 3.8 to 5.5, and reproductive success peaked at 4.1 surviving offspring after 10.5 births (Strassmann and Gillespie, 2002). Among 176 children followed for eight years, an additional sibling increased the odds of childhood mortality by 26% (Strassmann, 2000). Another study using the longitudinal data found that childhood growth was negatively impacted by larger family size and siblings competed with each other for resources (Strassmann, 2011). Overall, these findings provide information about how large sibship size negatively influences childhood growth and survival. Since some of the female cohort members are beginning to have their own offspring, I analyzed offspring birth weight in relational to maternal health conditions.

The longitudinal data contains information on 41 mothers and their first-born offspring with two placental weights missing, and I used SPSS to conduct the analyses. As show in Figures 1 and 2, the distributions of birth weight and placental weight are slightly skewed, and the Q-Q plots demonstrate that both birth weight and placental are most likely not normally distributed. Therefore, I predominantly used Spearman's test to account for any deviations from normality and generate correlation coefficients. Additionally, neither the mother's age when she gave birth nor the sex of the infant was significantly related to low birth weight, as the p-values were 0.365 and 0.822, respectively. Thus, neither variable was treated as a cofounding variable. As Figure 3 illustrates, the population of mothers is also relatively young, so it is possible that some of the mothers are still growing and not yet at their adult height.

The descriptive statistics show that the mean offspring placental weight is 471 grams and the data varies from 340 to 680 grams with a standard deviation of 83 (normal placental weight ranges from about 454 to 907 grams). The mean offspring birth weight is 2527 grams, which is slightly above the low birth weight threshold, and the range was 1100 to 3400 grams with a standard deviation of 490. I focused my analyses on maternal systolic blood pressure, body fat percentage, body mass index, maternal childhood height, maternal height in adulthood, and placental weight in relation to low birth weight. Based on the findings from the literature, I predicted: maternal systolic blood pressure will be inversely related with offspring birth weight (Buchbinder et al., 2002; Barker et al., 1990); higher values of body fat percentage, body mass index, maternal childhood height, and maternal height in adulthood will be associated with a decreased prevalence of low birth weight (Winkvist et al., 1994; King, 2003; Miller, 2010; Ramakrishnan et al., 1999; Martin et al., 2004; Barker, 1998; Veena et al., 2004); placental weight and low birth weight will be inversely related (Lumey, 1998).

A. *Results*

I conducted a binary logistic regression test on average maternal systolic blood pressure and the binary birth weight variable (0=normal, 1=low: 2500 grams or less) to test the correlation between high blood pressure and low birth weight (Buchbinder et al., 2002). The results shown in Table 5 indicate that maternal systolic blood pressure did not significantly influence low birth weight risk (p-value=0.261). The frequency analysis and Figure 4 show that maternal systolic blood pressure ranged from 97 to 140 mm Hg, which is within the range of high systolic blood pressure.

Next, I looked at maternal body fat percentage and body mass index in relation to low birth weight. A higher percentage of maternal body fat, which was measured about two years

before the mothers gave birth, was found to significantly (p-value=0.048) decrease the risk of having children with low birth weight. The logistic regression odds ratio was 0.868 with a 95% confidence interval of 0.754 to 0.999. Thus, maternal body fat has a protective effect with a 13% decreased risk of having low birth weight offspring with each one-unit increase in body fat percentage. Although maternal body mass index, which was measured at the same time as body fat percentage, was not found to significantly (p-value=0.133) decrease the risk for low birth weight, the results might reach significance with a larger sample size. The odds ratio was 0.735 with a 95% confidence interval of 0.492 to 1.099. For every one-unit increase in maternal BMI, the risk of having a low birth weight offspring decreases non-significantly by 26.5%.

I then examined maternal height during childhood in relation to low birth weight. The binary logistic regression analyses show that maternal childhood height and adult height z-scores based on the World Health Organization height for age standards (World Health Organization, 2005) have a non-significant effect on low birth weight. The odds ratio for the maternal childhood height z-score was 0.678 with a 95% confidence interval of 0.311 to 1.474 and the odds ratio for the maternal adult height z-score was 0.708 with a 95% confidence interval of 0.262 to 1.918. Therefore, taller maternal adult height cannot be considered protective against low birth weight in this small sample. However, the maternal childhood height z-score has a smaller confidence interval than the maternal adult height z-score, and the results are approaching taller childhood height being protective against low birth weight, which could be evaluated in the future with a larger sample size.

Maternal childhood height will most likely have a protective effect based on how research studies show that women who experienced stunted childhood growth have a higher risk of giving birth to low birth weight offspring (Ramakrishnan et al., 1999). Stunting was also

taken into consideration and the relationship with low birth weight was not statistically significant as indicated in Table 5 (p-value=0.605 and odds ratio=1.481).

Since the literature demonstrates that the placenta compensates in order to protect the developing fetus during periods of famine and fasting (Lumey, 1998; Alwasel et al., 2010), I looked at the correlation between birth weight and placenta weight. The bivariate correlation results show that birth weight and placental weight are positively correlated with a correlation coefficient of 0.545 and a p-value equal to 0.000. However, when only the low birth weight cases were examined, placental weight and birth weight were negatively correlated with a coefficient of -0.465 and a p-value equal to 0.003.

B. *Discussion*

The results of the analyses support some of my predictions and findings from the low birth weight literature. The non-significant relationship between maternal systolic blood pressure and offspring birth weight may be due to the small sample size (N=39). As additional longitudinal data is collected, further research could look into how low birth weight influences blood pressure as the children grow and develop.

The significant effect of maternal body fat percentage on risk of having low birth weight infants has important implications about how maternal body composition influences birth weight. Since a higher body fat percentage is protective against low birth weight, there may be more in utero space for the fetus to grow and develop (Martorell and Zongrone, 2012; Walton and Hammond, 1938). A mother with more fat stores has greater energy reserves compared to a mother with a lower percentage of body fat and therefore may be able to supply her offspring with more resources (Winkvist et al., 1994). With a larger sample size, this can be further

explored and expanded to look into the influence of maternal depletion on low birth weight after multiple pregnancies.

Since studies show that a mother's childhood height impacts offspring birth weight (Veena et al., 2004; Hypponen, Power, and Smith, 2004), I predicted that girls who were taller in childhood would have a lower risk of giving birth to low birth weight offspring. Although taller childhood height tended to protect against low birth weight, the results of maternal childhood height and maternal stunted childhood growth were not significantly related with low birth weight. These findings may be due to the small sample size or there may be unknown confounding variables. Therefore, these analyses should be repeated once more data is collected and factors such as resource availability and psychological stresses during childhood should be taken into consideration (Gavin et al., 2011; Gavin et al., 2012).

The inverse correlation between placental weight and low birth weight was expected, since enlarged placental weight was a compensatory mechanism in response to events such as the Dutch famine and Ramadan (Lumey, 1998; Alwasel et al., 2010). However, in the Dutch famine study birth weight was protected by increased placental weight and the analyses, as shown in Table 6 indicate that larger placental weight occurs with low birth weight. Since the Dogon people eat a diet that consists of mainly millet, they are most likely more chronically undernourished than the Dutch people, who were exposed to famine for four months. Therefore, the placenta may increase in size as a compensatory mechanism, but may not be able to completely protect fetal growth and development, and prevent low birth weight among Dogon offspring. Future research on the placental weight-birth weight relationship is suggested, and future studies could explore how maternal micronutrient levels in the serum and blood influence placental and birth weights (Matthews, Yudkin, and Neil, 1999).

CONCLUSION

My extensive literature review illustrates that a wide range of factors influence and perpetuate the intergenerational transmission of low birth weight. Pregnancies that occur within eighteen months or less of each other increase the risk of having low birth weight offspring due to the insufficient amount of time for maternal micronutrient repletion. Both gestation and lactation contribute to maternal depletion, and varying degrees of maternal depletion occur among all women regardless of their initial nutritional status.

Family size also influences nutritional depletion, which is evident by the correlation between larger family size and lower vitamin D and vitamin A levels. Larger sibship size is associated with increased low birth weight prevalence and higher childhood mortality risks. These relationships between larger family size and adverse health outcomes may be due to both maternal depletion after many pregnancies and heightened resource competition within larger families. Therefore, it is important to look at both maternal health conditions and family dynamics when studying the factors that cause low birth weight.

Maternal birth and childhood health conditions also influence the risk for low birth weight. A mother who was born low birth weight has an increased risk of giving birth to low birth weight offspring (Price, Hyde, and Coe, 1999; Hypponen and Power, 2004). The regulation of imprinted genes through DNA methylayion or histone acetylation can either enhance or suppress low birth weight prevalence (Ishida et al., 2012; Apostolidou et al., 2007). Overall, my literature review demonstrates that both environmental and genetic factors exert an influence on low birth weight. Although the exact mechanisms of low birth weight transmission are unknown since the research is ongoing, low birth weight is most likely transmitted epigenetically.

Taking the factors that increase the prevalence and transmission of low birth weight into consideration, I analyzed Dogon data on birth weight. The results did not show a significant correlation between maternal systolic blood pressure and low birth weight. Higher maternal body fat percentage was significantly associated with a decreased risk of having low birth weight children. Maternal height during childhood and stunted childhood growth were not significantly related to low birth weight, but the trend was for a higher maternal childhood height z-score to protect against low birth weight. Placental weight and low birth weight were inversely correlated, which supports how the placenta compensates in size (Lumey, 1998; Alwasel et al., 2010). Although the results are limited by the small sample size due to the ongoing nature of the study, the results conform to some of the findings from the literature.

Overall, my analyses show that there is a need to do further research once more data is collected. However, my analyses also provide some direction for future research. The mother's birth weight could be obtained and then studied in the comparison to offspring birth weight to investigate whether an intergenerational birth weight correlation exists. Additionally, epigenetic analyses on placental samples could be done in order to study the imprinted genes that influence birth weight and the mechanisms that trigger increased placental weight with low birth weight. The current data set only includes information about first-born offspring, so once the mothers have more children, analyses could be extended to look at the relationship between sibship size and low birth weight.

In conclusion, low birth weight is an important public health issue, and the findings show that low birth weight most likely has significant evolutionary implications. Since low birth weight tends to increase with larger sibship sizes, a trade-off exists between offspring quantity and quality. This trade-off serves to protect both offspring health and survival since larger

family size is associated with higher mortality and lower birth weight is related to stunted growth and hypertension in adulthood. Therefore, the negative consequences of low birth weight most likely contributed to evolutionary selection against larger family sizes in order to maximize offspring survival and reproductive success. Since the Dogon people are a traditional population that does not use contraception, analyses on birth weight data can provide insight on low birth weight as an evolutionary force.

APPENDIX

Table 1. The Influence of Family Size on Infant Mortality—Paris, France 17th and 18th Century Data (Charbonneau, 1970)	
Family Size	Infant Mortality Rate
4	0.172
5	0.267
6	0.250
7	0.180
8	0.237
9	0.310
10	0.244
11	0.282
12	0.298
13	0.192
14	0.286
15	No data
16	0.458
17	0.118
18	0.389

Table 2. The Influence of Family Size on Proportion of Children Dead at Age 20—Geneva, Switzerland, 16th-20th Century Data (Henry, 1956)	
Family Size	Proportion Dead at Age 20
2	0.29
3	0.23
4	0.26
5	0.26
6	0.34
7	0.38
8	0.39
9	0.40
10	0.46
11	0.50
> or = 12	0.48

Table 3. The Influence of Family Size on Proportion of Children Dead—Niakhar, Senegal, 20th Century Data (Ronsmans, 1995)	
Family Size	Proportion of Children Dead
1	0.6667
2	0.3300
3	0.3667
4	0.4454
5	0.3678
6	0.4074
7	0.4197
8	0.4587
9	0.4522
10	0.5102
11	0.5156
12	0.5582
13	0.6207
14	0.6429
15	0.6833
16	0.6458

Table 4. Sibship Size Influence on Height Compared to Only Children—Avon, England, 20th Century Data (Lawson and Mace, 2008)		
	Birth length	Growth per year
1 sibling	-4.4 mm	-2.3 mm
2 siblings	-5.2 mm	-2.4 mm
3 siblings	-6.4 mm	-2.4 mm
4 siblings	-8.7 mm	-2.3 mm

Table 5. Binary Logistic Regression SPSS Test Results				
Variables	P-value	Odds Ratio	Odds Ratio 95% CI	Comments
Systolic Blood Pressure & Low Birth Weight (LBW) (N=39)	0.261	0.962	[0.899, 1.029]	Non-significant results, with OR close to 1 results show the BP does not influence LBW
Maternal Body Fat Percentage & LBW (N=39)	0.048*	0.868	[0.754, 0.999]	Body fat significantly protects against LBW
Maternal BMI & LBW (N=39)	0.133	0.735	[0.492, 1.099]	Trend is towards higher BMI protecting against LBW
Maternal Childhood Height z-score & LBW (N=30)	0.326	0.678	[0.311, 1.474]	Trends is towards taller height protecting against LBW
Maternal Stunting & LBW	0.605	1.481	[0.334, 6.572]	Non-significant results
Maternal Adult Height z-score & LBW (N=39)	0.498	0.708	[0.262, 1.918]	Non-significant results

*Denotes statistical significance at the 5% level

Table 6. Bivariate Correlation SPSS Test Results		
Variables	P-Value	Correlation Coefficient
Placental Weight & Birth Weight (N=39)	0.000**	0.545
Placental Weight & LBW (N=13)	0.003**	-0.465

**Denotes statistical significance at the 1% level

Figure 1. Distribution of Dogon Birth Weight

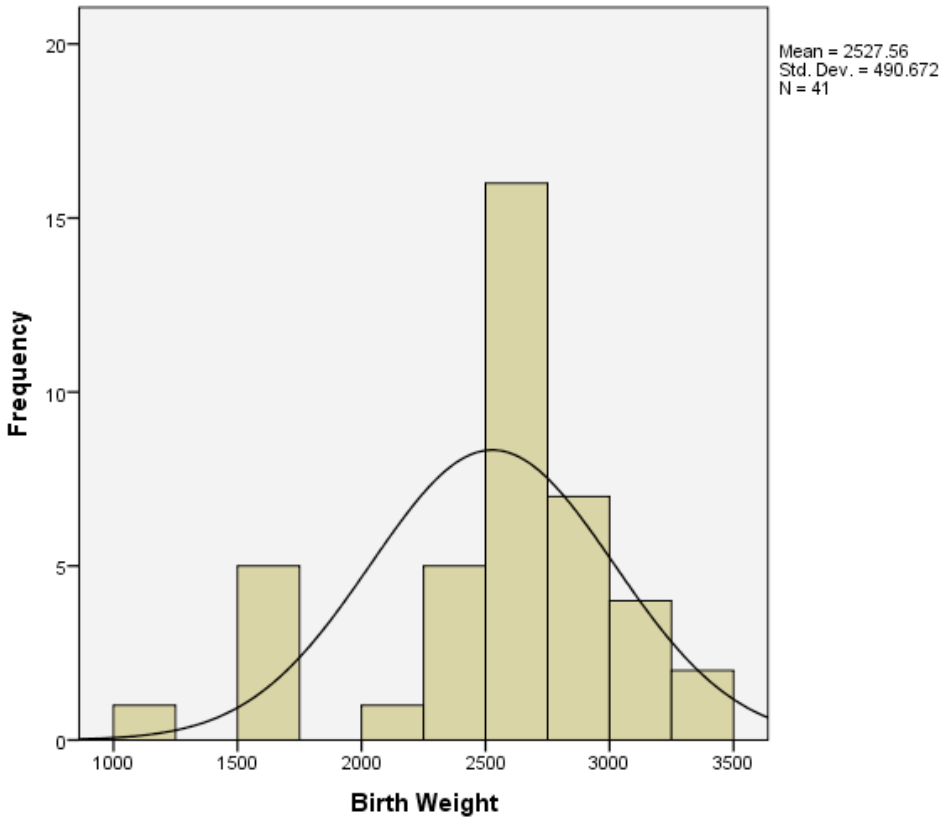


Figure 2. Distribution of Dogon Placental Weight

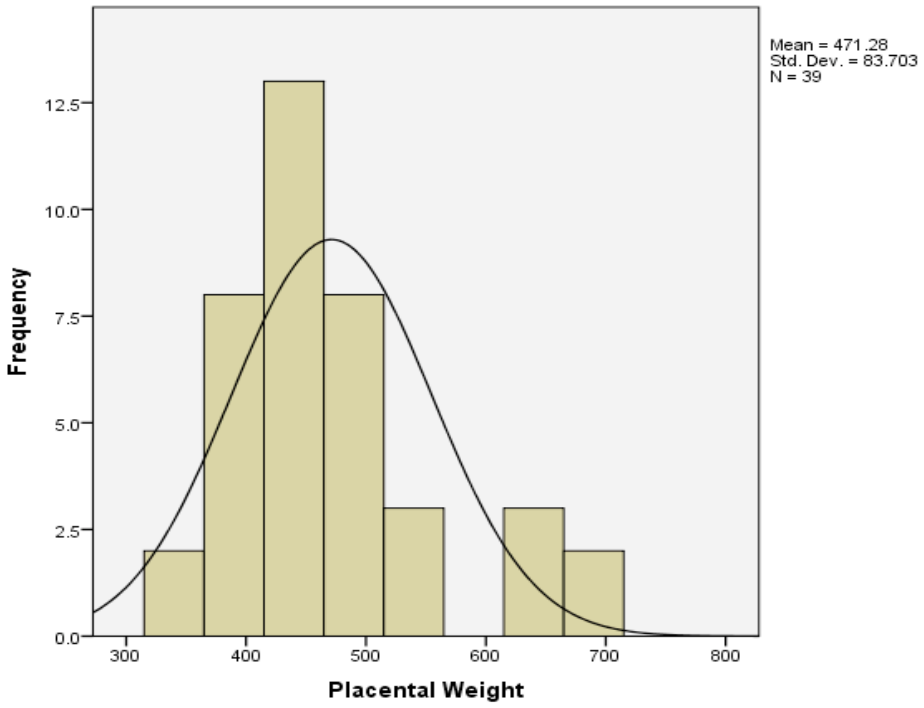


Figure 3. Distribution of Dogon Maternal Age

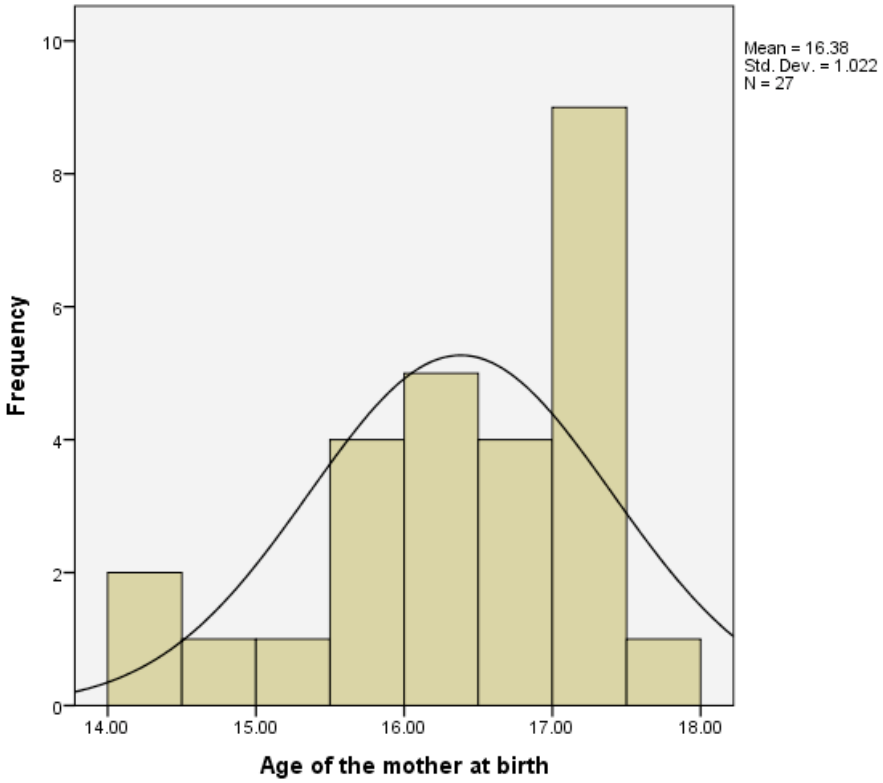
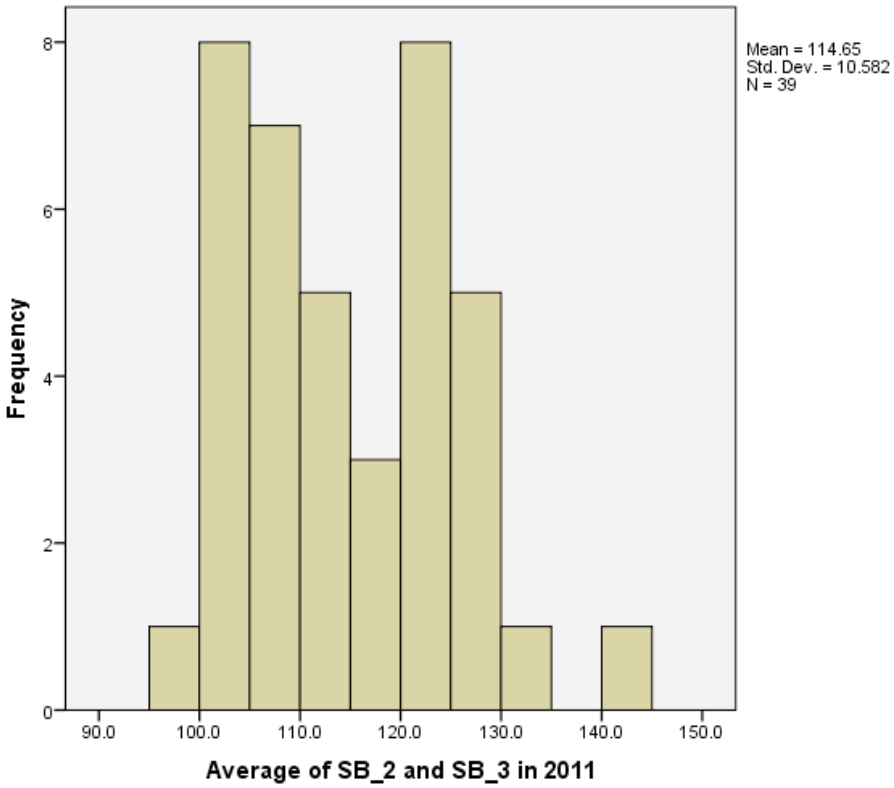


Figure 4. Distribution of Dogon Maternal Systolic Blood Pressure



WORKS CITED

Adair, L.S., and Popkin, B.M. 1992. Prolonged Lactation Contributes to Depletion of Maternal Energy Reserves in Filipino Women. *J Nutr* 122(8):1643-1655.

Adkins, R.M., Krushkal, J., Klauser, C.K., Magann, E.F., Morrison, J.C., and Somes, G. 2008. Association between small for gestational age and paternally inherited 5' insulin haplotypes. *Int J Obes* 32:372-380.

Adkins, R.M., Somes, G., Morrison, J.C., Hill, J.B., Watson, E.M., Magann, E.F., and Krushkal, J. 2010. Association of Birth weight With Polymorphisms in the *IGF2*, *H19*, and *IGF2R* Genes. *Pediatr Res* 68(5):429-434.

Akpede, G.O., Solomon, E.A., Jalo, I., et al. 2001. Nutritional rickets in young Nigerian children in the Sahel savanna. *E Afri Med J* 78(11):568-575.

Alberman, E., Filakti, H., Williams, S., Evans, S.J.W., and Emanuel, I. 1991. Early influences on the secular change in adult height between the parent and children of the 1959 birth cohort. *Ann Hum Biol* 18:127-136.

Aliyu, M.H., Jolly, P.E., Ehiri, J.E., and Salihu, H.M. 2005. High Parity and Adverse Birth Outcomes: Exploring the Maze. *Birth* 32:45-59.

Alwasel, S.H., Abotalib, Z., Aljarallah, J.S., Osmond, C., Alkharaz, S.M., Alhazza, I.M., Badr, G., and Barker, D.J.P. 2010. Changes in Placental Size during Ramadan. *Placenta* 31(7):607-610.

Apostolidou, S., Abu-Amero, S., O'Donoghue, K., Frost, J., Olafsdottir, O., Chavele, K. M., Whittaker, J. C., Loughna, P., Stanier, P., & Moore, G. E. 2007. Elevated placental expression of the imprinted *PHLDA2* gene is associated with low birth weight. *J Mol Med* 85:379-387.

Baird, D. 1985. Changing problems and priorities in obstetrics. *Br J Obstet Gynaecol* 92:115-121.

Bakketeig, L.S., and Hoffman, H.J. 1979. Perinatal mortality by birth order within cohorts based on sibship size. *BMJ* 2:693-696.

Barker, D.J.P., Bull, A.R., Osmond, C., and Simmonds, S.J. 1990. Fetal and placental size and the risk of hypertension in adult life. *BMJ* 301:259-262.

Barker D.J.P. 1998. *Mothers, Babies and Health in Later Life.* London: Churchill Livingstone.

Barker, D.J.P. 2004. The Developmental Origins of Adult Disease. *ACN* 23(6):588S-595S.

Barker, D.J.P., Bull, A.R., Osmond, C., and Simmonds, S.J. 1990. Fetal and Placental Size And Risk of Hypertension In Adult Life. *BMJ* 301:259-262.

Berg, B.N. 1965. Dietary restriction and reproduction in the rat. *J Nutr* 87:344-348.

Buchbinder, A., Sibai, B.M., Caritis, S., Macpherson, C., Hauth, J., Lindheimer, M.D., Klebanoff, M., Vandorsten, P., Landon, M., Paul, R. 2002. Adverse Perinatal outcomes are significantly higher is severe gestational hypertension than in mild preeclampsia. *AJOG* 186:66-71.

Cain, A.C., and Cain, B.S. 1964. On Replacing A Child. *J Child Psychol Psychiatry* 3(3):443-456.

Chan, K.K.L., Ho,L.F., and Lao, T.T. 2003. Nutritional intake and placental size in gestation diabetic pregnancies – a preliminary observation. *Placenta* 24(10):985-988.

Charbonneau, Hubert. 1970. Ourouvre-au-Perche aux 17e et 18e Siècles: Étude de Démographie Historique. Paris: Presses Universitaires de France.

Coall, D.A., and Chisholm, J. S. 2003. Evolutionary perspectives on pregnancy: maternal age at menarche and infant birth weight. *Social Science & Medicine* 57:1771-1781.

Cohen, J.E. 1975. Childhood Mortality, Family Size and Birth Order in Pre-Industrial Europe. *Demography* 12(1):35-55.

Colen, C.G., Geronimus, A.T., Bound, J., and James, S.A. 2006. Maternal Upward Socioeconomic Mobility and Black—White Disparities in Infant Birthweight. *Am J Public Health* 96:2032-2039.

Collins J.W. Jr, David, R.J., Rankin, K.M., ad Desireddi, J.R. 2009. Transgenerational effect of neighborhood poverty on low birth weight among African Americans in Cook County, Illinois. *AJE* 169:712-717.

Collins, J.W. Jr., Rankin, K.M., and David, R.J. 2011. African American Women's Lifetime Upward Economic Mobility and Preterm Birth: The Effect of Fetal Programming. *Am J Public Health* 101:714-719.

Cuco, G., Arija, V., Iranzo, R., et al. 2006. Association of maternal protein intake before conception and throughout pregnancy with birth weight. *Acta Obstet Gynecol Scad* 85(4):413-421.

De, B., Lin, S., Lohsoonthorn, V., and Williams, M.A. 2007. Risk of preterm delivery in relation to maternal low birth weight. *Acta Obstetricia et Gynecologica* 86:565-571.

De Stavola, B.L., Leon, D.A., and Koupil, I. 2011. Intergenerational Correlations in Size at Birth and the Contribution of Environmental Factors. *AJE* 174:52-62.

Desai, S. 1995. When Are Children from Large Families Disadvantaged? Evidence from Cross-National Analyses. *Population Studies* 49:195-210.

DeSweemer, C. 1984. The influence of child spacing on child survival. *Popul Stud* 38:47-72.

Downey, D.B. 1995. When Bigger in Not Better: Family Size, Parental Resources, and Children's Educational Performance. *Am Sociol Rev* 60:746-761.

Drake, A.J., and Liu, L. 2010. Intergenerational transmission of programmed effects: public health consequences. *TEM* 21:206-213.

Durrani, A.M., and Rani, A. 2011. Effect of maternal dietary intake on the weight of the newborn in Aligarh city, India. *Niger Med J* 52(3):177-181.

Emanuel, I., Filakti, H., Alberman, E., and Evans, S.J.W. 1992. Intergenerational Studies of Human Birth-Weight from the 1958 Birth Cohort 1. Evidence for a Multigenerational Effect. *BJOG* 99(1):67-74.

Farina, A., Dini, B., Mattioli, M., Rosa, S., and Rizzo, N. 2010. Offspring birth weight in second-generation 'small for gestational age' infants. *Prenat Diagn* 30:551-554.

Fowden, A. L., Coan, P. M., Angiolini, E., Burton, G. J., and Constancia, M. 2011. *Prog Biophys Mol Biol* 106, 281-288.

Fujita, M., Shell-Duncan, B., Ndemwa, P., Brindle, E. Lo, Y., Kombe, Y., ad O'Connor, K. 2011. Vitamin A Dynamics in Breastmilk and Liver Stores: A Life History Perspective. *Am J Hum Biol* 23:664-673.

Gavin, A.R., Hill, K.G., Hawkins, J.D., and Maas, C. 2011. The Role of Maternal Early-Life and Later-Life Risk Factors on Offspring Low Birth Weight: Findings From a Three-Generational Study. *J Adolesc Health* 49:166-171.

Gavin, A.R., Thompson, E., Rue, T., and Guo, Y. 2012. Maternal Early Life Risk Factors for Offspring Birth: Findings from the Add Health Study. *Prev Sci* 13:162-172.

Gebre-Medhin, M., Vahlquist, A., Hofvander, Y., Uppsall, L., and Vahlquist, B. 1976. Breast milk composition in Ethiopian and Swedish mothers. I. Vitamin A and beta-carotene. *Am J Clin Nutr* 29:441-451.

Gennser, G., Rymark, P., and Isberg, P.E. 1988. Low birth weight and risk of high blood pressure in adulthood. *BMJ* 296:1498-1500.

Godfrey, K.M., Redman, C.W.G., Barker, D.J.P., and Osmond, C. 1991. The effect of maternal anaemia and iron deficiency on the ratio of fetal weight to placental weight. *BJOG* 98:886-891.

Godfrey, K.M, and Robinson, S. 1998. Maternal nutrition, placental gowth, and fetal programming. *Proc Nutr Soc* 57(1):105-111.

Gray, R.H. 1981. Birth Intervals, Postpartum Sexual Abstinence and Health. In: Page, H.J., and Lesthaege, R., editors. Child-Spacing in Tropical Africa: Traditions and Change. New York: Academic Press.

Gray, R.H. 1984. Maternal reproduction and child survival. *Am J Public Health* 74:1080-1081.

Hämäläinen, H., Hakkarainen, K., and Heinonen, S. 2003. Anaemia in the first but not in the second or third trimester is a risk factor for low birth weight. *Clin Nutr* 22(3):271-275.

Henry, Louis. 1956. Anciennces Familles Genevoises; Étude Démographique: 16e-20e Siècle. Paris: Presses Universitaires de France.

Hypponen, E., Power, C., and Smith G.D. 2004. Parental growth at different life stages and offspring birthweight: an intergenerational cohort study. *Paediatr Perinat Epidemiol* 18:168-177.

Ishida, M., Monk, D., Duncan, A.J., Abu-Amero, S., Chong, J.H., Ring. S.M., Pembrey, M.E., Hindmarsh, P.C., Whittaker, J.C., Stainer, P., and Moore, G.E. 2012. Maternal Inheritence of a Promoter Variant in the Imprinted *PHLDA2* Gene Significantly Increases Birth Weight. *Am J Hum Gen* 90(4):715-719.

Jablonka, E., and Lamb, M. 2005. Evolution in four dimensions. Genetic, epigenetic, behavioral, and symbolic variation in the history of life. Cambridge, MA: MIT Press.

James, W.H. 1968. Stillbirth and birth order. *Ann Hum Genet* 32:151-162.

Jasienska, G. 2009. Low birth weight of contemporary African Americans: an intergenerational effect of slavery?. *Am J Hum Biol* 21:16-24.

Juntunen, S.T.K, Läärä, E.J, and Kauppila, A.J.I. 1997. Grand Grand Multiparity and Birth Weight. *Obstet Gynecol* 90(4):495-499.

King, J.C. 2003. The Risk of Maternal Nutritional Depletion and Poor Outcomes Increases in Early or Closely Spaced Pregnancies. *J Nutr* 133:17325-17365.

Kjolhede, C.L., Stallings, R.Y., Dibley, M.J., Sadjimin, T., Dawiesah, S., and Padmawati, S. 1995. Serum retinol levels among preschool children in Central Java: demographic and socioeconomic determinants. *Int J Epidemiol* 24: 399-403.

Klebanoof, M.A., Secher, N.J., Mednick, B.R., and Schulsinger, C. 1999. Maternal size at birth and the development of hypertension during pregnancy: a test of the Barker hypothesis. *Arch Internal Med* 159:1607-1612.

Knodel, J., and Hermalin, A.I. 1984. Effects of birth rank, maternal age, birth interval, and sibship size on infant and child mortality: evidence from 18th and 19th century reproductive histories. *Am J Public Health* 74:1098-1106.

Kochanek, K.D., Kirmeyer, S.E., Martin, J.A., Strobino, D.M, and Guyer, B. 2012. Annual Summary of Vital Statistics: 2009. *Pediatrics* 129(2);338-348.

Koura, G.K., Ouedraogo, S., Le Port, A., Watier, L., Cottrell, G., Guerra, J., Choudat, I., Rachas, A., Bouscaillou, J., Massougbodji, A., and Garci, A. 2012. Anaemia during pregnancy: impact on birth outcome and infant haemoglobin level during the first 18 months of life. *Trop Med Int Health* 17:283-291.

Kuzawa, C.W. 2005. Fetal origins of developmental plasticity: are fetal cues reliable predictors of future nutritional environments? *Am J Hum Biol* 17:5-21.

L'Abée, C., Vrieze, I., Kluck, T., Erwich, J.J.H.M., Stolk, R.P., and Sauer, P.J.J. 2011. Parental factors affecting the weights of the placenta and the offspring. *J. Perinat. Med.* 39:27-34.

Lack, D. 1947. The significance of clutch-size (part I-II). *Ibis* 89:302-352.

Laskey, M.A., and Prentice, A. 1997. Effect of pregnancy on recovery of lactational bone loss. *Lancet* 349:1518-1519.

Lawson, D.W., and Mace, R. 2008. Sibling configuration and childhood growth in contemporary British families. *Int J Epidemiol* 37:1408-1421.

Lawson, D.W., and Mace, R. 2011. Parental investment and the optimization of human family size. *Proc R Soc A: Biol* 366:333-343.

Lenders, C.M., McElrath, T.F., and Scholl, T.O. 2000. Nutrition in adolescent pregnancy. *Cuur Opin Pediatr* 12:291-296.

Leon, D.A., and Moser, K.A. 2012. Low birth weight persists in South Asian babies born in England and Wales regardless of maternal country of birth. Slow pace of acculturation, physiological constraint or both? Analysis of routine data. *J Epidemiol Community Health* 66:544-551.

Lim, A.L., Ng, S., Leow, S.C.P., Choo, R., Ito, M., Chan, Y.H., Goh, S.K., Tng, E., Kwek, K., Chong, Y.S., Gluckman, P.D., and Ferguson-Smith, A.C. 2012. Epigenetic state and expression of imprinted genes in umbilical cord correlates with growth parameters in human pregnancy. *J Med Genet* 49:689-697.

Lumey, L.H. 1998. Compensatory placental growth after restricted maternal nutrition in early pregnancy. *Placenta* 19:105-111.

Lumey, L.H., and Stein, A.D. 1997. Offspring birth weights after maternal intrauterine undernutrition: a comparison with sibships. *Am J Epidemiol* 146:810-819.

"Macronutrient." *Merriam-Webster*.com. Merriam-Webster, 2013. Web. 1 April 2013.

Martin, R.M., Smith, G.D., Frankel, S., and Gunnell, D. 2004. Parents' growth in childhood and the birth weight of their offspring. *Epidemiol* 15:308-316.

Martorell, R., and Zongrone, A. 2012. Intergenerational influences on child growth and undernutrition. *Paediatr Perinat Epidemiol* 26 Suppl 1:302-314.

Masho, S.W., and Archer, P.W. 2011. Does maternal birth outcome differentially influence the occurrence of infant death among African Americans and European Americans?. *MCH* 15:1249-1256.

Mathews, F., Yudkin, P., and Neil, A. 1999. Influence of maternal nutrition on outcome of pregnancy: prospective cohort study. *BMJ* 319:339-343.

Merchant, K., Martorell, R., and Haas, J. 1990. Maternal and fetal responses to the stresses of lactation concurrent with pregnancy and of short recuperative intervals. *Am J Clin Nutr* 52:280-288.

"Micronutrient." *Merriam-Webster*.com. Merriam-Webster, 2013. Web. 1 April 2013.

Miller, E.M. 2010. Maternal hemoglobin depletion in a settled northern Kenyan pastoral population. *Am J Hum Biol* 22:768-774.

Majid, M.A., Badawi, M.H., al-Yaish, S., Sharma, P., el-Salam, R.S., and Molla, A.M. 2000. Risk factors for nutritional rickets among children in Kuwait. *Pediatr Int* 42(3):280-284.

Nault, F., Desjardins, B., and Legare, J. 1990. Effects of Reproductive Behaviour on Infant Mortality of French-Canadians during the Seventeenth and Eighteenth Centuries. *Pop Stud* 44(2):273-285.

Nilsson, P.M., Li, X., Sundquist, J., and Sundquist, K. 2009. Maternal cardiovascular disease risk in relation to the number of offspring born small for gestational age: national, multi-generational study of 2.7 million births. *Acta Paediatrica* 98:985-989.

Omariba, D.W.R., Rajulton, F., and Beaujot, R. 2008. Correlated mortality of siblings in Kenya: The role of state dependence. *Demog Res* 18:311-335.

Ozumba, B.C., and Igwegbe, A.O. 1992. The challenge of grandmultiparity in Nigerian obstetric practice. *Int J Gynecol Obstet* 37:259-264.

Painter, R.C., Osmond, C., Gluckman, P., Hanson, M., Phillips, D.I.W., and Roseboom, T.J. 2008. Transgenerational effects of prenatal exposure to the Dutch famine on neonatal adiposity and health in later life. *Int J Obstet and Gynaecol* 115(10):1243-1249.

Pearl, M., Braveman, P., and Abrams, B. 2001. The Relationship of Neighborhood Socioeconomic Characteristics to Birthweight Among 5 Ethnic Groups in California. *Am J Public Health* 91:1808-1814.

Petry, C.J., Seear, R.V., Wingate, D.L., Acerini, C.L., Ong, K.K., Hughes, I.A., and Dunger, D.B. 2011. Maternally transmitted foetal *H19* variants and associations with birth weight. *Hum Genet* 130:663-670.

Price, K.C., Hyde, J.S., and Coe, C.L. 1999. Matrilineal transmission of birth weight in the rhesus monkey (Macaca mulatta) across several generations. *Obstet Gynecol* 94:128-134.

Ramakrishnan, U., Martorell, R., Schroeder, D.G., and Flores, R. 1999. Role of intergenerational effects on linear growth. *J Nutr* 129(2S):544S-549S.

Rasmussen, K.M., and Fischbeck, K.L. 1987. Effect of repeated reproductive cycles on pregnancy outcome in ad libitum-fed and chronically food-restricted rats. *J Nutr* 117:1959-1966.

Rona, R.J., Swan, A.V., and Altman, D.G. 1978. Social factors and height of primary schoolchildren in England and Scotland. *J Epidemiol Comm Health* 32:147-154.

Ronsmans, C. 1959. Patterns of Clustering of Child Mortality in a Rural Area of Senegal. *Pop Stud* 49(3):443-461.

Sanna, E., and Danubio, M.E. 2009. Are changes in body dimensions of adult females from Italy (Sardinia and Latium) related to secular trend?. *J Compar Hum Biol* 60(5):451-460.

Scholl, T.O., Stein, T.P., and Smith, W.K. 2000. Leptin and maternal growth during adolescent pregnancy. *Am J Clin Nutr* 72:1542-1547.

Seidman, D.S., Dollberg, S., Stevenson, D.K., and Gale, R. 1991. The effects of high parity and socioeconomic status on obstetric and neonatal outcome. *Arch Gynecol Obstet* 249:119-127.

Seidman, D.S., Gale, R., Slater, P.E., Ever-Hadani, P., and Harlap, S. 1987. Does Grand Multiparity Affect Fetal Outcome? *Int. J. Gynaecol. Obstet.* 24:1-7.

Selling, K.E., Carstensen, J., Finnström, O., and Sydosjö, G. 2006. Intergenerational effects of preterm birth and reduced intrauterine growth: a population-based study of Swedish mother-offspring pairs. *Int J Gyneocol Obstet* 113(4):430-440.

Shah, P.S., and Shah, V. 2009. Influence of the maternal birth status on offspring: A systematic review and meta-analysis. *Acta Obstetricia et Gyneocologica* 88:1307-1318.

Sipilä, P., von Wendt, L., and Hartikainen-Sorri, A.-L. 1990. The grand multipara—still an obstetrical challenge? *Arch Gynecol Obstet* 247:187-195.

Smerieri, A., Petrarli, M., Ziveri, M.A., Volta, C., Bernasconi, S., and Street, M.E. 2011. Effects of Cord Serum Insulin, IGF-II, IGFBP-2, IL-6 and Cortisol Concentrations on Human Birth Weight and Length: Pilot Study. *PLoS ONE* 6(12):e29562.

Smith, D.G., Hart, C., Upton, M., et al. 2000. Height and risk of death among men and women: aetiological implications of associations with cardiorespiratory disease and cancer mortality. *J Epidemiol Community Health* 54:97-103.

Sowers, M., Corton, G., Shapiro, B., Jannausch, M.L., Crutchfield, M., Smith, M.L., Randolph, J.F., and Hollis, B. 1993. Changes in bone density with lactation. *JAMA* 268:3130-3135.

St-Pierre, J., Hivert, M.F., Perron, P., Poirier, P., Guay, SP., Brisson, D., and Bouchard, L. 2012. *IGF2* DNA methylation is a modulator of newborn's fetal growth and development. *Epigenetics* 7(10):1125-1132.

Stein, A.D., and Lumey, L.H. 2000. The Relationship between Maternal and Offspring Birth Weights after Maternal Prenatal Famine Exposure: The Dutch Famine Birth Cohort Study. *Hum Biol* 72(4):641-654.

Stewart, R.J., Preece, R.F., and Sheppard, H.G. 1975. Twelve generations of marginal protein deficiency. *BJN* 33:233-253.

Strassmann, B.I. 2000. Polygyny, family structure, and child mortality: A prospective study among the Dogon of Mali. In: Cronk, L., Chagnon, N., and Irons, W., editors. Adaptation and Human Behavior: An Anthropological Perspective. New York: de Gruyter, p. 49-67.

Strassmann, B.I., and Gillespie, B. 2002. Life-history theory, fertility and reproductive success in humans. *Proc R Soc Lond* 269:553-562.

Strassmann, B.I. 2011. Cooperation and competition in a cliff-dwelling people. *PNAS* 108:10894-10901.

Swamy, G.K., Edwards, S., Gelfand, A., James, S.A., and Miranda, M.L. 2010. Maternal age, birth order, and race: differential effects on birthweight. *J Epidemiol Community Health* 66:136-142.

Tobi, E.W., Slagboom, P.E., van Dongen, J., Kremer, D., Stein, A.D., Putter, H., Heijmans, B.T., and Lumey, L.H. 2012. Prenatal Famine and Genetic Variation Are Independently and

Additively Assoicated with DNA Methylation at Regulatory Loci with *IGF2*/*H19*. *PLoS ONE* 7(5):e37933.

Urbina, E.M., Srinivasan, S.R., Tang, R., Bond, M.G., Kieltyka, L., and Berenson, G.S. 2002. Impact of multiple coronary risk factors on the intima-media thickness of different segments of carotid artery in health young adults (The Bogalusa Heart Study). *Am J Cardiol* 90(9):953-958.

van den Berg, G., van Eijsden, M., Vrijkotte, T.G.M., and Gemke, R.J.B.J. 2013. Suboptimal maternal vitamin D status and low education level as determinants of small-for-gestational-age birth weight. *Eur J Nutr* 52:273-279.

van Eijsden, M., Smitts, L.J.M., van der Wal, M.F., and Bonsel, G.J. 2008. Association between short interpregnancy intervals and term birth weight: the role of folate depletion. *Am J Clin Nutr* 88:147-153.

Veena, S.R., Kumaran, K., Swarnagowri, M.N., Javakumar, M.N., Leary, S.D., Stein, C.E., Cox, V.A., and Fall, C.H. 2004. Intergenerational effects on size at birth in South India. *Paediat Perinat Epidemiol* 18:361-370.

Ventura, S.J., Martin, J.A., Curtin, S.C., and Mathews, T.J. 1995. Report of final natality statistics, 1995. *Mon Vital Stat Rep* 45:77S.

Walton, A., and Hammond, J. 1938. The maternal effects on growth and conformation in Shire horse-Shetland pony crosses. *Proc R Soc B Biol* 125:311-335.

Wedge, P., Alberman, E., and Goldstein, H. 1970. Health and height in children. *New Society* 16:1044-1045.

Wells, J.C., Hallal, P.C., Reichert, F.F., Dumith, S.C., Menezes, A.M., and Victora, C.G. 2011. Associations of birth order with early growth and adolescent height, body composition, and blood pressure: prospective birth cohort from Brazil. *Am J Epidemiol* 174:1028-1035.

Whincup, P.H., Cook, D.G., and Papacosta, O. 1992. Do maternal and intrauterine factors influence blood pressure in childhood?. *Arch Dis Childh* 67:1423-1429.

Winkvist, A., Jalil, F., Habicht, J.-P., and Rasmussen, K.M. 1994. Maternal energy depletion is buffered among malnourished women in Punjab, Pakistan. *J Nutr* 124:2376-2385.

Wong, S.S. 1990. Birth Order and Birth Weight of Saudi Newborns. *Perspec Public Health* 110:96-97.

World Health Organization. 2005. *Department of Nutrition* (World Health Organization, Geneva).

Yassin, M.M., and Lubbad, A.M.H. 2010. Risk Factors Associated With Nutritional Rickets Among Children Aged 2 to 36 Months Old in the Gaza Strip: A Case Control Study. *Int J Food Nutr Public Health* 3(1):33-45.

Zhu, B.-P., Haines, K.M., Le, T., McGrath-Miller, K., and Boulton, M.L. 2001. Effect of the interval between pregnancies on perinatal outcomes among white and black women. *Am J Obstet Gynecol* 185:1403-1410.