The Influence of Race on Gestational Exercise and Birth Outcomes

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In the United States, long-standing racial disparities in adverse birth outcome are prominent among the non-Hispanic Black (NHB) population, particularly when compared to Caucasians. Although maternal physical activity during pregnancy has been shown to improve birth measures and reduce the risk of adverse birth outcome among both NHBs and the general population, there exists a gap in the current literature as to whether the degree of response to maternal physical activity is the same among different racial groups. The primary purpose of this study is to investigate the influence of maternal exercise on birth outcomes in NHB infants compared to Caucasian infants. Secondary purposes of this study are to investigate the effect of maternal exercise on preterm infant health and to compare both overall and modality-specific compliance among NHB and Caucasian participants enrolled in exercise interventions. We hypothesized that infants born to NHB exercisers would have similar gestational age and markers of neonatal health at birth relative to infants of Caucasian exercisers, and that any racial disparities observed would be found among control participants. We also hypothesized that preterm infants born to exercisers would have reduced hospital stay and improved measures of health compared to control, and that compliance among participants would be similar regardless of race. Participants engaged in 150 minutes of moderate intensity exercise (60-85% HRmax) through three 50 minutes sessions per week; beginning at 16 weeks gestation and continuing through delivery. Controls did not engage in exercise training. Maternal measures of age, pre-

pregnancy BMI, maternal/parental education levels, and compliance were collected from questionnaires and training logs. Infant measures of gestational age, length of hospital stay, head to abdominal circumference ratio, birth weight, mode of delivery, and 1 and 5 minute Apgar scores were collected from birth records. Mann-Whitney U and independent t-tests were used to compare maternal and infant measures between races, while ANOVA and chi-square tests were used to analyze compliance and proportions of adverse birth. Analyses also included binomial logistic and linear regressions. With the exception of birth weight, which was significantly lower among NHB infants ($p=0.036$) due to a higher prevalence of low birth weight, there were no differences in measures of neonatal health and adverse birth outcome between infants born to compliant Caucasian exercisers and those born to compliant NHB exercisers. A pattern of reduced hospital stay and improved markers of infant health was observed among preterm infants born to exercisers, and modality-specific compliance was found to vary significantly both within and between races. The results of this study suggest that 1) In addition to infants of different races responding similarly to maternal exercise, racial disparities in birth outcomes may be partially attenuated by maternal exercise; with maternal exercise influencing birth outcomes by fostering more favorable gestational age at birth. 2) Infants exposed to maternal exercise can still potentially gain health benefits when born preterm. 3) Among NHB populations, aerobic exercise should be recommended in order to maximize the likelihood of compliance with physical activity guidelines and foster greater improvement in birth outcomes. Further research is needed, but our study supports existing literature that maternal exercise benefits infant health, while adding to our understanding of the degree of response among different races.

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by

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Chapter I. Introduction

Background

Infant mortality rate serves as an important marker by which the reproductive health of a population can be measured (4). Birth outcomes, a category of measures that describe infant health at birth, are strongly associated with infant mortality (59). Adverse birth outcomes such as preterm birth (PTB), low birth weight (LBW), and macrosomia lead to decreased rate of infant survival and increased infant mortality rates (19, 43, 84), as well as increased hospital stay and accumulated costs (57, 7). Multiple studies of recent infant birth/death data show that over a third of infant mortality in the United States is due to an elevated percentage of preterm births and associated health complications (61). Compared to other developed nations, the United States has a high preterm birth rate (59).

Although preterm birth rates have been on a steady decline in the US since peaking in 2006, there exists significant racial disparities amongst non-Hispanic Blacks (alternatively referred to as African Americans in literature), who consistently exhibit the highest rates of preterm birth and death due to preterm birth complications relative to other racial groups in the US (61, 19). Racial disparities expand beyond preterm birth to other birth outcome measures, with non-Hispanic Blacks having the highest rates of infant mortality, low birth weight and small size for gestational age (43, 16, 28), as well as elevated rates of cesarean delivery (61). These racial disparities in birth outcomes extend to infants of biracial parentage, although disparities are not as pronounced when compared to those of infants born to two non-Hispanic Black parents (42, 37). While paternal race has been shown to influence birth outcomes, current literature points to maternal race having the most profound influence on risk of adverse birth outcome (27, 76). Although the exact causes of racial disparities in birth outcome are not fully understood, current research indicates that they are likely the result of complicated interactions between behavioral (35, 52, 41) and socioeconomic (26, 35, 39, 40) factors amongst the non-Hispanic Black community.

With elevated risk of infant mortality in the United States serving as a credible threat to mothers and their offspring, reducing risk of the adverse birth outcomes that contribute to infant mortality is a crucial public health concern. Maternal physical activity during pregnancy has been shown to be an effective low-cost and non-pharmacological method of fostering more favorable birth outcomes and measures of neonatal health (53, 23, 47). Physical activity during pregnancy has been associated with favorable birth weight by reducing risk of low birth weight (Clapp 2000, Hatch), macrosomia (14, 78), and small for gestational age (54). More importantly, physical activity during pregnancy has been found to correlate with decreased risk of preterm birth (53, 56). While the beneficial effect of physical activity during pregnancy on birth outcomes and infant health has been exhibited among both non-Hispanic Blacks (71) and the general populations (53, 54, 47), comparative studies detailing how race affects the degree of response to maternal physical activity remain limited.

Specific Aims and Hypotheses

Specific Aim #1: Investigate the influence of exercise on birth outcomes in non-Hispanic Black infants compared to Caucasian infants.

- Hypothesis #1: Gestational age at birth, markers of neonatal health (eg. birth weight, head-to-abdominal circumference ratios, Apgar scores), and the rates of adverse birth outcome among non-Hispanic Black infants exposed to exercise will be similar to those of Caucasian infants exposed to exercise during pregnancy. If any racial disparities in birth outcomes are observed, they will be present among control participants.

Specific Aim #2: Investigate the effect of exercise during pregnancy on the health of preterm infants by comparing the hospital stay and health markers of preterm infants exposed to maternal exercise to those of preterm infants of control participants.

- Hypothesis #2: Preterm infants born to exercisers will have improved markers of health as well as reduced hospital stay and accumulated cost compared to preterm infants born to control participants. We believe these improvements will be found in both Caucasian and non-Hispanic Black preterm infants.

Specific Aim #3: Compare the overall and modality-specific (aerobic, resistance, circuit) compliance of non-Hispanic Black and Caucasian participants enrolled in the exercise intervention protocol.

- Hypothesis #3: Compliance levels amongst non-Hispanic Black participants and Caucasian participants enrolled in the exercise intervention groups of the study will be similar.

Scope of this Study

The research performed in this study was carried out in conjunction with the ongoing "ENHANCED by Mom" study (65), and is subject to the preexisting design of this active randomized control trial. Retrospective analysis of previously collected ENHANCED data limits the scope of this study to the variables and data already collected by the study. The hospital at which a participant delivers her child also acts as a limitation, as the ENHANCED study only has access to the birth records of participants who deliver at Vidant Medical Center in Greenville, NC. When available, the birth records of participants obtained from other facilities were included in our analyses. Delimitations of the study include specific recruitment criteria such that participants 18-40 years of age and have a Body Mass Index (BMI) of 18.5-34.9. A lack of substance use and significant chronic metabolic, heart, and pulmonary disease is also controlled for. Physical activity of participants will be supervised and recorded by staff members to ensure safety, as well as accuracy of measures and high compliance.

Definition of Terms

Racial Disparity – In reference to measures of health, racial disparities refer to a higher instance of illness or death experienced by one racial population over another.

Birth Outcomes – A category of measures that describe infant health at birth. These include, but are not limited to; birth weight, gestational age at birth, preterm/full term classification, and mode of delivery.

Infant Mortality Rate – The number of deaths of infants under 1 year of age per 1000 live births in an annual period within a geographic region.

Minority Race – A group of a certain race that constitute a minority of the overall population

Non-Hispanic Blacks (NHB) – Individuals of African racial background that do not hail from Hispanic countries such as Cuba, Mexico, Puerto Rico, and Costa Rica. In literature, non-Hispanic Blacks are alternatively referred to as African Americans or Blacks.

Caucasians – Individuals of European descent. In literature, Caucasians are alternatively referred to as non-Hispanic Whites or Whites.

Pre-Pregnancy BMI – A women's body mass index prior to pregnancy, measured as body weight in kilograms divided by the square of body height in meters.

Exercise Modality – The type or form of exercise designed to elicit a specific type of response from the body of the participant.

Aerobic Training – Continuous, rhythmic exercise that raises the heart rate (HR) and depends predominantly on aerobic metabolism in order to meet energy demands. In this study, aerobic training was performed with the use of treadmills, elliptical machines, stationary bikes, and rowing machines.

Resistance Training – Exercise focused on utilizing muscular contractions against a resisting force to facilitate muscular strength and endurance, and that raises HR. In this study resistance forces were achieved using weight machines, dumb bells, resistance bands, and bodyweight.

Circuit Training – Exercising in a manner that raises HR and involves completing numerous cycles of various exercises in order to improve both strength and cardiovascular endurance. In this study, cycles consisted of a mixture of both aerobic and resistance training cycles performed in quick succession.

Gestational Age – A measure of infant growth and development time measured in weeks from the mother's last recorded menstruation.

Preterm Birth – Any birth occurring prior to 37 weeks gestational age.

Low Birth Weight – A birth weight of less than 2500 g.

Very Low Birth Weight – A birth weight of less than 1500 g.

Macrosomia – A birth weight greater than 4000 g, as described by the American College of Obstetrician and Gynecology (6).

Head-to-Abdominal Circumference Ratio (HC/AC) – A ratio of infant head circumference to abdominal circumference used to assess proportional growth of the child.

Apgar Score – A qualitative measure used to summarize the health of a newborn child. Apgar scores assess skin color, pulse rate, reflex, activity level, and respiration. Each component is graded from 0-2, with the total sum serving as the final Apgar score. Measures are completed at 1 minute and 5 minutes following birth.

Compliant – participants who attended at least 80% of their 3 weekly training assignments from 16 weeks GA to delivery.

Noncompliant – participants who fail to achieve 80% attendance rate.

Chapter II. Review of the Literature

Introduction to the Literature

The purpose of this study is to determine if there are differences in exercised-induced pregnancy outcomes amongst non-Hispanic Black and Caucasian infants. Specifically, we hypothesize non-Hispanic Black infants exposed to exercise during gestation will show similar rates of preterm birth and markers of infant health relative to Caucasian infants exposed to exercise during gestation, indicated by birth weight, circumference ratios, APGAR scores, and length of hospital stay. Additionally, we wished to investigate whether preterm infants receive health benefits from maternal exercise, as well as analyze how maternal race affects compliance within an exercise intervention protocol. Accordingly, this review of literature will focus on preterm birth and measures of neonatal health, racial disparities in preterm birth and neonatal health and their proposed causes, the safety of physical activity in pregnancy, the effects of maternal exercise on birth outcome and neonatal health, and effect of race on exercise training response.

Review of the Literature

Birth Outcomes and Measures of Neonatal Health

Measurements of infant mortality rates serve as an important metric by which health status of populations can be assessed, with higher percentages of infant mortality often indicative of deficits in access to quality medical care, maternal health, and socioeconomic status (59).

Adverse birth outcomes such as preterm birth, low birth weight, and macrosomia contribute to higher infant mortality and are topics of intense study (19, 43, 84).

In the United States infant mortality has been a long-standing public health issue (61). Although infant mortality has decreased significantly in the US from the early 1900s due to improvements in public health and medical technology (4), the US continues to exhibit higher infant mortality than other developed nations (59). In a CDC analysis of 2010 international birth data the United States was found to have the highest infant mortality in a comparison to Europe, Australia, and select East Asian nations. Compared to Sweden, the nation with the most favorable infant mortality, the US had a 69% higher rate of infant mortality. In their report, MacDorman et al. concluded that 39% of this elevated infant mortality compared to Sweden was explained by rate of preterm birth, of which the US had significantly higher percentage of than the next leading nation (9.8% vs. 8.9% in Hungary)(59).

Due to their strong association with health risk and infant mortality, preterm birth status and gestational age at birth are regarded as reliable markers of neonatal health. Analysis of 2010 US birth/death data by Matthews et al. found that 35.2% of all infant death was due to preterm birth-related complications (61). Likewise, investigation into the causes of excess infant mortality in the Southern United States found preterm birth to be the second leading contributor (50). Further analysis of 2010 infant mortality rates by period of gestational age showed that infant mortality rate decreased with increasing gestational age, with preterm infants <32 weeks gestational age having the highest risk of death (61). This trend reflects the fact that infants that spend more time *in utero* achieve greater physiological development, better preparing them for life outside of the womb and enhancing their survivability.

Like gestational age at birth, birth weight has been found to be a reliable marker of neonatal health. While birthweight is closely associated with gestational age, the two do not exactly correspond, nor are low birth weight and preterm status mutually exclusive. Low birth weight is most often associated with preterm birth or intrauterine growth restriction (43), and is also partially responsible for the increased rates of infant morbidity and mortality in the US. In the aforementioned analysis of 2010 US birth/death data, infants who were of low birth weight (<2500 g) had a mortality rate 24 times higher than infants of healthy weight (≥2500 g). Mortality rate for infants of very low birth weight (<1500 g) was in turn 100 times higher than those of healthy weight. Infants of the lowest birth weight category (<1000 g) made up only 0.7% of US births in 2010, yet they were responsible for 47% of all infant deaths that year (61).

Although low birth weight tends to garner greater attention regarding its negative effects on birth outcome, neonate macrosomia (birth weight >4000 g) is also associated with poor birth outcomes and increased neonatal health risk. In a cohort study of over 5 million mothers of live singleton or still-births the perinatal health consequences of high birth weight were assessed. While infants of 4000-4499 g were not found to be at increased morbidity or mortality, infants born at 4500-4999 g had greater risk of still-birth, mortality, injury during delivery, and neonatal asphyxia compared to infants of healthy weight. When infants exceeded a birth weight of 5000 g, these risks further increased and a heightened risk of sudden infant death syndrome was also exhibited (84).

In addition to their associations with survivability and neonatal health, birth weight and preterm status have implications on the cost and length of infant stay in the hospital or its Neonatal Intensive care Unit. In 2011, the average length of stay and cost for a preterm infant was 14.3 days and $21,500, compared to only 3.4 days and $3,200 for the average infant.

Similarly, infants of low birth weight had an average hospital stay of 17.7 days with an average cost of $27,200 (57). According to a report compiled by the US Institute of Medicine in 2007, the total cost burden on US healthcare due to preterm birth amounts to approximately $26 billion annually (7).

Among the methods used to assess neonatal health at the time of birth, perhaps the most well-known is the Apgar scoring system. Developed in 1952 by Dr. Virginia Apgar, this system allows rapid assessment of neonatal health using skin color, heart rate, reflexes, muscle tone, and respiration effort. Each component is assigned a score of 0-2, with the total sum constituting the final Apgar score (1, 67). Apgar score is assessed at 1 and 5 minutes post-delivery, with the 1-minute score serving as a measure of the infant's tolerance of the birthing process and the 5 minute score representing how well the infant is tolerating its new environment outside its mother's womb (5).

Despite its development over 60 years ago, the Apgar scoring system continues to be validated, with several studies focusing on its use on preterm infants (58, 48). In preterm infants Apgar score has been found to be closely associated with multiple measures of neonatal health and birth outcome. In a cohort study of 1105 preterm births, birth weight and gestational age were found to be associated with increasing Apgar score at both 1 and 5 minutes. Apgar scores of <3 at 1 minute and <6 at 5 minutes were also significantly associated with low birth weight, gestational age, and mode of delivery (48). In a study of the association between Apgar score and infant mortality, Li et al. found that births with low 5-minute Apgar scores incurred high mortality rate, particularly when they were preterm. Among births with high Apgar score, mortality rate decreased with advancing gestational age. In analyzing these patterns using a large diverse population, Li et al. concluded that the Apgar score was valid for both term and preterm infants, as well as both non-Hispanic Black and non-Hispanic white populations (58).

Among the measurements collected at birth, the circumference of infant head, chest, and abdomen are commonly recorded. Infant head-to-abdomen circumference ratio is a valuable tool that allows assessment of growth proportionality in unborn fetuses and neonates (21). Typically, a symmetrical head-to-abdomen circumference ratio is associated with normal healthy infant growth and development, with an elevated ratio serving as risk factor for adverse birth outcomes. Study of premature infants born <33 weeks gestational age found that occurrence of asymmetrical head-to-abdomen circumference ratios during development was associated with severe intrauterine growth restriction (68). Furthermore, elevated head-to-abdomen ratio has been associated with increased perinatal mortality, low birth weight, and a decreased gestational age at birth (28).

Racial Disparities in Birth Outcomes

Disparities in preterm birth and other adverse birth outcomes in racial and ethnic populations have been long-standing and well-documented in comparative analysis of United States birth data. These disparities are often the most pronounced in non-Hispanic Black populations, particularly when compared to Caucasian populations (60, 69, 16, 29, 26). For this study, we are looking primarily at racial differences in preterm birth and low birth weight, as well as APGAR scores and head-to-abdominal circumference ratios.

As is the case with the general US population, one of the greatest contributors to infant mortality amongst non-Hispanic Blacks is preterm birth. In the United States, non-Hispanic Blacks have historically suffered from significantly higher rates of preterm birth and infant death due to preterm-related complication than any other racial group (Figure 1)(69, 61). Black women are approximately 60% more likely to give birth preterm compared to White mothers (63), and carry significantly higher risk of a previable birth (<26 weeks gestational age)(29). This elevated risk of preterm birth affects women of all levels of socioeconomic status of the non-Hispanic Black population, ranging from mothers residing in low-income urban areas (66) to those in high income rural neighborhoods (26).

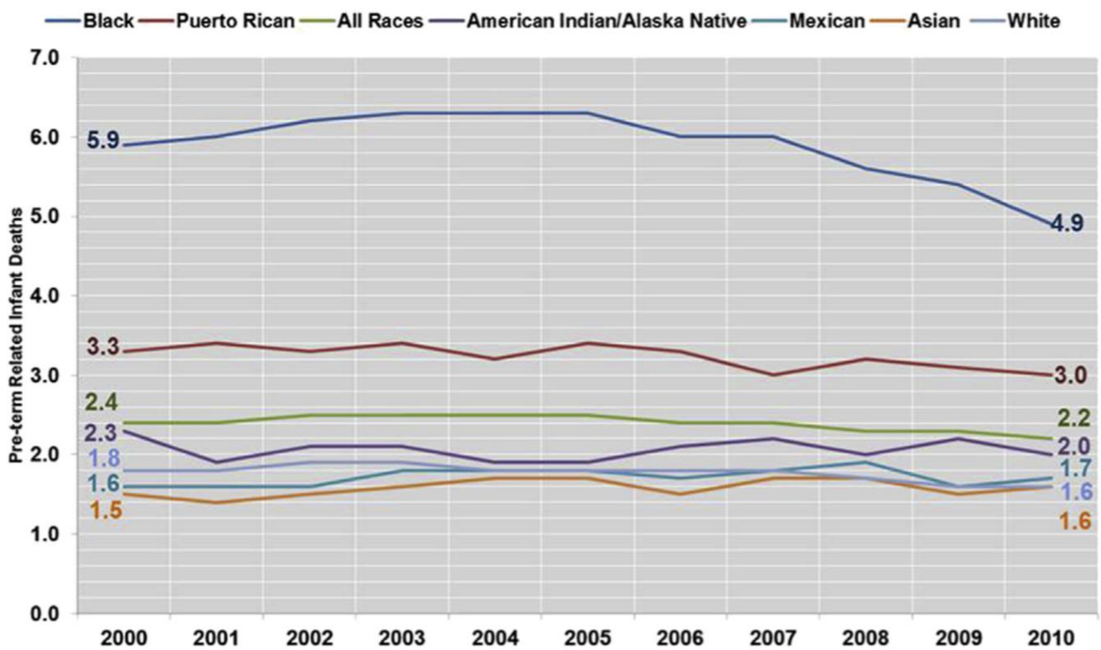

Figure 1. Preterm-related infant deaths per 1,000 live births by racial/ethnic group, 2000 to 2010. (From Mathews TJ, McDorman MF. Infant mortality statistics from the 2010 period linked birth/infant death data set. Natl Vital Stat Rep 2013;62(8):1-26.)

From 1989 to 2006, the racial disparity in preterm birth between non-Hispanic Blacks and other races decreased on both absolute and relative scales. However, a cohort study of racial and ethnic disparities in infant mortality by Rossen and Schoendorf found that the decreasing preterm birth disparity during this period was primarily due to worsening rates of preterm birth amongst Hispanics and Caucasians; as opposed to marked improvements in non-Hispanic Black preterm birth rates (69). In fact, during the late 90s and early 2000s, preterm birth rates amongst non-Hispanic Blacks were on the rise, albeit at a slightly slower rate than their Hispanic and non-Hispanic White counterparts (60). In 2006, preterm birth amongst non-Hispanic Blacks and non-Hispanic Whites peaked, with both in steady decline through 2013 (60, 19, 20). Although this recent decline is promising, the racial disparity in preterm birth rates has remained constant, with non-Hispanic blacks still at significantly higher risk compared to other races (19)(Figure 2).

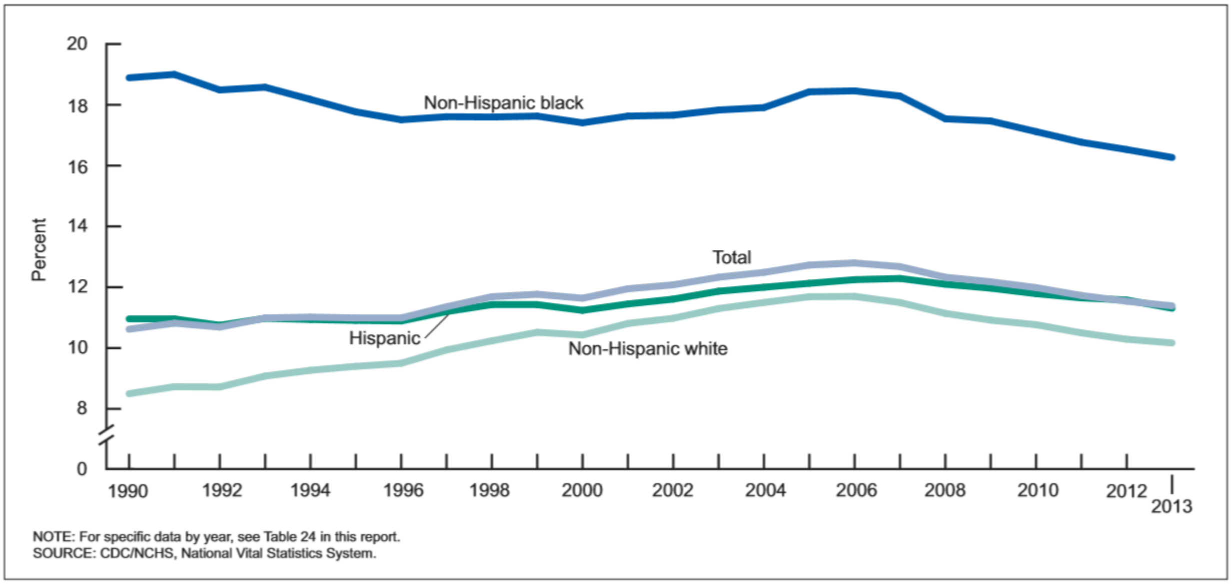

Figure 2. Preterm birth rates, by race and Hispanic origin of mother: United states, 1990-2013 (From Martin JA, et al. Births: Final Data for 2013. Natl Vital Stat Rep 2015;64(1):10.)

Low birth weight amongst non-Hispanic Blacks is also subject to significant racial disparity (61, 43, 16, 28, 77). In 2013, the rate of low birth weight amongst non-Hispanic black infants was more than double that of non-Hispanic White infants (11.46% vs. 5.18%)(61). While much of this racial disparity in low birth weight is due to elevated rates of preterm birth, it can also be caused by intrauterine growth restriction, something which non-Hispanic Blacks are also at an elevated risk of occurring (43). Interestingly, racial disparity in macrosomia trends in the opposite direction, with Caucasians being at higher risk than non-Hispanic blacks (60).

As with preterm birth and birth weight, racial disparities also exist within Apgar scores of non-Hispanic Black and non-Hispanic White infants. Analysis of Apgar scores among a cohort of 1105 preterm infants found that both mean 1-minute and 5-minute Apgar scores for black infants were significantly lower than that of white infants (7[4,8] and 8[7,9] vs 5[3,7] and 8[6,9])(48). With higher scores, Black infants had a higher survival rate during the neonatal period (birth to 1 month) but a lower rate in the post-neonatal period (58).

When discussing racial disparities in birth outcome and neonatal health, biracial parentage must also be addressed. Infants of biracial non-Hispanic Black and Caucasian have been shown to carry increased risk of adverse birth outcomes such as premature birth and low birth weight compared to Caucasian infants, but lesser risk than non-Hispanic Black infants (42, 37, 76). Although Black paternal race has been found to be a predictor of very low birth weight in biracial infants (Fulda), Collins et al. found that infants born to Black mothers and White fathers had greater odds of low birth weight than those of White mothers and Black fathers (27). These findings are supported by those of Srinivasjois et al, who performed meta-analysis of eight separate studies encompassing over 26 million births in order to review birth outcomes of mixed race infants to those of homogeneous racial parentage. This analysis found that in addition to biracial infants having a risk of adverse birth outcome between that of homogeneous White and homogeneous Black infants, maternal race had greater influence than paternal race in regards to birth outcome (76).

Proposed Reasons for Racial Disparities

The reasons behind preterm birth and birth outcome disparities are complex and include a multitude of interacting factors not entirely understood. Compelling data exists for both behavioral (35, 52, 41) and socioeconomic/sociostructural (26, 35, 39, 40) determinants, indicating that an intersection of the two may be at work. Genetic variation may also be a factor, as illustrated by genotype study (36) and investigations into the risk of biracial offspring (16, 76, 42, 37, 27).

Socioeconomic factors serve as indirect influences on birth outcome and infant health, and act through mediating variables such as access to medical care, education, and stress levels (35). In addition to having greater instances of preterm birth, southern regions of the US have poorer economic factors than the rest of the country. Hirai et al. (50) found these areas have a disproportionately high population of Black births, which account for 59% of the regional disparity. The effect of increased socioeconomic detriments and racial inequality on the health of African Americans is encapsulated in the “weathering hypothesis” proposed by Geronimus et al. (40). When applied to non-Hispanic Black mothers, the weathering hypothesis states that maternal health and birth outcome are influenced by socioeconomic pressures and social stigmatisms experienced throughout gestation and throughout a woman’s entire life (39, 29). It is worth noting that although those of Latino descent in the United States share similar socioeconomic factors with non-Hispanic Blacks, they have a noticeably lower risk of adverse birth outcome (16, 35, 63). This would indicate that while Latinos and non-Hispanic Blacks share many socioeconomic traits, there are traits exclusive to non-Hispanic Blacks that yield a greater degree of health detriment that require further study (16).

Moving beyond socioeconomic factors, the role of heredity appears to play a part in racial disparities as well. As discussed in the prior section of this literary review, children of biracial parentage have been shown to have higher risk of adverse birth outcomes than those of homogeneous White parentage, yet less than those of homogeneous Black parentage (76, 42).

Although studies have detailed influence of paternal race, the general consensus is that maternal race had the most significant influence on birth outcome (76). However it is also worth noting that disparities in biracial birth outcomes could also be the result of ethnic socioeconomic factors such as culture, diet, access to education and medical care, and poverty.

The precedent of ethnic background superseding racial background is supported by the decreased risk of preterm birth and low birth weight amongst Black Hispanic women when compared to that of non-Hispanic Black counterparts. These Black Hispanic women share the same African ancestry as non-Hispanic blacks, yet hail from nations such as Cuba, Puerto Rico, and the Dominican Republic (16). The risk of adverse birth outcome in these Black Hispanic mothers is more akin to that of their Latina/Hispanic counterparts than that of non-Hispanic Blacks. Another example comes from epidemiological research of the birth weight of US-born Blacks, African-born Blacks, and US-born Whites. Despite sharing the same racial background, US-born Blacks had a significantly higher incidence of low birth weight and lower mean birth weight than African-Born blacks. Although incidence of low birth weight was still higher in African-born Blacks than US-born Whites, the two groups had near-identical mean birth weights (3446 g vs. 3333 g)(28).

Behavioral factors prior to and during pregnancy have been shown to influence pregnancy outcomes and have thus been a topic of investigation in ascertaining the causes of racial disparities in birth outcomes (35, 71, 41, 81). However, the results of behavioral factors contributing to racial disparities are often mixed. Through analysis of health behaviors, socioeconomic factors, infant survival, and time of neonatal/post-neonatal deaths, one study (35) found that although behavioral factors were partially responsible for racial disparities in infant mortality and adverse birth outcomes, socioeconomic factors served as more powerful determinants. Likewise, study of preconception health indicators in racial populations was unable to explain racial disparities in low birth weight (77). These findings, coupled with that of Finch et al., indicated that behavioral factors during a pregnancy carry greater influence on pregnancy outcome than those prior to pregnancy.

Physical activity behaviors are of particular note to this study. Although data on the prevalence of exercise during pregnancy among various races can be difficult to ascertain, Whitaker et al. found that African American women less frequently expressed intention to meet physical activity guidelines during pregnancy during a qualitative interview study (81). This is supported by Evenson and Wen, who found that objectively measured moderate to vigorous intensity physical activity was less prevalent amongst non-Hispanic Black women than among Caucasians (32). Evidence is growing to support that physical activity during pregnancy has the potential to foster more favorable birth weight and gestational age, and can help attenuated racial disparities in adverse birth outcome. Non-Hispanic Black mothers that fail to engage in such activity do not reap these benefits, and may suffer increased risk of adverse birth outcome because of it.

Safety of Physical Activity During Pregnancy

A common concern for mothers is the safety of exercise during pregnancy, with mothers often expressing fear for their child's health and the possibility of inducing preterm labor (33, 31). This trepidation can often result in women who do engage in physical activity failing to meet exercise recommendations and guidelines (41). Despite these fears still being commonplace in modern times, aerobic (30, 25, 33), resistance (82, 12), combination (circuit) and flexibility/yoga (13) exercise have all been proven to be safe during pregnancy. However, gestational exercise guidelines from the American College of Obstetricians and Gynecology (ACOG) must be followed in order to ensure safety of both a mother and her child (2). These guidelines consist of relative and absolute contraindications to exercise (3) (Table 1).

Absolute Contraindications to Aerobic Exercise During Pregnancy	Relative Contraindications to Aerobic Exercise During Pregnancy
Hemodynamically significant heart disease	Severe anemia
Restrictive lung disease	Unevaluated maternal cardiac arrhythmia
Incompetent cervix/cerclage	Chronic bronchitis
Multiple gestation at risk for premature labor	Poorly controlled type I diabetes
Persistent second or third trimester bleeding	Extreme morbid obesity
Placenta previa after 26 weeks gestation	Extreme underweight (body mass index <12)
Premature labor during the current pregnancy	History of extremely sedentary lifestyle
Ruptured membranes	Intrauterine growth restriction in current pregnancy
Pregnancy induced hypertension	Poorly controlled hypertension/preeclampsia
	Orthopedic limitations
	Poorly controlled seizure disorder
	Poorly controlled thyroid disease
	Heavy smoker

Table 1. Relative and Absolute Contraindications to Aerobic Exercise During Pregnancy. (ACSM's guidelines for exercise testing and prescription. 8th ed. Philadelphia (PA): Wolters Kluwer and Lippincott Williams & Wilkins; 2010. p. 185.

For women with uncomplicated pregnancies and no contraindications to exercise, ACOG recommends 150 minutes of moderate intensity physical activity each week. Regarding exercise modality, ACOG recommends that women engage in activities such as walking, low-impact aerobics, modified yoga, running/jogging, and strength training, while avoiding contact sports and activities with a high risk of falling (2).

Effects of Physical Activity During Pregnancy on Birth Outcome and Neonatal Health

Exercise during pregnancy has been shown to produce a multitude of health benefits for both a mother and her child. Besides benefits such as reduced risk of gestational diabetes and maternal weight gain, both of which can negatively impact infant health, exercise during pregnancy is associated with more favorable gestational age and weight at birth (53, 56, 23, 54).

Through the use of both objectively and subjectively measured physical activity, the influence of exercise on birth outcome has been studied extensively. Analysis of birth records and self-reported physical activity among 87,232 participants of the Danish National Birth Cohort found a significant reduction in preterm birth amongst the 40% of women who reported being active (53). Review of 27 publications examining leisure-time physical activity and gestational age at birth by Kahn et al. found 11 studies reporting a lower risk of preterm birth among women who engaged in physical activity (56). While 14 of the studies analyzed found no association between physical activity and improved gestational age at birth, it is worth noting that more than half of these studies involved self-reported activity levels collected up to 5 years post-delivery or exercise interventions that failed to meet physical activity guidelines set by ACOG.

Evidence of the protective effect of exercise on reducing preterm birth is not isolated to studies of the general public. Specifically, non-Hispanic Blacks have been shown to achieve this protective effect with increased levels of leisure time physical activity. In analyzing self-reported physical activity of non-Hispanic Black women who participated in the Baltimore Preterm Delivery Study, Sealy-Jefferson et al. found that women who walked with purpose more than 30 minutes a day on most days of the week had lower prevalence of preterm birth than those that did not (71). It is important to note that walking for purpose satisfies ACSM's definition of moderate intensity physical activity (3, 45), and that performing 30 minutes per day on most days of the week would meet the recommendation of 150 minutes per week set by ACOG.

Although a multitude of studies have linked maternal physical activity to increased gestational age and reduced rates of preterm birth, there is a gap in the current literature as to whether preterm infants exposed to maternal physical activity may receive health benefits compared to those born to sedentary mothers. Besides reductions in preterm birth, maternal physical activity is associated with other infant health benefits such as more favorable birth weight (53, 14, 47), reduced time spent in labor (15), and quicker delivery (46). It stands to reason that infants born preterm may still receive benefits from maternal physical activity, making further research into this topic a worthwhile endeavor.

The effect of maternal physical activity on infant birth weight is particularly interesting, as evidence exists for a multidirectional effect. Leisure time physical activity during pregnancy has been associated with heavier infants and a reduced risk of low birthweight both among general populations (23, 47) and among non-Hispanic Black populations (52). Conversely, maternal physical activity is also associated with lighter, leaner babies (24) as well as reduced risk of macrosomia (14, 78). This mediating effect on birth weight is perhaps best evident in the work of Juhl et al. in which exercising women had a decreased risk of having a child that was small for gestational age or large for gestational age (54). It would appear this effect carries over to low birth weight and macrosomia as well, with infant birth weight shifting towards the optimal weight range with exposure to exercise.

Although the benefits of maternal physical activity and exercise on infant health are well documented, the prevalence of maternal physical activity remains troubling. In addition to the aforementioned racial disparities in maternal physical activity levels, women often report engaging in less physical activity with pregnancy (32) and as they progress further into a pregnancy (66). Additionally, there exists notable differences in the prevalence of different exercise modalities among female exercisers. Among the general population, multiple studies have found females to be less likely to engage in strength training exercises, due to fears of becoming muscular and perceived as masculine (51, 79, 83). This reluctance to engage in strength training only furthers during pregnancy, due to fears of harming their child or inducing preterm labor (30, 33). As previously mentioned however, these fears are unfounded so long as the resistance training program is properly designed and implemented by a trained professional (70). The ENHANCED by Mom program is unique in this regard, as all exercise participants engage in an intervention designed and supervised by staff trained in kinesiology at East Carolina University's College of Health and Human Performance.

Effect of Race on Exercise Training Adaptations

Compelling evidence exists for race lacking influence on the degree of training response a person gains through exercise (18, 73, 62). Much of this data comes from the HERITAGE Family Study, one of the few large-scale studies of exercise response to include Black and White participants of both genders and a large range of ages. Skinner et al. found race to have no influence on improvements in aerobic fitness, with both Black and White races producing high, medium, and low responders following 20 weeks of standardized training (73). Likewise, race was found to account for less than 1% of variation in changes to subject's heart rate and blood pressure during submaximal exercise among healthy adults (18). Although race has found to have little influence on exercise response in the general population, there is a current gap in the literature as to whether or not this is the case among infants exposed to maternal exercise. While prior training was associated with varying response to exercise in studies of the general population, exposing an infant to the effects of exercise during the earliest point of its life negates the concern of prior training adaptations.

Summary

Racial disparities in birth outcomes such as preterm birth and birth weight are most profound among non-Hispanic Blacks in the United States. The reasons behind these racial disparities are complex and not fully understood, with neither behavioral nor socioeconomic factors fully explaining them. As preterm birth and low birth weight having substantial impact on life expectancy and healthcare spending, these birth outcomes and the racial disparities they carry are of great importance to public health. While exercise has been shown to decrease preterm birth, macrosomia, and low birth weight in the general population and among non-Hispanic blacks, these studies are often based on self-reported physical activity rather than objectively measured exercise or fail to meet ACOG recommended exercise levels. Additionally, there exists a current gap in the literature as to whether or not the benefits of maternal exercise are similar among non-Hispanic Black and Caucasian infants. If exercise is to be prescribed as a low-cost and non-pharmacological method for improving birth outcomes in high-risk populations such as non-Hispanic Blacks, then the effectiveness of maternal exercise intervention in fostering healthy infants amongst various races must be understood. This study aims to compare the degree of response maternal exercise has on fostering favorable birth outcomes between newborns of non-Hispanic Black race and Caucasian race using a structured and objectively-measured exercise intervention that meets current physical activity guidelines for pregnant women.

Chapter III. Study Design and Methods

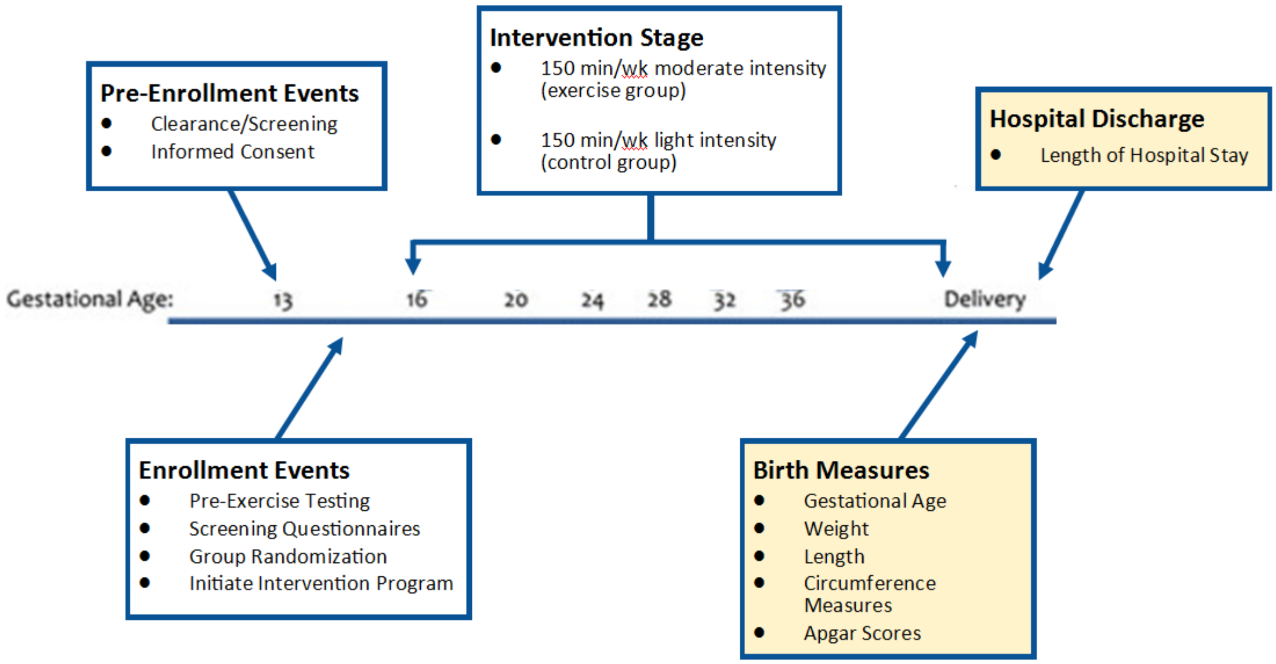

Figure 3. ENHANCED by Mom Study Timeline

Study Recruitment and Participants

This study was a retrospective analysis of a randomized control study, with data collected from records of the ENHANCED by Mom project (Figure 3). Therefore, this study was subject to additional limitations and delimitations of the ENHANCED study design.

Participants recruited to the ENHANCED study were healthy women with low-risk singleton pregnancies that were cleared to engage in regular physical activity by their physician after being screened for contraindications to exercise. Recruitment criteria was also delimited to those of 18-40 years of age; a pre-pregnancy BMI of 15.8-34.9; no usage of alcohol, tobacco, or recreational drugs; and not taking medications for mental health disorders or chronic disease. An exclusion criteria was also set for those with pre-existing hypertension, diabetes, cardiovascular disease, or any comorbidities that may affect fetal growth or well-being. Subjects were recruited via mass emails, flyers placed in the Greenville NC area at local obstetrics/gynecology clinics.

Participant screening and clearance occurred prior to 16 weeks gestation, with participants required to provide consent and a letter from their physician clearing them to engage in regular physical activity, as well as complete a treadmill testing visit. Participants did not begin exercising until 13-16 weeks gestation so as to reduce the likelihood of morning sickness during training or miscarriage while enrolled in the study. Following the initiation of the exercise intervention at 13-16 weeks gestation, participants continued training until delivery. All study protocols were approved by the East Carolina Institutional Review Board.

Initial Fitness Testing

After providing consent and physician clearance, all participants enrolled in the ENHANCED study performed initial fitness testing consisting of a modified Balke treadmill test (Figure 4). The test is intended to determine each participant's target heart rate zone; to be used during their exercise training to accurately assess exercise intensity. The Balke protocol was selected for its submaximal nature, and due to it being validated amongst pregnant populations (64).

Before each treadmill test is administered, a ParvoMedics TrueMax 2400 metabolic cart was calibrated by a trained member of the study according to manufacturer specifications. Gas calibration was completed using a standard gas canister containing 16% oxygen, 4% carbon dioxide, and 80% nitrogen, and flow meter calibration was performed using a standard 3 liter syringe. Following calibration of the metabolic cart, each participant's height, weight, resting heart rate, and resting blood pressure were recorded. Each participant was given a description of the testing protocol before being fitted with a Polar heart rate monitor and breathing circuit. Each test began with 3 minutes of resting VO2 measurement as a baseline measurement, after which the Balke protocol began. Participant heart rate, blood pressure, and rating of perceived exertion were recorded in the last 30 seconds of each stage. Participants continued to progress through the protocol stages until either reaching 75% of their heart rate reserve, signaling the researcher to end the test, or completing all stages of the protocol. Once the testing protocol was ended, a cool down phase was conducted to allow the participant's heart rate and blood pressure to return to normative values.

Modified Balke Protocol *(VO_2peak pre-exercise testing)*						
Stage	Minute	Speed (mph)	Grade (%)	HR (bpm)	BP	RPE
Warm-up	0-5	3.0	0			
1	0-2	3.0	0			
2	2-4	3.0	2			
3	4-6	3.0	4			
4	6-8	3.0	6			
5	8-10	3.0	8			
6	10-12	3.0	10			
7	12-14	3.0	12			
8	14-16	3.2	12			
9	16-18	3.4	12			
10	18-20	3.6	12			

Figure 4. Modified Balke Protocol

Randomization and Exercise Protocol

After completing their treadmill testing session participants were randomly assigned to one of three exercise modality groups (Aerobic, Circuit, or Resistance) or a non-exercise control group. Participants of all exercise groups were required to complete 3 supervised training sessions per week at one of two approved university facilities. Exercise sessions were scheduled in advance, with sessions available from 7am to 7pm on weekdays and 8:30-11:00am on Saturdays.

At the start of each exercise session, participants were fitted with a Polar heart rate monitor and wrist-watch to assess heart rate prior to, during, and after their training session. Before performing a 5 minute aerobic warm up, participants were seated and their resting heart rate and blood pressure was recorded by a member of the research team. Aerobic participants were supervised in performing 45 minutes of moderate intensity (60-85% HRmax) exercise via treadmill, elliptical, rowing machine, or recumbent bike. In order to ensure that participants remained within the appropriate heart rate zone for moderate intensity equipment speed, resistance, and incline were manipulated. Aerobic participants were allowed to complete their training session using multiple pieces of exercise equipment, so long as they remained within their designated heart rate training zone.

Both the circuit and resistance groups engaged in 45 minutes of supervised moderate intensity exercise as well, with the resistance group doing so through the use of free weights, weight machines, and resistance bands, and the circuit group undergoing alternating bouts of 4-6 resistance exercises and 5 minute bouts of aerobic exercise. Both resistance and circuit training participants performed a variety of resistance exercise that worked all major muscle groups. In order to keep circuit and resistance participants at a moderate intensity, participants were encouraged not to spend excessive time resting between sets or when moving between exercise machines. Additionally, heart rate measures were supplemented with rating of perceived exertion.

The intensity and cumulative weekly exercise duration of each exercise intervention group meets the minimum physical activity recommendation (150 min/wk moderate intensity) set by the American College of Obstetricians and Gynecology (ACOG) for healthy pregnant women, as well as the minimum recommendation for the general population as described by ACSM (150 min/wk moderate intensity). The non-exercise control group performed a 5 minute warmup followed by 45 minutes of low intensity (<40% Hrmax) stretching and breathing exercises. (Figure 5). At the end of each training session, participants would again be seated so that measures of post-exercise heart rate and blood pressure could be recorded. Additionally, average heart rate during the participant's training session was also recorded.

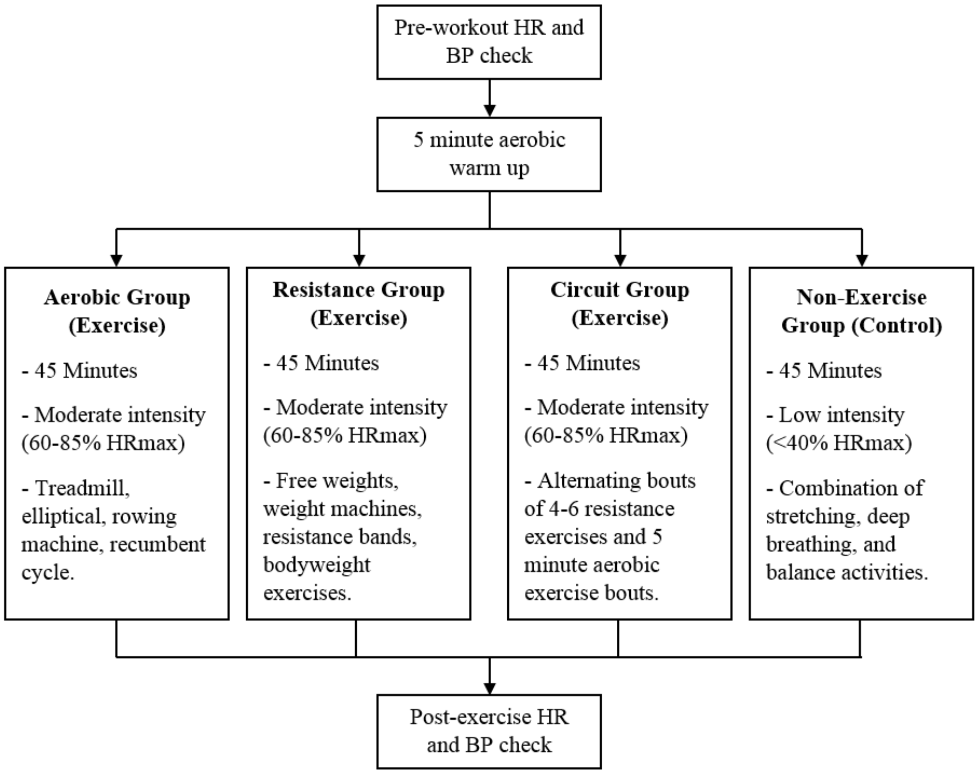

Figure 5. Maternal Training Protocol Outline

Maternal Measures

Maternal BMI, age, race, and parental education levels were obtained from screening questionnaires completed by each mother upon being recruited to the study. In order to assess parental education levels, the screening questionnaire contained questions as to both maternal and paternal education. Education was assessed using a scale ranging from 1 to 7 in which; 1=partial high school, 2=graduate equivalent degree (GED), 3=high school degree, 4=associate's degree, 5=bachelor's degree, 6=master's degree, and 7=doctorate degree. For this study, combined parental education was used as a proxy for socioeconomic status, due to higher education correlating to higher household income and lower unemployment rate (10). Despite holding equivalent levels of education, GED and high school degree were treated as separate and unequal levels of education in analyses due to findings of reduced income and lower socioeconomic status among GED recipients by the US Department of Education (74). Exercise intervention compliance was also calculated using each participant's weekly training logs. In order to be included in per-protocol analyses, a participant must have achieved an 80% compliance level. Participants who completed the intervention with less than 80% compliance were included in intent-to-treat analyses.

Infant Birth Measures

In consenting to participate in the ENHANCED study, participants also consented to give the study access to their electronic health records. In order for the study to access birth records, participants had to deliver at Vidant Medical Center in Greenville NC. In the event that a participant gave birth at another facility, that hospital would be contacted and a formal request for their birth records would be placed. Variables obtained from birth records included gestational age (GA), birth weight (BW), birth length (BL), and measures of neonatal health at birth. Measures indicative of neonatal health were head circumference (HC), abdominal circumference (AC), 1 minute and 5 minute Apgar scores, and mode of delivery. Gestational age was used to classify each infant as preterm (<37 weeks gestational age) or full term (≥37 weeks gestational age), and HC and AC measures were used to calculate infant head-to-abdominal circumference ratios (HC/AC). Mode of delivery was used to classify each birth as cesarean or non-cesarean delivery. From hospital birth records we were also given each infant's date and time of birth, as well as the date and time of their discharge from the hospital. Using these two values, we were able to calculate the length of hospital stay for each infant.

Statistical Analyses

Statistical analyses were completed using Statistical Package for the Social Sciences (SPSS) version 22.0. Alpha level was set *a priori* at $p<0.05$ for all analyses. Means comparisons were used extensively throughout our analyses. Prior to means analyses, normality of variables were determined using Shapiro-Wilk tests. Independent t-tests were used to compare means of normally distributed data, while Mann-Whitney U tests were performed to compare means of data that did not fit a normal distribution. Per-protocol analyses were performed using participants that met an inclusion criteria of 0.80 compliance. Intent-to-treat analyses were also performed, with these utilizing all non-drop participants regardless of their compliance level. In addition to initial means comparisons of the parental measures of control and exercise participants, three separate series of analyses were performed; each of which correlated with one of our three hypotheses. As this study focused on Caucasians and non-Hispanic Blacks, participants of other races (Hispanic, Asian, Brazilian) were excluded from our statistical analyses.

In order to test our hypothesis that non-Hispanic Black and Caucasian infants born to exercisers would have similar gestational age and measures of neonatal health at birth we used a combination of means comparisons, proportion comparisons, and both binomial logistic and linear regressions. Independent t-tests and Mann-Whitney U tests were used to compare maternal measures of Caucasian exercisers to those of non-Hispanic Black exercisers as well as to compare the birth outcome measures of their infants. Effect sizes for Mann-Whitney U tests were calculated using eta-squared, while the effect size of independent t-tests were performed using Hedge's g when the sample size was less than 20 and Cohen's d when the sample size exceeded 20. Chi-square tests were utilized to compare the rates of low birth weight, cesarean delivery, and preterm birth among Caucasian and non-Hispanic black exercisers. Comparisons of the rates of low birth weight, cesarean delivery, and preterm birth were also performed for Caucasian and non-Hispanic Black control participants in order to determine if there were any racial disparities among non-exercise control participants that may have been attenuated among exercisers.

Binomial logistic regressions were used to investigate the ability of race and other covariates to predict categorical birth outcomes of preterm birth, low birth weight, and cesarean delivery, and linear regression analyses were completed to investigate the ability of race and other covariates to predict continuous birth outcomes of gestational age, hospital stay, HC/AC, birth weight, and Apgar scores. In order for categorical variables such as race and exercise modality to be used in linear and logistic regressions, a dummy variable coding system (also known as a Boolean indicator or binary variable system) had to be implemented. This dummy coding system allowed one categorical variable outcome to be designated as a reference variable, to which other possible outcomes would then be compared to.

In order to test our hypothesis that preterm infants born to exercisers would show improved markers of health and reduced hospital stay compared to preterm infants born to control participants, means comparisons were again performed. Independent t-tests and Mann-Whitney U tests were used to compare hospital stay and birth measures of preterm exercise and preterm control infants. These comparisons were completed for both non-Hispanic Black and Caucasian races, as well as for all participants, regardless of race. After calculating the difference in hospital stay between preterm exercise and preterm control infants, cost analyses were performed to investigate the potential healthcare savings among mothers whose preterm infants were exposed to maternal exercise.

To test our final hypothesis; that non-Hispanic Black and Caucasian exercisers would have similar compliance levels, both overall and modality-specific compliance levels were compared between races. Both overall compliance and modality-specific compliance were compared between races using Mann-Whitney U tests. Comparisons of modality-specific compliance among Caucasian exercisers were compared using an ANOVA and post hoc Tukey tests, while comparisons among non-Hispanic black exercisers were completed using a Mann-Whitney U test. We also compared the maternal characteristics and birth measures of compliant and noncompliant exercisers using independent t-tests and Mann-Whitney U tests. Linear regressions were also used to investigate the influence of maternal characteristics and exercise modality on participant compliance.

Chapter IV. Results

Participants

Of the participants (N=178) initially enrolled in the study, 58 were randomly assigned to control and 91 were assigned to one of the exercise groups. Of the 91 participants assigned to exercise, 52 achieved a 0.80 compliance level (Figure 6).

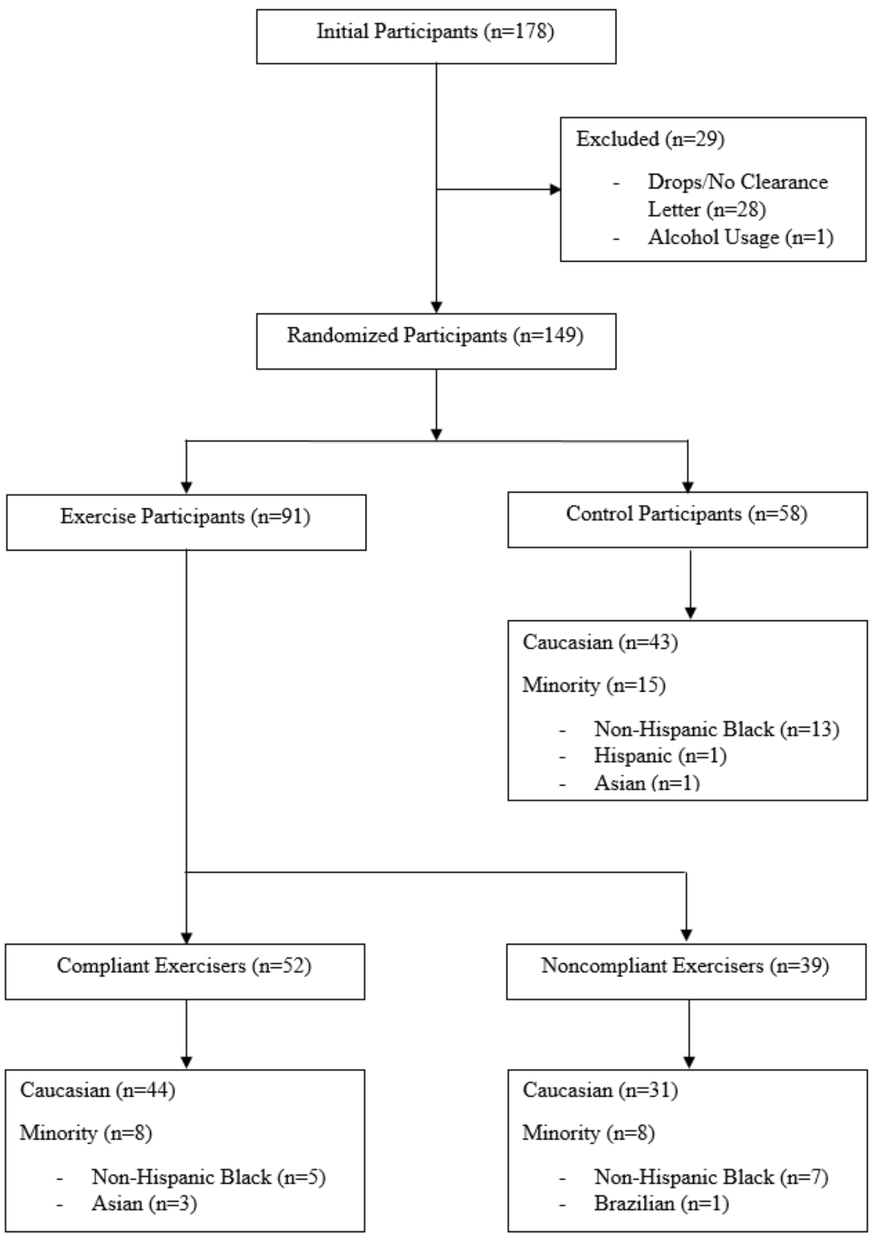

Figure 6. Consort Diagram of Study Participants

The average participant was 30.27±4.12 years of age, had a BMI of 24.75±4.25, and had an education level equivalent to a bachelor's degree. The average participant's partner held an associate degree, resulting in a combined parental education level that fell just short of a bachelor's degree equivalence. Table 2 illustrates the average participant measures for both control and exercise participants specifically. No significant differences in parental measures were observed between control and exercise groups.

Among exercisers, a greater proportion of participants were randomly assigned to aerobic exercise than to either circuit or resistance exercise. This trend was found to extend to all racial groups, with NHB participants having a disproportionately low randomization to resistance exercise compared to that of Caucasian Exercisers (Table 3). This was the result of random chance, due to the non-stratified randomization model used by the ENHANCED study.

Variable	Control	Exercise	p	Effect Size
Age (years)	29.78±4.53	30.56±3.89	0.624[†]	0.002
Pre-pregnancy BMI	25.44±5.01	24.42±3.73	0.444[†]	0.005
Maternal Education[1]	5.12±1.14	5.55±1.00	0.170[†]	0.027
Parental Education[2]	8.97±3.19	10.28±2.14	0.105[†]	0.035

Table 2. Parental Measures – Control vs. Exercise Participants

BMI – Body Mass Index (kg/m^2); Highlighted cells indicate normally distributed values
[1]Maternal Education: 1=Partial HS, 2=GED, 3=HS diploma, 4=Associate, 5=Bachelor, 6=Masters, 7=Doctorate
[2]Parental Education: 2=Partial HS, 4=GED, 6=HS diploma, 8=Associate, 10=Bachelor, 12=Masters, 14=Doctorate
[†]Analysis of nonparametric data completed using Mann-Whitney U tests

	Caucasian (n=75)	NHB (n=12)	All Exercisers (n=91)
Aerobic	41/75 = 54.7%	10/12 = 83.3%	53/91 = 58.2%
Circuit	14/75 = 18.7%	2/12 = 16.7%	16/91 = 17.6%
Resistance	20/75 = 26.7%	0/12 = 0%	21/91 = 23.1%

Table 3. Distribution of Exercise Participants Across Exercise Modalities

Hypothesis #1 Analyses – Racial Disparities in Birth Outcome among Infants Born to Exercisers

Parental Measures

In order to compare parental measures between Caucasian and non-Hispanic Black participants, exercise participants were divided into groups based on their racial background. Due to this investigation focusing on the effects of exercise, a per-protocol analysis was necessary due to the dose-response relationship between exercise and health outcomes. These analyses were restricted to exercise participants that met at least a 0.80 compliance level. After screening for compliance, 44 Caucasian and 5 non-Hispanic Black participants were identified as being compliant (Figure 6).

Table 4 depicts per-protocol comparisons between non-Hispanic Black and Caucasian participants. No significant differences were present between non-Hispanic Black exercisers and Caucasian exercisers in age, pre-pregnancy BMI, exercise compliance, education level, or combined parental education level.

Variable	Caucasian EX	NHB EX	P	Effect Size
Age (years)	31.06±2.85	34.20±4.32	0.115†	0.064
Pre-pregnancy BMI	22.78±3.18	24.55±6.01	0.954†	0.000
Compliance	0.92±0.07	0.90±0.09	0.446†	0.012
Maternal Education[1]	5.77±0.82	6.67±0.58	0.074†	0.114
Parental Education[2]	10.59±2.02	12*	0.165†	0.067

Table 4. Per-Protocol Parental Measures – Caucasian Exercisers vs. Non-Hispanic Black Exercisers

BMI – Body Mass Index (kg/m^2); EX – Exercise Participants; Highlighted cells indicate normally distributed values
[1]Maternal Education: 1=Partial HS, 2=GED, 3=HS diploma, 4=Associate, 5=Bachelor, 6=Masters, 7=Doctorate
[2]Parental Education: 2=Partial HS, 4=GED, 6=HS diploma, 8=Associate, 10=Bachelor, 12=Masters, 14=Doctorate
†Analysis of nonparametric data completed using Mann-Whitney U tests
*Of the five compliant NHB exercise participants analyzed, only one participant reported paternal education

Birth Measures

Birth measures were taken from the delivery records of the mothers described in the parental measures section of the results. The average infant born to participants in this study was delivered at 39.06±1.74 weeks gestational age and had a roughly 2.64±3.75 day hospital stay. Average infant head-to-abdominal circumference ratio was 1.11±0.09, with a birthweight of 3.37±0.54 kg and Apgar scores that increased from 8.01±1.27 at 1 minute to 8.78±0.58 at 5 minutes.

Per-protocol analyses comparing infants of Caucasian exercisers to those of non-Hispanic Black exercisers were completed (Table 5). Birth weight was found to be significantly lighter in non-Hispanic Black (p=0.036) exercisers compared to Caucasian exercisers. However, mean infant birth weight for both races were within the normal weight range. No other variables were significantly different between races.

Variable	Caucasian EX	NHB EX	p	Effect Size
Gestational Age (weeks)	39.26±2.02	38.32±1.81	0.276†	0.026
Hospital Stay (days)	2.14±1.48	1.89±0.63	0.836†	0.000
HC/AC	1.11±0.08	1.16±0.13	0.233†	0.032
Birth Weight (kg)	3.46±0.49	2.82±0.47	**0.036**	**1.325**
1 min Apgar	8.14±1.16	8.20±0.84	0.851†	0.000
5 min Apgar	8.76±0.58	9.0±0.0	0.329†	0.021

Table 5. Per-Protocol Infant Measures – Caucasian Exercisers vs. Non-Hispanic Black Exercisers

BMI – Body Mass Index (kg/m^2); EX – Exercise Participant; Highlighted cells indicate normally distributed values
†Analysis of nonparametric data completed using Mann-Whitney U tests

Low Birth Weight Among Participants

There were 9 instances of low birth weight among participants enrolled in the study. 4 infants of low birth weight were born to control participants (2 NHB, 2 Caucasian), and 5 were born to exercise participants (1 NHB, 4 Caucasian). Among the exercise participants who delivered infants of low birth weight, 3 were noncompliant (3 Caucasian). Several participants had incomplete birth records that prevented assessment of low birth weight status. Comparisons of the rate of low birth weight among participants were completed using participants with records that included birth weight (control valid n=49, compliant exercise valid n=47).

Proportions of low birth weight among Caucasians and non-Hispanic Blacks were compared among both control and compliant exercise participants (Table 6). Among control participants, non-Hispanic Blacks had a higher proportion of low birth weight compared to Caucasians that approached significance ($\chi 2=0.092$). Likewise, the proportion low birth weight of compliant non-Hispanic Black exercisers was higher than that of compliant Caucasian exercisers to a degree that approached significance ($\chi 2=0.068$). When looking at all participants by race, regardless of their randomly assigned group, non-Hispanic Blacks had a significantly higher proportion of low birth weight compared to Caucasians ($\chi 2=0.012$).

Intent-to-treat binomial logistic regressions were performed to ascertain the effect of non-Hispanic Black race and other covariates on the likelihood that a participant would deliver and infant of low birth weight (Table 7). The first regression model was constructed with NHB race and 4 other covariates as predictors of low birth weight ($p<0.001$, $R^2=1.00$). Although the overall model was significant, none of the covariates included in the model served as significant predictors of low birth weight. A second model was assembled with gestational age and compliance as predictors of low birth weight ($p<0.001$, $R^2=0.516$). In this second model, gestational age was a significant negative predictor of low birth weight ($p<0.001$, B= -1.02).

	Caucasian	NHB	Chi-Square ($\chi2$)
Control	2/40 = 5.0%	2/9 = 22.2%	0.092
Compliant Exercisers	1/42 = 2.38%	1/5 = 20.0%	0.068
Total	3/82= 3.66%	3/14 = 21.4%	**0.012**

Table 6. Proportion of Low Birth Weight within Race – Caucasian vs. Non-Hispanic Black

Model Variables	**p**	**B**	**Regression Results**
Low Birth Weight			R^2 (1.00)
-Race (NHB)	0.993	57657	
-Pre-Pregnancy BMI	1.000	0.197	Percentage Correct (100)
-Compliance	0.996	-3.089	
-Combined Education	0.997	7.766	Sig (<**0.001**)
-Gestational Age	0.993	-14.283	
Low Birth Weight			R^2 (0.516)
-Gestational Age	**0.000**	-1.020	
-Compliance	0.869	-0.181	Percentage Correct (94.9)
			Sig (<**0.001**)

Table 7. Intent-to-Treat Logistic Regression Models of Low Birth Weight

Cesarean Delivery Among Participants

There were 31 cesarean deliveries among participants enrolled in the study. 13 cesarean deliveries occurred among control participants (3 NHB, 10 Caucasian) and 17 occurred among exercise participants (3 NHB, 14 Caucasian). Among the exercise participants that delivered via cesarean, 9 failed to meet compliance (1 NHB, 8 Caucasian). Several participants had incomplete records that prevented mode of delivery from being assessed. Comparisons of cesarean delivery rate among participants were completed using participants with records that included mode of delivery (control valid n=49, exercise valid n=47).

Proportions of cesarean delivery among Caucasians and non-Hispanic Blacks were compared among both control and compliant exercise participants (Table 8). No significant differences were found between non-Hispanic Black and Caucasian participants, regardless of whether they were control participants ($\chi 2$=0.614) or exercise participants that met compliance criteria ($\chi 2$=0.153). Looking at all participants by race, regardless of their randomly assigned group, no significant differences were found in the proportion of cesarean delivery between non-Hispanic Black and Caucasian participants ($\chi 2$=0.178).

Intent-to-treat binomial logistic regressions were performed to ascertain the effect of race and other covariates on the likelihood that a participant would deliver via cesarean (Table 9). The first regression model was constructed with NHB race and 4 other covariates as predictors of cesarean delivery (p=0.146, R^2=0.177). Although the overall model failed to achieve significance, pre-pregnancy BMI was a significant positive predictor of cesarean delivery (p=0.032, B=0.174). In a follow-up model, pre-pregnancy BMI predicted cesarean delivery to a level that closely approached significance (p=0.050, R^2=0.05).

	Caucasian	NHB	Chi-Square ($\chi 2$)
Control	10/40 = 25.0%	3/9 = 33.3%	0.614
Compliant Exercisers	6/42 = 14.3%	2/5 = 40.0%	0.153
Total	16/82 = 19.5%	5/14 = 35.7%	0.178

Table 8. Proportion of Cesarean Delivery within Race – Caucasian vs. Non-Hispanic Black

Model Variables	p	B	Regression Results
Cesarean Delivery			R^2 (0.177)
-Race (NHB)	0.589	-0.554	
-Pre-Pregnancy BMI	**0.032***	0.174	Percentage Correct (77.8)
-Compliance	0.716	0.285	
-Combined Education	0.623	0.072	Sig (0.146)
-Gestational Age	0.120	-0.287	
Cesarean Delivery			R^2 (0.05)
-Pre-Pregnancy BMI	0.050	0.096	Percentage Correct (76.8)
			Sig (0.050)

Table 9. Intent-to-Treat Logistic Regression Models of Cesarean Delivery

*Although models 1 failed to achieve significance, Pre-Pregnancy BMI was a significant predictor of cesarean delivery in both models. Model 3 was constructed by removing non-significant covariates from Models 1 and 2.

Preterm Birth Among Participants

There were 14 preterm infants (Gestational Age <37 weeks) born to participants enrolled in the study. 7 preterm infants were born to control participants (2 NHB, 5 Caucasian) and 7 were born to exercise participants (1 NHB, 6 Caucasian). Among the exercise participants who delivered preterm, 3 of the Caucasian participants failed to meet compliance. Several participants had incomplete records that prevented gestational age and preterm status from being assessed. Comparisons of preterm birth rate among participants were completed using participants with records that included gestational age at time of birth (control valid n=48, exercise valid n=47).

Proportions of preterm birth among Caucasians and non-Hispanic Blacks were compared among both control and compliant exercise participants (Table 10). While no significant differences were found between non-Hispanic Black and Caucasian control participants ($\chi2=1.00$), the proportion of preterm birth rate among compliant non-Hispanic Black exercisers was significantly higher than that that of compliant Caucasian exercisers ($\chi2=0.026$). Looking at all participants by race, regardless of their randomly assigned group, no significant differences were found in the proportion of preterm birth among non-Hispanic Black and Caucasian participants ($\chi2=0.165$).

Intent-to-treat binomial logistic regressions were performed to ascertain the effect of race and other covariates on the likelihood that an infant is born preterm (Table 11). An initial model was constructed with NHB race and 3 other covariates as predictors of preterm birth (p=0.808, R^2=0.05). A follow-up model consisting of only non-Hispanic Black race as also failed to predict the likelihood of preterm birth (p=03739, R^2=0.02) (Table 19).

The influence of specific exercise modality on preterm birth was also addressed in our analyses. Of the compliant exercisers that delivered preterm, 2 were assigned to aerobic exercise, 1 to circuit exercise, and 2 to resistance exercise. Comparison of the proportions of preterm birth in each exercise modality failed to yield significant differences, as did comparisons to the proportion of the control group that delivered preterm (Table 12). A per-protocol binomial logistic regression found that exercise modality failed to predict preterm birth (p=0.635, R^2=0.022). Likewise, a per-protocol linear regression found that exercise modality was not a significant predictor of gestational age (p=0.217, R=0.188, R^2=0.013).

	Caucasian	NHB	Chi-Square ($\chi 2$)
Control	5/40 = 12.5%	1/8 = 12.5%	1.00
Compliant Exercisers	3/42 = 7.14%	2/5 = 40.0%	**0.026**
Total	8/82 = 9.76%	3/13 = 23.1%	0.165

Table 10. Proportion of Preterm Birth within Race – Caucasian vs. Non-Hispanic Black

Model Variables	**p**	**B**	**Regression Results**
Preterm Birth			R^2 (0.05)
-Race (NHB)	0.326	0.990	
-Pre-Pregnany BMI	0.873	-0.016	Percentage Correct (89.1)
-Compliance	0.608	-0.723	
-Combined Education	0.608	0.098	Sig (0.808)
Preterm Birth			R^2 (0.01)
-Race (NHB)	0.433	0.553	
			Percentage Correct (89.4)
			Sig (0.451)

Table 11. Intent-to-Treat Logistic Regression Models of Preterm Birth

Proportion Preterm (Preterm/Total)	Proportion Preterm (Preterm/Total)	Chi-Square (χ2)
Aerobic (2/30 = 6.7%)	Circuit (1/11 = 9.1%) Resistance (2/9 = 22.2%) Control (6/50 = 12%)	0.797 0.190 0.447
Circuit (1/11 = 9.1%)	Resistance (2/9 = 22.2%) Control (6/50 = 12%)	0.432 0.786
Resistance (2/9 = 22.2%)	Control (6/50 = 12%)	0.422

Table 12. Comparison of Proportion of Preterm Birth within Exercise Modalities

Linear Regressions

The first linear regression model was constructed with non-Hispanic Black race and 4 other covariates as predictors of gestational age ($p=0.004$ $R=0.500$ $R^2=0.186$). In this first model, maternal age was a significant negative predictor ($p=0.004$, $B= -0.369$) of gestational age. Exercise compliance was found to be a significant positive predictor of gestational age ($p=0.008$, $B=0.325$). These findings suggest that while increasing maternal age was associated with reduced gestational age, greater exercise dosage was associated with increased gestational age.

The second model was constructed with non-Hispanic Black race and 5 other covariates as predictors of hospital stay ($p<0.001$ $R=0.599$ $R^2=0.291$). In this model, gestational age was found to be a significant negative predictor of hospital stay ($p<0.001$, $B= -0.548$), indicating that infants with greater gestational age at birth spend less time in the hospital.

Model 3 was constructed with non-Hispanic Black race and 5 other covariates as predictors of HC/AC ($p<0.001$ $R=0.604$ R^2=0.0.295). Increasing maternal age was found to be a significant positive predictor of HC/AC ($p=0.020$, $B=0.303$) and gestational age was found to be a significant negative predictor ($p=0.01$, $B= -0.447$). This indicates that increasing maternal age and decreased gestational age at birth were both associated with less favorable HC/AC among our participants.

Our regression model of the relationship between non-Hispanic Black race and birth weight was the only model in which race was a significant predictor of birth outcome (p=0.001, B= -0.314). This fourth model was constructed with non-Hispanic Black race and 5 other covariates as predictors of birth weight ($p<0.001$ $R=0.802$ $R^2=0.605$). In addition to NHB race acting as a significant negative predictor of birth weight, parental education was also a significant negative predictor (p=0.001, B= -0.300) and gestational age was found to be a significant positive predictor ($p<0.001$, B=0.632).

Regression models investigating the relationship between Apgar scores and non-Hispanic Black race failed to reach significance (1 min p=0.201, 5 min p=0.468) regardless of the covariates included in the regressions. In the regression model of 1 min Apgar scores, maternal age was a significant negative predictor (p=0.047, B= -0.300). No variables were found to be significant predictors of 5 minute Apgar scores. Removal of nonsignificant covariates in follow up regressions to both models failed to produce significant regression models.

Model Variables	p	Std. Beta Coefficient	Regression
GA(weeks)			R (0.500)
-Race (NHB)	0.194	-0.160	
-Age	**0.004**	-0.369	R^2 (0.25)
-Pre-Pregnancy BMI	0.894	0.017	Adj. R^2 (0.186)
-Compliance	**0.008**	0.325	
-Combined Education	0.906	-0.015	Sig (**0.004**)
Hospital Stay			
-Race	0.587	0.063	R (0.599)
-Age	0.464	0.092	
-Pre-Pregnancy BMI	0.266	-0.136	R^2 (0.359)
-Compliance	0.779	-0.033	Adj. R^2 (0.291)
-Combined Education	0.647	-0.56	
-Gestational Age	**0.000**	-0.548	Sig (<**0.001**)
HC/AC			
-Race	0.830	0.025	R (0.604)
-Age	**0.020**	0.303	
-Pre-Pregnancy BMI	0.287	-0.132	R^2 (0.365)
-Compliance	0.751	-0.038	Adj. R^2 (0.295)
-Combined Education	0.616	-0.062	
-Gestational Age	**0.001**	-0.447	Sig (<**0.001**)
Birth Weight			
-Race	**0.001**	-0.314	R (0.802)
-Age	0.624	0.046	
-Pre-Pregnancy BMI	0.839	0.019	R^2 (0643)
-Compliance	0.219	0.110	Adj. R^2 (0.605)
-Combined Education	**0.001**	-0.300	
-Gestational Age	**0.000**	0.632	Sig (<**0.001**)
1 min Apgar			
-Race	0.334	-0.133	R (0.376)
-Age	**0.047**	-0.300	
-Pre-Pregnancy BMI	0.783	-0.040	R^2 (0.142)
-Compliance	0.794	-0.037	Adj. R^2 (0.046)
-Combined Education	0.694	-0.057	
-Gestational Age	0.613	0.074	Sig (0.201)
5 min Apgar			
-Race	0.908	-0.016	R (0.309)
-Age	0.210	-0.192	
-Pre-Pregnancy BMI	0.312	0.152	R^2 (0.095)
-Compliance	0.334	-0.141	Adj. R^2 (-0.005)
-Combined Education	0.915	-0.016	
-Gestational Age	0.353	-0.141	Sig (0.468)

Table 13. Linear Regression of NHB Maternal Race Relative to Birth Outcomes*

*Exclusion of nonsignificant covariates in follow up analyses failed to significantly increase the strength of regression models. Nonsignificant covariates were reported to highlight variations in covariates ability to predict the various birth outcomes listed.

Hypothesis #2 Analyses – The Protective Effect of Maternal Exercise for Preterm Infants

Preterm Hospital Stay and Birth Measures Analyses

Hospital stay analyses were performed using only exercise participants that achieved a 0.80 compliance level or greater. No significant difference in hospital stay was observed between preterm and full term infants exposed to exercise, both in comparisons within races and within pooled groups of all exercise participants (Table 14). Additionally, no significant difference (p=1.00) in hospital stay was observed between preterm infants born to Caucasian exercisers compared to those born to non-Hispanic Black exercisers.

Although not statistically significant, the mean hospital stay of preterm infants born to control participants was greater than that that of preterm infants born to compliant exercisers for among both Caucasians and non-Hispanic Blacks (Table 15). The overall difference in hospital stay between preterm control and preterm exercise infants approached significance (p=0.094) and had a large effect size (ES=1.13). Although differences in hospital stay between preterm control and preterm exercise infants failed to reach significance among either racial group, a moderate effect size (ES=0.75) was found among non-Hispanic Blacks, and a small effect size (ES=0.26) was found among Caucasians. No significant difference in hospital stay was observed between full term infants born to control participants and full term infants born to exercise participants, regardless of race.

Analyses of infant birth measures among preterm infants born to control participants and preterm infants born to compliant exercisers found 1 minute Apgar scores were significantly (p=0.033) lower among preterm infants born to control participants. Although no other infant birth measures were significantly different between groups (Table 16), all variables were more favorable among preterm infants born to exercisers. A moderate effect size (ES=0.68) was also observed between groups for gestational age. When grouping participants by race, this pattern of more favorable birth measures among preterm infants born to exercisers was also found among both Caucasian and NHB exercisers (Table 17-18). The difference in 1 minute Apgar scores approached significance among Caucasians (p=0.055), and moderate effect sizes were observed for gestational age and birth weight among NHB participants (ES=0.75 for both variables).

Group	Preterm Hospital Stay (days)	Full Term Hospital Stay (days)	p	Effect Size
Caucasian EX	2.03±0.48	2.15±1.53	0.541†	0.009
NHB EX	2.11±0.91	1.74±0.54	0.564†	0.083
All EX	2.06±0.57	2.12±1.44	0.528†	0.008

Table 14. Hospital Stay – Preterm Infants of Exercisers vs. Full Term Infants of Exercisers

EX – Compliant Exercise Participants; Highlighted cells indicate normally distributed values
†Analysis of nonparametric data completed using Mann-Whitney U tests

Group	Preterm Control Hospital Stay (days)	Preterm Exercise Hospital Stay (days)	p	Effect Size
Caucasian	10.80±13.02	2.03±0.48	0.180†	0.26
NHB	21.49	2.11±0.91	0.221†	0.75
All	12.58±12.44	2.06±0.57	0.094	1.13

Table 15. Hospital Stay – Preterm Control vs Preterm Exercise

†Analysis of nonparametric data completed using Mann-Whitney U tests

	Preterm Control	Preterm Exercise	p	Effect Size
Gestational Age (weeks)	35.05±1.62	35.96±0.85	0.289	0.68
Birth Weight (kg)	2.58±0.57	2.67±0.35	0.855†	0.00
HC/AC	1.27±0.10	1.20±0.08	0.464†	0.05
1 min Apgar	7.33±1.21	8.80±0.45	**0.033**†	0.45
5 min Apgar	9.0±0.0	9.0±0.0	1.000†	0.00

Table 16. Infant Measures – Preterm Control vs Preterm Exercise

†Analysis of nonparametric data completed using Mann-Whitney U tests

	Preterm Control	Preterm Exercise	p	Effect Size
Gestational Age (weeks)	35.48±1.38	35.67±1.04	0.834	0.15
Birth Weight (kg)	2.72±0.50	2.84±0.09	0.643	0.29
HC/AC	1.27±0.11	1.20±0.08	0.653†	0.03
1 min Apgar	7.2±1.3	9.0±0.0	0.055†	0.53
5 min Apgar	9.0±0.0	9.0±0.0	1.00†	0.00

Table 17. Infant Measures – Caucasian Preterm Control vs Caucasian Preterm Exercise

†Analysis of nonparametric data completed using Mann-Whitney U tests

	Preterm Control	Preterm Exercise	p	Effect Size
Gestational Age (weeks)	32.90	36.4±0.28	0.22†	0.75
Birth Weight (kg)	1.86	2.42±0.50	0.22†	0.75
HC/AC	1.27	1.20±0.12	1.00†	0.00
1 min Apgar	8.0	8.50±0.71	0.48†	0.25
5 min Apgar	9.0	9.0±0.0	1.00†	0.00

Table 18. Infant Measures – NHB Preterm Control vs NHB Preterm Exercise

†Analysis of nonparametric data completed using Mann-Whitney U tests

Preterm Hospital Stay Cost Analysis

Utilizing 2011 data reported by the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization project, we were able to calculate the approximate daily hospital stay cost for a preterm infant. Dividing the average hospital cost of preterm infants ($21,500) by their average length of hospital stay (14.3 days) yielded a daily hospital stay cost of $1503.50. By multiplying this daily hospital stay cost by the difference in mean hospital stay between preterm infants born to control participants and preterm infants born to compliant exercisers, we were able to calculate the projected healthcare savings due to reductions in hospital stay. Compliant non-Hispanic Black exercise participants had a projected savings of $29,137.83 due to a 19.38 day reduction in preterm hospital stay, while compliant Caucasian exercisers had a $13,185.70 projected saving due to a 8.77 day reduction in preterm hospital stay. On average, preterm infants born to exercisers spent 10.52 fewer days in the hospital than preterm infants born to control participants, resulting in a $15,816.82 savings (Table 17).

Group	Preterm Control – Preterm Exercise Hospital Stay Difference	Hospital Care Cost Differential
Caucasian	8.77	$13,185.70
NHB	19.38	$29,137.83
All	10.52	$15,816.82

Table 17. Cost Analysis of Reduced Hospital Stay among Preterm Infants Born to Exercisers

Hypotheses #3 Analyses – Race, Exercise Modality, and Exercise Intervention Compliance

Exercise Modality Compliance Levels and Overall Compliance Analyses

Although Caucasian exercisers had a slightly greater overall compliance than NHB exercisers (Figure 7), this difference was found not to be significant (p=0.197). However, it is worth noting that while the mean overall compliance of Caucasian exercisers (0.81±0.16) is above the 0.80 per-protocol threshold, the mean overall compliance of NHB exercisers (0.74±0.19) falls below this threshold.

ANOVA analysis found significant differences (p=0.005) in compliance across exercise modalities among Caucasian exercisers (Table 20). Post-hoc analyses (Table 21) revealed that among Caucasian participants, circuit exercise compliance was significantly (p=0.005) greater than resistance exercise compliance, and that aerobic exercise compliance was greater than resistance compliance to a degree that closely approached significance (p=0.053). Differences in compliance across exercise modalities were also found among non-Hispanic Black exercisers, whose aerobic compliance was greater than circuit compliance to a degree that approached significance (p=0.085).

Compliance of circuit exercisers was significantly higher among Caucasian participants (p=0.038) than NHB participants. No significant differences were observed in aerobic exercise compliance between Caucasian and NHB participants (p=0.455). The absence of NHB participants assigned to resistance exercise prevented comparisons of resistance compliance from being conducted across race or across exercise modalities (Table 20).

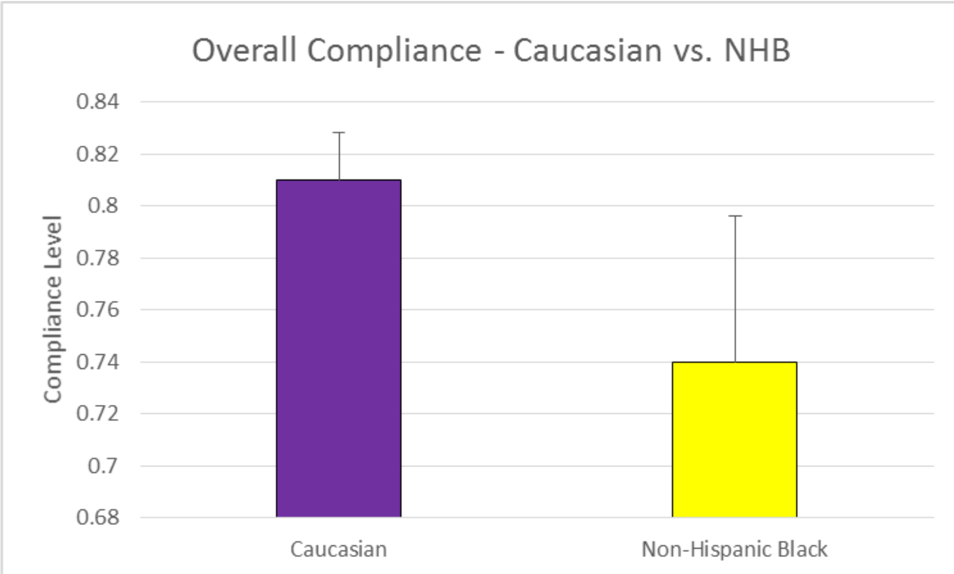

Figure 7. Overall Compliance – Caucasian Exercisers vs. NHB Exercisers*

*Overall Caucasian Compliance = 0.81±0.16, Overall NHB Compliance = 0.74±0.19

	Aerobic	Circuit	Resistance	p[1]
Caucasian	0.83±0.15	0.90±0.12	0.73±0.16	**0.005**
NHB	0.79±0.16	0.51±0.25	-	0.085[†]
p[2]	0.455[†]	**0.023**[†]	-	

Table 20. Exercise Modality Attendance – Caucasian vs. NHB

[1]Between-group analysis of weekly exercise attendance across modalities (1-way ANOVA unless otherwise stated)
[2]Means comparisons of exercise modalities between Caucasian and NHB participants
[†]Analysis of nonparametric data completed using Mann-Whitney U tests

Exercise Group	Mean Diff.	95% CI	p
Aerobic			
-Circuit	-0.07	-0.18-0.04	0.255
-Resistance	0.09	0.00-0.19	0.053
Circuit			
-Resistance	0.17	0.04-0.29	**0.005**

Table 21. Post Hoc Exercise Modality Attendance Analysis – Caucasian*

*Post-Hoc analyses of Caucasian exercise attendance performed using Tukey tests

Compliant vs. Noncompliant Exercisers

Participants were classified as compliant if they completed at least 80% of their training sessions from 16-36 weeks gestation at a sufficient moderate intensity and 50 minute duration. Participants who failed to do so were classified as noncompliant. Overall, compliant exercisers were significantly older (p=0.049) and had significantly higher education level (p=0.020) than noncompliant exercisers. In comparing compliant and noncompliant exercisers by racial background, compliant Caucasian exercisers had significantly higher education levels (p=0.030) than noncompliant Caucasians. Compliant NHB exercisers were also found to be older than and have a higher education than noncompliant NHB exercisers at levels that approached significance (p=0.069 and p=0.068, respectively). In comparing the birth outcomes of noncompliant and compliant exercisers, no significant differences were found among racial groups or pooled groups of all participants regardless of race (Tables 22-24).

Intent-to-treat linear regressions were constructed to investigate the effect of various covariates on exercise compliance (Table 25). The first model consisted of 4 predictors of exercise participant compliance, including NHB race (p=0.012, R=0.530, R^2=0.205). Maternal age was a significant positive predictor of compliance (p=0.005, B=0.485), and pre-pregnancy BMI predicted compliance to a degree that approached significance (p=0.069, B= -0.311). A second regression model was constructed to investigate the influence of exercise modality on overall compliance, using aerobic exercise as a reference variable (p=0.093, R=0.229, R^2=0.031). This second regression found that resistance exercise was associated with a significantly lower overall compliance compared to aerobic exercise (p=0.045). A third regression using resistance exercise as a reference variable (p=0.093, R=0.229, R^2=0.031) found that resistance exercise was associated with lower overall compliance than circuit exercise that approached significance (p=0.066).

Variable	Noncompliant	Compliant	p	Effect Size
Compliance	0.66±0.12	0.92±0.07	**<0.001**†	0.736
GA (weeks)	39.17±1.80	39.68±1.63	0.745†	0.001
Hospital Stay (days)	2.73±3.28	2.12±1.37	0.619†	0.003
HC/AC	1.09±0.06	1.12±0.09	0.352†	0.010
Birth Weight (kg)	3.40±0.52	3.38±0.51	0.853	0.040
1 min Apgar	7.92±1.44	8.12±1.10	0.831†	0.001
5 min Apgar	8.76±0.64	8.78±0.55	0.973†	0.000

Table 22. Compliant vs Noncompliant Exercisers – All Participants

†Analysis of nonparametric data completed using Mann-Whitney U tests

Variable	Noncompliant	Compliant	P	Effect Size
Compliance	0.66±0.11	0.92±0.07	**<0.001**†	0.729
GA (weeks)	39.1±1.94	39.26±1.61	0.841†	0.001
Hospital Stay (days)	2.58±3.54	2.14±1.48	0.942†	0.000
HC/AC	1.09±0.06	1.11±0.08	0.458†	0.008
Birth Weight (kg)	3.44±0.55	3.46±0.49	0.878	0.037
1 min Apgar	7.90±1.47	8.14±1.16	0.617†	0.003
5 min Apgar	8.80±0.48	8.76±0.58	0.944†	0.000

Table 23. Compliant vs Noncompliant Exercisers – Caucasian

†Analysis of nonparametric data completed using Mann-Whitney U tests

Variable	Noncompliant	Compliant	p	Effect Size
Compliance	0.63±0.17	0.90±0.09	**0.007**	1.829
GA (weeks)	39.82±0.85	38.32±1.81	0.103	1.098
Hospital Stay (days)	3.20±1.92	1.89±0.63	0.163	0.883
HC/AC	1.10±0.06	1.16±0.13	0.351	0.682
Birth Weight (kg)	3.28±0.29	2.82±0.47	**0.103**	1.203
1 min Apgar	7.83±1.47	8.20±0.84	0.844†	0.003
5 min Apgar	8.50±1.23	9.0±0.0	0.662†	0.083

Table 24. Compliant vs Noncompliant Exercisers – NHB

†Analysis of nonparametric data completed using Mann-Whitney U tests

Model Variables	p	Std. Beta Coefficient	Regression
Compliance -Race (NHB) -Age -Pre-Pregnancy BMI -Combined Education	 0.616 **0.005** 0.069 0.432	 0.071 0.485 -0.311 0.124	R (0.530) R^2 (0.281) Adj. R^2 (0.205) Sig (**0.012**)
Compliance -Circuit Exercise -Resistance Exercise	 0.768 **0.045**	 0.032 -0.219	R (0.229) R^2 (0.053) Adj. R^2 (0.032) Sig (0.093)
Compliance -Circuit Exercise -Aerobic Exercise	 0.066 **0.045**	 0.234 0.256	R (0.229) R^2 (0.053) Adj. R^2 (0.032) Sig (0.093)

Table 25. Linear Regressions of Exercise Participant Compliance*

*Exclusion of nonsignificant covariates in follow up analyses failed to significantly increase the strength of regression models. Nonsignificant covariates were reported to highlight variations in covariates ability to predict the various birth outcomes listed.

Chapter V. Discussion

We hypothesized that infants born to non-Hispanic Black mothers who engaged in exercise during pregnancy would have similar gestational age and markers of neonatal health at birth relative to infants of Caucasian women that exercised during pregnancy, and that racial disparities in birth outcomes would still be present among control participants. We also hypothesized that preterm infants born to exercisers would have reduced hospital stay and improved measures of health compared to control, and that compliance among participants would be similar regardless of race. 1) We found that with the exception of birth weight, which was significantly lighter among infants of NHB (p=0.036) participants due to a higher prevalence of low birth weight, there were no differences in measures of neonatal health and preterm birth between infants born to Caucasian exercisers and those born to NHB exercisers. 2) In our comparisons of hospital stay we found that among all races; preterm infants born to control participants had a longer hospital stay than preterm infants born to compliant exercise participants, although these differences failed to achieve statistical significance (p=0.094). A trend in more favorable birth measures was also observed among preterm infants born to compliant exercisers was observed in both races, and pooled group of all compliant exercisers. 3) We found that although overall compliance did not differ between races, the modality of the exercise performed had significant impact on compliance both within and between races.

Hypothesis #1 – Racial Disparities in Birth Outcomes among Infants Born to Exercisers

In comparing the birth outcomes of compliant exercisers between races, we observed a lack of racial disparities among NHB participants and Caucasian participants, with the notable exception of birth weight. Although the mean birth weight of both races fell within the healthy range of 2.5-4.0 kg, birth weight was significantly lower among NHB participants (p=0.036). This reduced mean birth weight was the result of a higher proportion of NHB exercisers delivering infants of low birth weight compared to Caucasian exercisers. In addition to approaching significance among compliant exercisers ($\chi2$=0.068), this increased proportion of low birth weight among NHBs extended to the control group ($\chi2$=0.092), resulting in a higher overall proportion of low birth weight among NHBs that was statistically significant ($\chi2$=0.012).

While we also observed a significantly higher proportion of preterm birth among compliant NHB exercisers than compliant Caucasian exercisers ($\chi2$=0.026), this difference in preterm birth prevalence between races failed to extend to our control participants ($\chi2$=1.00) or our overall population ($\chi2$=0.165). A likely explanation for this increased prevalence of preterm birth among compliant NHB exercisers would be simple chance occurrence coupled with a small NHB sample size, rather than this being an example of a racial disparity in birth outcome. Our regression analyses found NHB race not to be a significant predictor of preterm birth or gestational age, further supporting that this difference in preterm birth prevalence between races was the result of chance, or else some other unknown factor among our NHB exercise participants.

Through linear regressions analysis we found exercise dosage measured via compliance to be a significant predictor of gestational age, with increasing compliance correlating with increased gestational age at birth. Given this significant positive relationship between compliance and gestational age, exercise during pregnancy may serve as an important tool in increasing gestational age at birth and potentially preventing preterm births. Although exercise compliance failed to significantly predict birth variables other than gestational age, our regressions did reveal a potential indirect influence of compliance on other measures of neonatal health. Regression analyses found gestational age to be a significant predictor of hospital stay, HC/AC, and birth weight; with increased gestational age correlating with more favorable values. Given the significant predictive effect and positive relationship between compliance and gestational age, increased dosage of exercise during pregnancy may lead to improved birth outcomes via increased gestational age at birth.

It is also worth noting that with the exception of birth weight, NHB race failed to significantly predict birth outcomes in any of our regression models. Gestational age was found to be the most prevalent predictor of birth outcomes, with exercise compliance and maternal age acting as significant predictors of gestational age. Maternal age was also found to be a significant predictor of HC/AC, as well as a predictor of 1 minute Apgar scores. Additionally, our binomial logistic regressions found that increased pre-pregnancy BMI was a significant predictor of cesarean delivery; a relationship that is well-established in existing literature (38, 17). Our findings suggest that while maternal race may exert some influence on birth outcomes, maternal characteristics such as age, exercise habits, and BMI play a much more crucial role in determining risk of adverse birth outcome. These findings are particularly important in that both exercise habits and BMI are modifiable factors that can be influenced through behavior changes. Public health initiatives focused on increasing physical activity and controlling BMI would therefore be invaluable tools for fostering more favorable birth outcomes.

One explanation as to why maternal exercise could help attenuate racial disparities in birth outcome may lie in the anti-inflammatory and stress relieving properties of exercise. The Weathering Hypothesis proposed by Geronimus hypothesizes that racial disparities in African American women's health are the result of cumulative exposure to socioeconomic disadvantages, discrimination, and the resulting chronic stress (39). When subject to stress the human body releases cortisol, which has been found to play an important role in influencing the production of inflammatory cytokines such as IL-6 and IL-1β; both of which have been associated with preterm birth (80). Additionally, chronic stress has been found to increase levels of inflammatory C-reactive protein and susceptibility to infections associated with preterm birth (72). Conversely, exercise has been shown to reduce cortisol levels through what has been termed the cross stressor adaptation hypothesis (75). Due to regular exercise activating similar stress system to those of psychosocial stress, the body adapts in a manner that blunts cortisol production and reduces the intensity of response to non-physical stress (22). By reducing cortisol release in pregnant NHB women, the metabolic pathways associated with preterm birth that stem from cortisol release may also be dampened. Regular exercise has also been associated with reduced C-reactive protein (34) and reduced feelings of anxiety and depression (44), both of which serve to only further reduce risk of stress-induced reductions in gestational age and associated birth outcomes.

Hypothesis #2 – The Protective Effect of Maternal Exercise for Preterm Infants

In our comparisons of hospital stay among preterm infants, we found mean length of hospital stay to be 10 days longer among infants of the control group compared to those born to exercisers. This difference between groups approached significance (p=0.094), and resulted in an estimated $15816 reduction in hospital and healthcare expenses. Reductions in hospital stay among exercisers were found to extend to all racial groups, and were most pronounced among NHB participants. In comparing birth measures of preterm infants, we found 1 minute Apgar scores to be significantly higher among preterm infants born to exercisers than those born to control participants (p=0.033). Gestational age, birth weight, and HC/AC were also found to be more favorable among preterm infants born to exercisers, albeit to a degree that failed to reach significance. This pattern of more favorable birth measures among preterm infants born to compliant exercisers was also exhibited among both NHB and Caucasian participants.

Despite lacking significance, these improved markers of health and hospital stay among preterm infants born to compliant exercisers depict an overall trend of improved health when preterm infants have been exposed to maternal exercise. Increased 1 minute Apgar scores also show preterm infants born to exercisers being more immediately adaptable to life outside of their mother's womb. These data support our hypothesis that preterm infants exposed to exercise would have reduced hospital stay and improved markers of health compared to preterm infants born to control participants. The lack of significance that we observed could be the result of our study's small sample size. Given the promising findings in our study and the current lack of research on the influence of maternal exercise on preterm infant health, we believe that further research is warranted.

Interestingly, our comparisons of the rate of preterm birth within intervention groups failed to find significant differences between control and compliant exercise participants. This contradicts previous studies that have found reduced rates of preterm birth among mothers that engaged in exercise during their pregnancy (53, 71). Nonetheless, our results illustrate that even if exercise during pregnancy fails to reduce a mother's risk of delivering preterm, it can still foster improved infant health even in the occurrence of a preterm delivery.

Hypothesis #3 – Race, Exercise Modality, and Exercise Intervention Compliance

Although our hypothesis that the compliance of NHB and Caucasian exercise participants would be similar was supported by a lack of significant difference in overall compliance between races, we found significant variations in compliance when comparing different exercise modalities. These variations were found both within individual races and when comparing NHBs to Caucasians. Caucasian exercisers had higher compliance for circuit and aerobic training than for resistance training (p=0.005 and p=0.053, respectively), NHB exercisers had higher compliance for aerobic training than circuit training (p=0.085). Given the drastic differences observed in compliance between aerobic and circuit modalities for NHB exercisers, and preexisting literature detailing preference for aerobic exercise among females (9), we believe that these differences would likely achieve significance in a larger sample size. We found no significant difference in aerobic compliance between Caucasians exercisers and NHB exercisers. However, circuit training compliance was significantly higher among Caucasian exercisers than NHB exercisers (p=0.023).

One possible explanation for the differing compliance observed among exercise modalities in our study may lie in women's perceptions of resistance exercise as well as their personal preferences of exercise modality. As discussed in the literature review section, strength training is often less prevalent among females than it is in males, primarily due to misconceptions that females who engage in resistance training run the risk of becoming "bulky" or being perceived as masculine (51, 79, 83). These misconceptions and stigmas may explain why resistance training had the lowest compliance among Caucasians, and lead us to believe that resistance training compliance would have also been low amongst NHBs had any been randomized to that exercise modality. Among women who do engage in a strength training, Caucasian women have been shown to be significantly more compliant than NHBs (11). If NHB women are even less likely to engage in strength training than Caucasian women, the resistance training components of our circuit training protocol may be the cause of lower circuit training compliance observed amongst NHB exercisers.

Our findings that compliant exercisers were older and more highly educated were significant in comparisons that included all exercisers (p=0.049; p=0.02) and approached significance in comparisons of solely NHB exercisers (p=0.069; p=0.068). This should not come as a surprise, as ours is not the first study to come to this conclusion (49, 55). Additionally, linear regressions found maternal age and assignment to aerobic exercise modality to be significant predictors of compliance (p=0.001; 0.045, respectively).

In comparisons of birth measures between noncompliant and compliant exercisers we failed to find significant differences. This lack of variation in birth outcomes may indicate that an exercise dosage below ACOG recommendations can still convey infant health benefits. While the noncompliant exercisers failed to achieve our per-protocol threshold of 0.80, their mean compliance was still in the mid-sixty percent range for all racial groups. At a 0.65 compliance level, an exercise participant would still have accumulated an average of 97 minutes of moderate intensity physical activity per week. Given the dose-response nature of exercise, it stands to reason that these noncompliant individuals would still experience some level of protective effect against adverse birth outcomes. These findings are of particular importance to pregnant women who struggle to meet physical activity guidelines set by ACSM and ACOG, as they may still stand to elicit benefits to their child's health through whatever exercise they are able to accumulate each week.

Limitations

Although our study has many strengths, it does suffer from several limitations. Our sample size is small, particularly for those of NHB race. Due to lower recruitment of minority and NHB participants, our sample fails to accurately represent the population of the region where this study took place. While 16.7% (25/149) of our randomized sample population consisted of NHBs, the United States Census Bureau estimated the NHB/African American population in the city of Greenville NC to be approximately 38.7% in the year 2016 (8). Additionally, the relatively high mean education level of our NHB participants is not representative of the local NHB population.

There were also numerous factors that we were unable to control for among our participants such as nutrition, social support, and stressors encountered during their pregnancy. Our analyses were restricted to physical activity and exercise performed during pregnancy, with no accounting for initial fitness or physical activity habits prior to pregnancy. While our study does have the strength of utilizing objectively-measured exercise and physical activity, we were not able to control for variations in occupational physical activity and activities of daily living among our participants.

Most notably, the use of compliance as a measure of exercise dose is subject to error. Participant's compliance levels only reflect their attendance with the exercise intervention protocol, and not the intensity at which they performed their assigned exercise. Although research team members encouraged participants to work within their target heart rate training zones, participants of equal compliance levels could theoretically have significant differences in exercise dose due to variations in exercise intensity during training. Similarly, our use of parental education level as a proxy for socioeconomic status is also subject to error. While higher education levels have been found to correlate to higher socioeconomic status, variations in income amongst individuals of comparable education levels is common and well documented. Additionally, a participant's report of higher education does not signify that they are currently employed, or that they are employed in a position that correlates to their educational background.

Future Research

While the results of this study serve as a valuable insight into the influence of race on maternal exercise and birth outcomes, further research is required to fill in the gaps in the current literature regarding these subjects. In order to more accurately assess exercise dosage during pregnancy, future analyses could utilize measures of average training heart rate recorded for each training session. Participants who more frequently worked within their target heart rate zone or who worked at higher levels of their designated heart rate training zone are likely to have achieved a greater exercise dosage than those that failed to meet intensity criteria on a regular basis. Additionally, previous analyses of ENHANCED by Mom study data have utilized metabolic equivalents (METs) to measure exercise dosage. Using Ainsworth et al.'s Compendium of Physical Activities, exercise modality can be matched with its corresponding MET value, allowing exercise intensity to be estimated.

Future studies of exercise compliance among different races could benefit from measuring compliance at different points throughout a mother's pregnancy in addition to overall compliance. Multiple studies of maternal exercise behavior have found that women are less likely to engage in physical activity as their pregnancy progresses. It would be interesting and potentially worthwhile to see if women of different races maintain physical activity levels into late pregnancy, or if some races are more likely to discontinue exercise than others. Additionally, this would allow researchers to investigate if there is a stage of pregnancy during which exercise is more effective in enhancing birth outcomes for high-risk minority populations such as non-Hispanic Blacks.

In future studies removed from the ENHANCED by Mom study protocol, a different randomization model could allow for stronger analyses of how exercise modality effects compliance among different races. The randomization model in this study inadvertently lead to a disproportionate percentage of NHB participants being assigned to aerobic exercise compared to the percentages assigned to resistance and circuit exercise. Additionally, the distribution of NHB participants across exercise modalities was significantly skewed towards aerobic exercise compared to the distributions across modalities among Caucasian exercisers. The utilization of a stratified randomization model in future studies would help to ensure that the assignment of participants across exercise modalities remains equal and consistent among different races. A larger sample size and increased recruitment efforts among NHB populations would also aid in ensuring a sample that it representative of the actual population.

Conclusions

Overall, our study saw a lack of significant variation in birth measures between infants born to Caucasian exercisers and those born to NHB exercisers. This suggests that in addition to those of different races responding similarly to maternal exercise, racial disparities in birth outcomes may be partially attenuated by maternal exercise. 1) Our data depicted an overall lack of racial disparities among infants born to women who exercised during pregnancy, save for birth weight, and resulted findings that maternal exercise was significant predictor of infant gestational age. Maternal exercise may indirectly influence other infant birth outcomes by fostering more favorable gestational age. We found maternal characteristics of age, exercise compliance, and pre-pregnancy BMI to be more significant predictors of birth outcome than maternal race. 2) While our results did not indicate a significant reduction in the rate of preterm birth among individuals who exercised during pregnancy, a trend of reduced hospital stay and improved measures of infant health was exhibited among preterm infants that were exposed to maternal exercise. 3) While overall compliance did not differ between exercisers of different race, significant differences were found between exercise modalities. Among NHB populations, aerobic exercise should be recommended in order to maximize the likelihood of compliance with guideline and foster more improved birth outcomes.

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Appendix

Appendix A: IRB Approval Letter

EAST CAROLINA UNIVERSITY
University & Medical Center Institutional Review Board
4N-64 Brody Medical Sciences Building· Mail Stop 682
600 Moye Boulevard · Greenville, NC 27834
Office **252-744-2914** · Fax **252-744-2284** ·
www.ecu.edu/ORIC/irb

Notification of Continuing Review Approval: Expedited

From:	Biomedical IRB
To:	Linda May
CC:	Debra Peaden
Date:	2/9/2018
Re:	CR00006640 UMCIRB 12-002524 ENHANCED by Mom

The continuing review of your expedited study was approved. Approval of the study and any consent form(s) is for the period of 2/8/2018 to 2/7/2019. This research study is eligible for review under expedited categories #2, #5, #7. The Chairperson (or designee) deemed this study no more than minimal risk.

Changes to this approved research may not be initiated without UMCIRB review except when necessary to eliminate an apparent immediate hazard to the participant. All unanticipated problems involving risks to participants and others must be promptly reported to the UMCIRB. The investigator must submit a continuing review/closure application to the UMCIRB prior to the date of study expiration. The investigator must adhere to all reporting requirements for this study.

Approved consent documents with the IRB approval date stamped on the document should be used to consent participants (consent documents with the IRB approval date stamp are found under the Documents tab in the study workspace).

The approval includes the following items:

Document	Description
14-014-Pregnancy Study.pdf(0.01)	Recruitment Documents/Scripts
Aerobic Home Exercise Sheet(0.01)	Additional Items
Circuit Home Exercise Sheet(0.01)	Additional Items
CLEAN-Maternal Consent- ENHANCED-IRB 12-002524-Amendment25-122017(0.04)	Consent Forms
CLEAN-Pedatric Consent- ENHANCED-IRB 12-002524-Amendment17-020817(0.02)	Consent Forms
Clinic cover letter 12-20-13.docx(0.01)	Recruitment Documents/Scripts
Clinic Letter of Support - Dolbier, Kim, & May.pdf(0.01)	Recruitment Documents/Scripts
Combined contact permission card 12-20-13.docx(0.01)	Recruitment Documents/Scripts
Combined research flyer 12-20-13.docx(0.01)	Recruitment Documents/Scripts
Dietary Assessment(0.01)	Surveys and Questionnaires
Email Campaign- ENHANCED(0.01)	Recruitment Documents/Scripts
ENHANCED by Mom study timeline(0.01)	Recruitment Documents/Scripts
ENHANCED Protocol 12-002524 Amendment 25-122017-CLEAN(0.09)	Study Protocol or Grant Application
ENHANCED%20Timeline-2014.pdf(0.01)	Additional Items
Exercise Motivations Inventory(0.01)	Surveys and Questionnaires
Exercise Session Log Sheets(0.01)	Additional Items
Expanded Behavioral Regulation for Exercise Questionanire(0.01)	Surveys and Questionnaires
Facebook Ad- headline-083116 Amendment 14(0.01)	Recruitment Documents/Scripts

Document	Description
Facebook Ad- Mockup- 083116- Amendment 14(0.01)	Recruitment Documents/Scripts
International Physical Activity Questionnaire(0.01)	Surveys and Questionnaires
Link to ENHANCED by Mom- website(0.01)	Recruitment Documents/Scripts
Magazine Ad-083116-Amendment 14(0.02)	Recruitment Documents/Scripts
Maternal Measurements Form(0.01)	Additional Items
Modified Balke Protocol.docx(0.01)	Standardized/Non-Standardized Instruments/Measures
Modified Physical Activity Questionnaire020817(0.04)	Surveys and Questionnaires
Photo Informed Consent(0.01)	Consent Forms
Psychological Need Satisfaction in Exercise Scale(0.01)	Surveys and Questionnaires
Recruitment Criteria Card (0.04)	Recruitment Documents/Scripts
Resistance Home Exercise Sheet(0.01)	Additional Items
Sheffield FFQ.doc(0.02)	Surveys and Questionnaires
Stretching Home Exercise Sheet(0.02)	Additional Items

The Chairperson (or designee) does not have a potential for conflict of interest on this study.