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Lauren Nelson Date

Preterm birth, neighborhood deprivation, and first grade educational attainment:

An analysis of multiplicative interaction and spatial heterogeneity

By

Lauren Nelson

Master of Public Health

Epidemiology

Michael Kramer, PhD

Faculty Thesis Advisor

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B.S., Point Loma Nazarene University, 2008

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An abstract of

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Abstract

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Objectives
Early childhood development is important for school readiness and educational attainment and has a lasting affect on health. There is evidence that both preterm birth and neighborhood deprivation are independently associated with school readiness and educational attainment, however there has been little examination of their combined effect. This analysis assessed for multiplicative interaction and spatial heterogeneity of the influence of preterm birth and neighborhood deprivation on the risk of failing the math portion of the Georgia Criterion-Referenced Competency Test (CRCT) in first grade.
Methods
Data is from the Georgia Birth to School Cohort. Birth and standardized test records were linked for 97,747 children born from 1998 to 2002 in the five core counties of Atlanta. Interaction was assessed using multivariable logistic regression and spatial heterogeneity was assessed using geographically weighted regression (GWR).
Results
The logistic regression models indicated that when adjusting for maternal age, marital status, education level, race, child sex, insurance status, smoking during pregnancy, and quality of prenatal care, there was evidence of significant interaction between preterm birth and neighborhood deprivation. For those who were born preterm (less than 37 weeks gestation), there was no significant effect of deprivation on the risk of failing the math portion of the CRCT (aRR: 1.00, 95% CI: 0.97, 1.04). For those born at term, there was a significant effect of deprivation on failing (aRR: 1.04, 95% CI: 1.02, 1.06). The GWR suggests that there is spatial heterogeneity in the relationship between preterm birth, neighborhood deprivation, and failure of the math CRCT. Among preterm births, deprivation appeared to have a larger effect in the northwest and eastern areas of the region. Among term births, deprivation had a greater effect in the northeast and in parts of the northwest and south.
Conclusion
This analysis provides evidence of significant multiplicative interaction and substantial spatial heterogeneity of preterm birth and neighborhood deprivation when predicting risk of failing the math portion of the CRCT in first grade. Further research should establish these spatial differences to better target interventions that aim to improve early childhood development.

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Literature Review

Introduction

Early childhood development is important for school readiness and educational attainment and has a lasting effect on health throughout childhood and into adulthood. The development of sensorimotor, socio-emotional, and language-cognition skills is influenced by a child's physical health, family, and larger social system (1). More specifically, research suggests that a child's development is affected by a wide range of factors including birth weight, gestational age, maternal age, maternal health, and parenting (2-4). Proper cognitive development is important in early childhood as it indicates the level of a child's readiness to begin school, which in turn influences later educational outcomes. Those who fail to reach their full developmental potential have greater risk of economic, social, and health problems later in life, making early child development important to understand and promote (5).

Neighborhood factors have been linked to individual health in a large amount of research. An individual's neighborhood is a dynamic entity with physical and social attributes that influence both physical and mental health and social well-being (6). Specifically, measures of neighborhood deprivation can indicate an individual's risk for mortality and morbidity and of particular interest, can predict outcomes of a child's cognitive development and educational attainment (7, 8).

Additionally, there is a large body of research that links preterm birth to many pediatric and adult health outcomes. Preterm birth is a birth that happens before 37 complete weeks of gestation (9). The causes of preterm birth are complicated and include various genetic, social, and physical health factors. An infant that is born preterm has an increased risk of mortality and morbidity in neonatal stages and in to adulthood(10, 11), and has a greater risk of poor cognitive development and poor educational attainment (12, 13).

While there is evidence supporting a relationship between neighborhood poverty and cognitive development and preterm birth and cognitive development, there is a lack of knowledge about how neighborhood and preterm birth may work together to influence cognitive development in early childhood. The purpose of this analysis is to assess these relationships and evaluate for multiplicative interaction between neighborhood deprivation and preterm birth using multivariable logistic regression. Additionally, the potential variation of influence of neighborhood and preterm birth over space will be assessed using geographically weight regression.

Cognitive Development, School Readiness, & Educational Attainment

Early childhood is an important time for an individual's sensorimotor, social-emotional, and language-cognitive development. The development of each of these depends on the context of the child's physical well-being, their family, and larger social network (1). Data from the 2007 National Survey of Children's Health for children ages 4 months to 5 years indicates that over 40% of parents in the United States reported one or more concern about their child's physical, behavioral, or social development. In Georgia, more than 38% of parents reported one or more concern about their child's development (14). This report suggests that proper development in early childhood is a relevant concern in the United States population today.

One way to measure how a child has developed in early years is to consider educational outcomes throughout schooling. Longer-term educational outcomes to consider include retention rates, drop-out rates, educational achievement, test scores, and years of schooling completed. School readiness is also important to consider. It refers to skills at the start of school that children need to best profit from the educational experiences of formal schooling. These skills include motor skills, self-care, self-regulation, and pre-academic skills like basic knowledge of letters and numbers (15). In addition, before starting school, it is just as important for a child to be physically health, to be able to communicate, to be curious and excited to learn, and to be socially appropriate by taking turns and sharing (16). Poor school readiness has been linked to truancy, drop out rates, special education placement, and achievement test scores. Between 30 and 40% of children entering kindergarten in the United States are estimated to not be ready for school (17). In a study by Lee and Burkman, they found evidence that most American students who start school significantly behind their peers can never close the gap and the gap may even become greater over time (18).

Bronfenbrenner's ecological model of human development suggests that a complex web of embedded social contexts shapes these developmental processes. Larger social structures influence development through more proximal context directly involving children. More specifically, larger socioeconomic structures and cultures may influence parenting norms and parental access to education resources influencing a child's outcomes (19). This model suggests that it is important to understand both the individual-scale and larger scale influence on child development.

Hediger et al. used data from the third National Health and Nutrition Examination Survey done from 1988-1994 on children born in the United States to determine risk factors for delays in motor and social development as assessed by the Bayley Scales of Infant Development, Gesell scale, and the Denver Developmental Screening Test. They determined that low parental education level, older maternal age, higher birth order, birth weight less than 2,500 grams, delivery before 37 weeks of gestation, and race are associated with delays in motor and social development. After adjusting for demographic factors, they found that birth weight was the most important indicator of delays (2).

Other factors that pose risk for poor cognitive development in childhood are maternal health and parenting. Several studies determine maternal health to be a predictor of a variety of developmental outcomes. Kahn et al. performed a study of US children and determined that maternal health, specifically depression, was associated with behavior and language development at age 3 (3). The Millennium Cohort study in the United Kingdom found an association between the self-reported health of mothers and their child's positive learning and development behavior.

They also found an association with parental engagement and caregiving that may mediate some of the relationship between maternal health and child development (20).

Belsky's ecological model of the determinants of parenting has been used as a framework for understanding the relationship between parenting and child development. Belsky's model suggests that quality of parenting is determined from the characteristics of the parent, contextual sources of stress and support, and characteristics of the child. In terms of promoting growth of a child, parental characteristics, specifically a parents' personal psychological resources, are considered to be the most important (4). A study by Bucker et al. determined that school-aged children that were exposed to early traumatic experiences including abuse, maltreatment, and neglect had a worse performance on attention, immediate verbal recall, and working memory tests than an age and sex matched control group (21).

There is also evidence of race being a risk marker for poor cognitive development, likely due to racial differences in allocation of opportunity. Phillips et al. determine there is a visible gap between white and black children at the start of elementary school and that the gap typically widens as children go through school (22). There is evidence that this racial gap continues into later schooling. In 2002, the National Assessment of Educational Progress found that only 16% of black twelfth grade students and 22% of Hispanic students had a solid performance in reading, while 42% of White students did. Similar patterns were also found for math, science, and writing (23). In addition to not doing well in later grades, disparities in school readiness are important as children who perform poorly in early grades also have a greater risk of not completing as much school and finding gainful employment in adulthood (24).

Data from the Quebec Longitudinal Study of Child Development examined the relationship between math, vocabulary, and attention at the start of kindergarten and health behaviors and academic performance at the end of fourth grade. They found that receptive vocabulary in kindergarten predicted fourth grade dietary habits, and higher math skills predicted increased physical activity. Overall, the math scores in kindergarten were the greatest predictors of academic outcomes at the end of fourth grade. This suggests that the knowledge and skills that children enter school with is important for both later achievement and health (25).

Overall, educational outcomes are important to measure as an indicator of cognitive development in early childhood. Children who fail to reach their full developmental potential have many lasting effects through adulthood. Those with mild-to-severe cognitive impairments or intellectual disabilities often have issue gaining employment. They are significantly affected by changes in the economy, earn less income, and have high rates of unemployment (5).

Neighborhoods

Data from the American Community Survey from 2011 estimates that 48.5 million people, or 15.9% of the population, in the United States live below the federal poverty line. This proportion is greater in Georgia, with 19.1% of the population living below the poverty line (26). Additionally, the American Community Surveys from 2006-2010 determined that in the United States, 67 million people, or 22.6% of the total population, live in census tracts where over 20% of the residents have an income below the federal poverty line. Further, 50.2% of people living in poverty live in a tract with greater than 20% of residents having an income below the poverty line. In Georgia, 29.5% of the population lives in a tract with greater than 20% poverty (27). This data demonstrates that a large number of people in Georgia and the United States are living below the poverty line and even more people live in census tracts with greater than 20% of the population living below the poverty line. While many poor individuals live in census tracts with a high density of poverty, the relative poverty of the neighborhood can vary making it possible for an individual to have different individual and neighborhood level poverty status. This ultimately makes it important to consider the influence of both individual and neighborhood levels of poverty on health.

An individual's neighborhood influences both physical and mental health of children and adults. Diez-Roux and Mair suggest a framework of the relationship between neighborhoods and health. They propose that residential segregation by race or socioeconomic status is related to inequalities in resource distribution. The combination of this segregation and lack of resources then influences neighborhood physical and social environments that in turn influence behavior and stress, and ultimately health (6). Physical environments that have proved important to consider include available areas for physical activity (28), local food availability (29, 30), and disorder and decay (31). Some characteristics of social environments that are important to consider are social support (32-34), safety (32, 35), residential stability (33, 34), demographic composition (31, 34), and ethnic density (31).

While there are several neighborhood attributes to consider, two that are important are neighborhood poverty and neighborhood deprivation. Neighborhood poverty is important to consider because it allows for assessing the direct relationship between neighborhood poverty level and health outcomes. Neighborhood deprivation is more helpful in understanding the multi-faceted and complicated natures of a neighborhood's socioeconomic status as it includes multiple domains of disadvantage including various measures of poverty, education, housing, and employment (36).

There are several proposed models that may explain the relationship between neighborhood deprivation and health. The collective resources model hypothesizes that people living in non-deprived areas have better health because there are more collective resources such as health services, social services, and job opportunities. Wealthier individuals and areas have the ability to attract more resources, but they also may have the ability to purchase goods and services privately or travel to access the services they desire. The effect of living in an area with greater resources is greater for those who are poorer because they may depend more on what is local. If those who are poorer do not have local resources, there will be negative implications on their health due to lack of access to care and other services (37).

The contagion model suggests that disadvantaged neighbors are a disadvantage themselves. Children that grow up in neighborhoods where much of the community engages in negative activities, such as crime and smoking, will be more likely to engage in those activities as they grow older. On the other hand, children that grow up in neighborhoods where common activities are more positive will grow up engaging in those positive activities. If negative activities are more associated with disadvantaged neighborhoods, then children growing up in these areas will be more likely to engage in negative behaviors than children growing up in more advantaged areas (38). Using this model, neighborhood poverty and deprivation can be linked to negative health outcomes through participation in risky behaviors that are norms for a neighborhood. Data from the National Health and Nutrition Examination Survey III indicates that the percent of respondents falling in to risk categories of high serum cotinine, excessive drinking, physical inactivity, and high serum triglycerides increased as the level of deprivation increased after adjusting for socio-demographic characteristics, body mass index, and various comorbidities (39).

Another model to consider is the local social inequity model. This model suggests that the disparity between an individual's socioeconomic status and the status of those living nearby affect health the most. If a poorer individual is living in an area that is generally wealthier, they may have worse health than if they were living in an area with others of comparable income level. When living in an area with those in a different income bracket, a poor individual may not be able to access or afford the services that are offered locally and in addition and may not feel like a member of the community (37).

Several studies have linked neighborhood factors, specifically poverty and neighborhood deprivation, to negative physical health outcomes for people of all ages. For example, the Diet and Health Study done by the American Association of Retired Persons determined that for adults ages 50 to 71 with self-rated good or excellent health, risk of mortality increased with increasing levels of socioeconomic deprivation (40). Additionally, the Whitehall II study of adults living in England determined that both individual-level and area deprivation were independently associated with poor self-rated health, poor mental health, and a higher waist-to-hip ratio (37). These findings were consistent with the collective resources model mentioned above.

Neighborhood poverty and deprivation have also been linked to mental health, specifically the internalization and externalization of problems. From the National Longitudinal Survey of Adolescent Health, it was determined that neighborhood concentration of poverty, as measured with census data, was significantly related to adolescent depressive symptoms after controlling for family and individual characteristics (41, 42). Those living in areas with higher concentration of poverty, lower proportion of whites, and with lower median household incomes had greater risk of depression in adolescence. Additionally, neighborhood poverty has been linked to externalizing problems that include violent behavior, aggression, conduct problems, and delinquency (43).

Neighborhood and child development

There is evidence of the relationship between various individual and familial socioeconomic factors and child development. In the 1990's, data from the Infant Health and Development program in the United States found that family income and poverty status are correlated with both the cognitive development and behavior of children after adjusting for family structure, maternal schooling, and other income related differences (44). More recently, the English Spring 2008 School Census used data from education records to determine that lower household socio-economic positions were associated with increased intellectual and developmental disabilities, but that greater deprivation was associated with lower rates of identification of these disabilities. Overall, the analysis indicates that children whose development is already compromised by low socioeconomic status are at an increased risk of exposure to social conditions that may further compromise their development (45).

Of greater interest in this analysis are the ways in which an individual's neighborhood may potentially influence early child development. Sampson et al. suggest two possible pathways for the relationship between neighborhood and child development. First, following the collected resources model, disadvantaged neighborhoods will likely have poor quality and poorly funded institutions that are critical to early development including schools and child care centers (46). Second, an example of the contagion model is the language environment of a neighborhood. Both the languages spoken and the properness of how a language is spoken can potentially influence a child's cognitive skills (46). Another potential pathway stems from the fact that poorer neighborhoods are often stressful and hazardous to live in. These stresses and hazards may isolate children from otherwise stimulating environments (47). Additionally, Wilson et al. suggest that collective socialization in neighborhoods provides support for children that may indirectly influence cognitive development. They suggest that there may be less positive role models in poorer neighborhoods (48). While this is not an extensive list of pathways, it is most likely that all of these pathways are intersecting and combining to explain the relationship between neighborhood and child development.

Research also shows evidence of the importance of considering multiple generations when trying to understand the relationship between neighborhood and a child's cognitive ability, suggesting that relevant pathways may begin long before a child is born. Sharkey et al. used data from the Panel Study of Income Dynamics that followed families over time since 1968 and followed-up with the 1997 and 2002 Child Development Surveys for children of parents in the original study. They found that a family's exposure to neighborhood poverty over two consecutive generations reduced the average child's cognitive ability by more than a half of a standard deviation (8).

Results from the United Kingdom Millennium Cohort Study suggest the importance of both individual and neighborhood level poverty. Children born in to poverty have lower cognitive test scores at age 3, 5, and 7. Additionally, they determined that continually living in poverty in early life has a cumulative effect on cognitive development. On measures of cognitive development, children who are seven years old and have lived in poverty since birth are greater than ten percentiles below children who have never lived in poverty (49). Additional data from this study also links neighborhood deprivation with greater reported problems with peers in preschool, but the association was moderated by cognitive ability (50).

In addition to the evidence of an association between neighborhood and child development, there is evidence supporting the relationship between neighborhood deprivation and educational outcomes. In a review of literature on the subject, McBride Murry et al. determined that characteristics of a disadvantaged neighborhood predict several academic outcomes. These outcomes include time spent on homework, math and reading test scores, and dropping out of school (51). Sastry and Pebley use data from the 2000-2001 Los Angeles Family and Neighborhood Survey to examine the potential family and neighborhood sources of socioeconomic inequality of children's achievement in both reading and math. They find that one third of the variation in math performance is associated with socioeconomic status differences, while one fifth of reading is explained by these differences. Using multi-level models, they find that living in a low-income neighborhood appears to have a larger impact on the inequality of test scores than coming from a low-income family (7), indicating the importance of considering socioeconomic status at the neighborhood level.

Dupere et al. examine the relationship between neighborhood advantage and children's achievement and determine that the magnitude of the association varies by the extent of neighborhood advantage. They find a non-linear association indicating that neighborhood effects are stronger for those in less advantaged neighborhoods. At about the 75^{th} percentile, the positive association between neighborhood advantage and children's achievement plateaus and the proportion of advantaged residents was no longer associated with higher achievement (52). The non-linearity of this association suggests a dynamic relationship between neighborhood deprivation and achievement that perhaps is more important among those living in neighborhoods with greater disadvantage.

Understanding the relationship between neighborhood socioeconomic status and academic and developmental outcomes in early childhood is important as the early neighborhood experiences that influence early childhood development set a child on a trajectory. A study in British Columbia, Canada of children followed from kindergarten through seventh grade indicated that neighborhood disadvantage experienced during kindergarten had a negative influence on reading level in grade seven (53). This suggests the important impact that early childhood neighborhood settings not only have on early childhood, but on in to adolescence as well.

The evidence of the relationship between neighborhood-level poverty and deprivation and health, specifically with measures of child development, provide insight for future interventions aiming to decrease disparities in child development. Simply, the research suggests that improving incomes of families living in high poverty will improve child development and specifically educational attainment early in elementary school. It strengthens the evidence for government funded programs like Head Start that work to improve the development of children at risk of not reaching their full developmental potential. Also, the evidence supports the need of welfare and other policies that give high priority to getting rid of persistent poverty for everyone, especially young children (54).

Preterm Birth

Any birth that takes places before 37 weeks of complete gestation is considered to be preterm. Births before 34 weeks of gestation are typically classified to be early preterm, while those occurring between week 34 and 37 are late preterm. Preterm birth has always been an important issue to consider, but has become more important as the rate of preterm births has risen significantly since 1990. In the United States, the peak rate of preterm births was in 2006 with 12.9% of births ending preterm. That was a 20% increase from the preterm birth rate in 1990. Since 2006, the preterm birth rates in the United States have slightly declined with 12% of births in 2010 ending preterm. More specifically, in 2010, 8.5% of births ended late preterm and 3.5% ended early preterm. Among singleton births, 10.3% ended before 37 weeks of gestation. The rates are higher in Georgia, with 14.1% of all births ending preterm in 2006 and 13.8% of births ending preterm in 2010. Since 1990, the rate of preterm births before 34 weeks has remained fairly constant; therefore most of the births accounting for increased rates happen between 34 and 36 weeks of gestation (9).

There are several reasons for a preterm birth. Preterm birth can be spontaneous or a result of a c-section. A c-section before a pregnancy reaches full term may be medically indicated or chosen for convenience or preference. Understanding and preventing preterm birth is important as each additional week of gestation decreases the likelihood of impairment (55) and improves functional outcomes in infants (56). At 34 weeks, the brain is only 65% of the full term brain weight. There is much growth of gyri, sulci, synapses, and dendritic arborization left to be done after 34 weeks of gestation (57).

There are many potential causes of preterm birth that are related to genes, environment, infections, nutrition, and behavior. The most significant predictor of preterm birth is having a previous preterm birth (58). Also, if a mother is born preterm, her risk for delivering preterm is increased (59). Some genetic factors that have been linked to preterm birth include cervical length (60), gene polymorphisms that are associated with race (61), and polymorphisms of TNF-α (62), IL-1, IL-4, and IL-6 (63).

Infections during pregnancy are also associated with preterm birth. Bacterial vaginosis is such an infection, with diagnosis earlier in pregnancy being predictive of a greater risk of preterm birth (64). About 22% of women who deliver preterm have a positive bacterial culture from amniotic fluid (65). There is also evidence that a microbial invasion of the amniotic cavity occurs in as many as 34%-75% of women who have a preterm birth due to premature rupture of membranes (66).

Maternal nutrition has been linked to fetal development and preterm birth, but the relationship is complicated. Maternal nutritional status affects fetal development (67) and the effects on fetal development, gestation length, and long-term disease may be linked (68). The fetus is at the end of the nutritional supply line from maternal intake and there are various factors along this supply line that can affect fetal nutrition (69). Also, increases in preterm birth have been associated with delayed childbearing and an increase in multiple gestations due to artificial reproductive technologies as both maternal age and multiple gestations provide greater risk for preterm birth (70).

In addition, preterm birth is associated with race and socioeconomic status. Non-Hispanic white women have a preterm birth rate of 10.8% and Hispanic women have a rate of 11.8% while non-Hispanic black women have a rate of 17.1% (9). The risk of preterm birth is approximately two times higher for African American women than for white women, even after adjusting for confounders (58, 71, 72). The source of the racial disparity is not completely understood, but studies have attributed some of the disparity to weathering or advanced aging (73), racial isolation and segregation (74), racial discrimination (75, 76), and differences in stress levels (77, 78). Adverse birth outcomes were most prevalent among women in the most sociologically disadvantaged groups in 93 of 106 studies included in a systematic review (79).

Neighborhood socioeconomic factors have also been associated with risk of preterm birth. In a study of eight geographic areas in Maryland, Michigan, North Carolina, and Pennsylvania, researchers found that for both non-Hispanic White women and non-Hispanic Black women, there was a significant increase in risk of preterm birth for those living in the fifth quintile of the deprivation index versus the first quintile even when adjusting for maternal age and education level. The difference in risk was more pronounced for the non-Hispanic Black women (80). A large population-based study of births from 1989 to 1997 in Missouri used multi-level modeling methods and found that women living in counties with a higher percentage of poverty are at an increased risk of preterm birth. Adjusting for individual level poverty and demographics reduced the odds ratio comparing those in the counties with highest poverty rate with those in the lowest quartile, but the association remained significant. (81)

Preterm birth is important to study because it is the leading cause of neonatal morbidity and mortality in infants with no congenital anomalies (10). It is a major contributor to various perinatal disorders that contribute to disability-adjusted life years because the disorders start at nearly the beginning of life (82). Infants that are born late preterm (after 34 weeks) experience morbidity during hospitalization more than three times more frequently than infants born at term. Additionally, infants born in late preterm have neonatal mortality rates greater than four times higher than infants born at term (11).

Preterm birth has been associated with several physical and mental health outcomes from infancy to adulthood. It puts infants at risk for severe acute and chronic medical conditions including intraventricular hemorrhaging with subsequent neurological dysfunction, respiratory distress, necrotizing enterocolitis, retinopathy of prematurity, and growth failure (83). There is also a greater risk of hypoglycemia, hyperbilirubinemia, transient tachypnea of the newborn, pulmonary hypertension, sepsis, meningitis, and pneumonia. Infants born preterm are more likely to have feeding intolerance and increased risk of extrauterine growth restriction (84). In adulthood, infants that were born preterm are at risk for developing hypertension, diabetes mellitus, atherosclerotic disease (85), and other chronic diseases.

Preterm birth and child development

Preterm birth has been associated with issues of brain development including volumes of the brain, white matter, grey matter, cerebellum, hippocampus, and corpus callosum (86). These brain development issues can be seen in to adolescence. Adolescents who were born preterm and low birth weight have a smaller brain size and smaller volume of thalamus and cerebellar white matter. Brain volume has been linked with lower IQ scores and negative language development, memory, motor skills, and executive functioning (87).

Preterm birth is also associated with cognitive development as each week of gestation improves cognitive outcomes (88). In a review by de Jong et al., when compared with those born at term, children and adults born moderate or late preterm had more school problems, worse cognitive functioning, more behavior problems, and more psychiatric disorders (89). Additionally, in a meta-analysis of births from 1980-2001, Bhutta et al. found that after age five, cognitive development was directly proportional to birth weight and gestational age (12).

While many studies provide evidence of a significant relationship, the National Institute of Child Health and Development Study of Early Child Care and Youth Development from 1991 to 2007 suggests there is not a relationship. They find that from age five to fifteen, those born late preterm do not have any differences in measures of cognition, achievement, social skills, and behavioral problems when compared to those born at term (90).

There have been several studies that have compared various measures of educational attainment among those born extremely preterm (before 28 weeks of gestation) and those born at term. In a cohort study in Cleveland, Ohio, 148 children born extremely preterm in 2001-2003 were compared with 111 term born peers to assess the relationship between extremely preterm birth and learning problems in kindergarten. Children that were born extremely preterm had lower mean standard scores on spelling and applied mathematics and higher rates of substandard learning in written language and mathematics as reported by their teacher (91). Additionally, all subjects were given comprehensive tests of cognitive development that assessed global cognitive ability, language, spatial and non-verbal reasoning, memory, motor, and executive functioning. The researchers found that there was greater prevalence of cognitive deficits among those born early preterm when compared to the group born at term, even when controlling for acquired verbal knowledge (92). Neonatal risk factors, impairment of early childhood neurodevelopment, and socioeconomic status were all found to be predictors of learning problems among extremely preterm children (91, 92). In a meta-analysis of studies of the influence of very preterm birth, defined as 33 weeks or less, children born very preterm and/or with very low birth weight scored

0.60 standard deviations lower on math tests than their term-born peers. In addition, they scored 0.48 standard deviations lower on reading and 0.76 standard deviations lower on spelling tests compared to term born peers (93).

While very preterm births have been the focus in the past, there has been a more recent push to understand differences in development and educational attainment between children born moderately preterm, typically between 32 and 36 weeks, and those born at term. In a systematic review, McGowan et al. synthesized data from 10 studies on the relationship between late preterm birth (at 34 to 36 weeks) and early childhood development from ages 1 to 7. When compared with term infants, they found that late preterm infants are at an increased risk of neurodevelopmental disabilities, poorer performance on standardized tests, and greater diagnoses of developmental delay up until age 7. Not surprisingly, they also found that children born late preterm have worse outcomes than term born, but better outcomes that those born very preterm. (13)

A study by Talge et al. of births from 1983 to 1985, where a preterm and term born child were matched on birth weight, determined that late-preterm birth (defined as 34 to 36 weeks) was associated with 2 to 3 times increased risk of having a full-scale or performance IQ below 85 and having higher level of internalizing and attention problems at age 6 after adjusting for maternal IQ, residence, and other socio-demographic factors (94). In New York City, researchers linked birth records from 1994 to 1998 to educational data that included third grade test scores. They found that children born preterm (32 to 34 weeks) or late preterm (34 to 37 weeks) had significantly higher odds of needing special education. In addition, those born preterm and late preterm had lower adjusted math and English scores. They found a linear association between test scores and gestational age up to 39 weeks (95).

Data from the Early Childhood Longitudinal Study-Kindergarten Cohort was used to compare learning difficulties from kindergarten to fifth grade among a nationally representative sample of children who started kindergarten in 1998 and were born moderately preterm (defined as 32-33 weeks), late preterm (34 to 36 weeks), or full term (after 36 weeks). Learning difficulties were assessed through standardized testing, teacher evaluations, individualized education programs, and special education services. On direct child assessment tests, late preterm children scored lower than full term children for reading, but not math in both kindergarten and first grade (96). Teacher academic rating scales also differed by birth status with late preterm infants scoring lower than full term in reading and math in kindergarten and first grade. Math abilities became more comparable in later grades. Similarly, children born late preterm had more need for independent educational plans and special education than those born full term in kindergarten and first grade, but in later grades, there was a similar need between the two groups. Late preterm had 24% increased odds for below average reading level in first grade, and a 22% increased odds for below average math score. Late preterm also had 30% increased odds for below average teacher rated reading at all grade levels while there was a 25% increased odds of below average teacher rated math at kindergarten, but there is no significant association for other grade levels. Late preterm infants had an elevated risk for needing special education in the early grades.

In addition to having a negative influence on health and development, preterm birth is an important issue to consider as it takes a large emotional and financial toll on both families and society at large. It is estimated to cost over $26.2 billion per year for acute care for preterm infants (97). In addition to costs for care, there are also costs for early intervention services. In 2003, it was estimated that the mean cost of early intervention services was $857. This cost was highest for those born between 24 and 31 weeks of gestation with the mean for that group being $5,393. The cost per infant decreased with longer gestation, indicating the economic importance of reducing incidence of preterm birth (98).

Research Questions

Neighborhood deprivation, preterm birth, and early child developmental outcomes are important public health issues. As discussed above there is much evidence of an association between neighborhood poverty and deprivation and a child's cognitive development. While this relationship is evident, it is also complicated with many potential factors influencing cognitive development along the way. There is also evidence of a strong relationship between preterm birth and negative cognitive developmental outcomes. This relationship is perhaps more straightforward, as increased gestational age is associated with increased positive cognitive development in children.

While there is substantial evidence of the independent relationships between neighborhood poverty and cognitive development and preterm birth and cognitive development, there are no analyses of how these two factors – neighborhood deprivation and preterm birth – may interact to influence risk of poor cognitive development. This analysis aims to answer the following questions:

1. Is there multiplicative interaction between neighborhood deprivation level and preterm birth when predicting risk for poor cognitive development, as measured by first grade standardized test scores?
2. Is there spatial interaction (effect modification of location) of the influence of preterm birth status and neighborhood deprivation on failure of first grade standardized tests?

Answering these two questions will have positive implications in the research field. Knowledge of the interaction between neighborhood deprivation and preterm birth will assist in the targeting of interventions. Perhaps only targeting one, neighborhood deprivation or preterm birth, will lead to desired increases in levels of cognitive development among children. Also important, this analysis will provide a foundation for the generation of future hypotheses that aim to examine how both the neighborhood and birth outcomes influence child development in the United States and specifically in Atlanta, Georgia.

Methods

Data

The Georgia Birth to School Cohort is a population-based retrospective cohort of children in Georgia that were followed from birth forward to first grade. The data is combined from two state-wide data sets that include birth records and standardized testing data. The birth records are for all live births from 1998 to 2002 to mothers living in Georgia at the time of giving birth. The standardized testing data is from the Georgia State Department of Education and contains scores on math, reading, and English language arts standardized Criterion-Referenced Competency Test (CRCT) for first grade attendees of Georgia public schools from 2004 to 2009. The two data sets were deterministically linked. In the initial state-wide dataset, approximately 53% of births were successfully linked to first grade test scores.

The state-wide data was restricted to the five core metropolitan Atlanta counties – Clayton, Cobb, DeKalb, Fulton, and Gwinnett. This included an initial 114,940 observations. For the purpose of this analysis, data was further restricted to include only mothers between the ages of 15 and 44 years and singleton births of birth weight greater than 500 grams and gestational age greater than 23 weeks. Births to 448 women were excluded for extremes of maternal age (350 ages 10 to 14, 98 ages 45 and older), 3,304 were excluded for plurality (3,091 twins, 207 triplets, and 6 quadruplets), 10 were excluded for birth weight below 500 grams, and 46 were excluded for gestational age less than 24 weeks. After these exclusions, there were 111,150 observations in the dataset.

The dataset for final analysis included only observations with complete data for the exposures, outcome, and covariates of interest. Observations for 154 children were excluded for missing CRCT math failure status, 1 for missing neighborhood deprivation index, 2 for missing mothers marital status, 5,804 for missing the Kotelchuck index of prenatal care, and 2,988 for missing maternal education level. Additionally, 5,428 observations were excluded due to residential addresses that were inaccurately geocoded to the street or census block level. The final dataset contained 97,747 observations.

Exposures

The research question focuses on the statistical interaction on the multiplicative scale of neighborhood deprivation and preterm birth when predicting standardized test performance for children in first grade in Georgia. Therefore, there are two exposures of interest: preterm birth and neighborhood socioeconomic status as measured by the Neighborhood Deprivation Index.

<u>Preterm birth</u>

Gestational age was determined using the date of the mother's last menstrual period and estimates reported on the birth certificate (99). Preterm birth was dichotomized to create two groups: preterm and term. Preterm birth was defined as all births at 36 weeks of gestation or less and a term birth was defined as any birth after 36 weeks of gestation.

<u>Neighborhood Deprivation</u>

Neighborhood is considered to be an individual's immediate residential environment with many potential physical and social factors that influence health (6). To measure neighborhood characteristics, census tract level data was used to approximate factors of each child's residential environment at birth. The United States Census Bureau defines a tract as being a small, relatively permanent subdivision of a county. Tracts are designed to represent groups of residents with homogeneous socio-demographic characteristics and living conditions. Each tract contains an average of 4,000 residents.

Maternal addresses were taken from the birth certificate records and were geocoded by the Office of Health Indicators for Planning (OHIP) of the Georgia Department of Public Health in order to identify each census tract. Thus the birth dataset was merged with an area-based dataset containing census tract level measures for each birth year. Census data was only available for births in the year 2000, however, using 1990 and 2010 Census data, information on each tract was extrapolated to match the birth year.

Neighborhood poverty was determined by estimating the percent of households at or below the poverty line in each census tract. For initial exploratory analysis, the poverty level variable was dichotomized to represent those living in a tract with 20% or more of the residents living below the federal poverty line versus those living in a tract with less than 20% living below the poverty line (27).

Neighborhood deprivation was calculated as the Neighborhood Deprivation Index using the methods of Messer et al. (36) and eight census variables that represent five different socioeconomic domains that are hypothesized to be associated with various health outcomes. These domains include income and poverty, education, employment, housing, and occupation. The variables representing the domains include percentage of males in management and professional occupations, percentage of residents living in crowded housing, percentage of households in poverty, female-headed households with dependents, households on public assistance, households earning less than $30,000 a year, percent of residents with less than a high school education, and the percent of residents that are unemployed. These eight variables were summarized using principal component analysis to create the Neighborhood Deprivation Index (NDI). Finally, the NDI was standardized with a mean of 0 and a standard deviation of 1. This standardization is a result of dividing the difference between a neighborhood's NDI and the overall mean NDI by the standard deviation of the NDI. With the standardized scale, a NDI of 1 indicates that a tract is 1 standard deviation more deprived than the average tract in Georgia. Similarly, a NDI of -1 indicates that a tract is 1 standard deviation less deprived than the average tract in Georgia. In the regression analyses, the NDI was treated as a continuous variable. For descriptive statistics and exploratory data analysis, the NDI was dichotomized as "deprived" and "not deprived". "Deprived" was defined as 1 or more standard deviation greater deprivation than average and “not deprived” was defined as less than 1 standard deviation greater deprivation than average.

Initial exploratory analyses were performed to determine if both neighborhood poverty level and NDI should be included in the final models. Poverty and NDI were determined to be highly correlated (Pearson correlation coefficient=0.94, p<0.001). Since the NDI includes the percent of the population living below the poverty level in each tract as well as other domains that may be influencing outcomes, the NDI was included in the final models rather than neighborhood poverty.

Outcome

<u>Failure of math CRCT</u>

While the exposure variables are factors from the time of birth, the outcome was measured several years later. The outcome of interest in this analysis was cognitive development in first grade. For the analysis, performance on first grade standardized tests was used as a proxy for cognitive development. Specifically for this analysis, the outcome was measured as failure to meet versus meet or exceed the standard of the math portion of the Georgia Criterion-Referenced Competency Test (CRCT). The test, given in kindergarten through eighth grade in all public schools in the state during the study period, is designed to assess students’ mastery of the content of the Georgia Performance Standards. It is considered to be a key indicator of student success and is one criterion in determining progress to the subsequent grade. This outcome variable was dichotomous, representing whether a student either failed to meet the standards or met the standards of the math portion of the CRCT.

Covariates

In addition to the main exposure variables, covariates were included to control for demographic information, individual socioeconomic status, mothers smoking status during pregnancy, and quality of prenatal care. Maternal demographics included were age, race, and marital status at time of giving birth. Additionally, the gender of the child, as reported on the birth certificate, was included. Maternal age was reported on the birth certificate and categorized into six five-year age groups. A new race variable was created using maternal race and maternal ethnicity as reported on the birth certificate. The categories of this new variable included non-Hispanic white, non-Hispanic Black, Hispanic, and other. Marital status was dichotomized as married and unmarried based on birth certificate data.

Individual socioeconomic status was controlled for by including maternal education and the payor of the medical costs associated with the birth. The mother's last completed grade of school at the time of giving birth was derived from birth certificate data. Four categories of education were created: completed less than high school, completed high school, completed one to three years of college or technical school, and completed four or more years of college or technical school. Payor status was dichotomized as Medicaid and other or unknown.

Smoking status during pregnancy was determined by report on the birth certificate. The variable was dichotomized to indicate any tobacco use during pregnancy or unknown/non-use during pregnancy. The Kotelchuck index was used to control for the adequacy of prenatal care. The index is categorized as inadequate, intermediate, adequate, and adequate plus based on when the mother started prenatal care and how many times she went (100).

Data Analysis

Descriptive statistics for all exposure, outcome, and covariates in the overall population were obtained using PROC FREQ in SAS 9.3 (Cary, NC). Chi-square tests were used to assess for significant differences of variables between the dataset before and after excluding observations with missing data and inaccurate geocoding. Additionally, descriptive statistics were attained for all variables using the same method for the portion of the population that was born preterm and the portion who lived in a neighborhood with a deprivation index at least one standard deviation greater than the mean.

To assess for significant bivariate associations between each covariate and the exposures and outcome, logistic and linear regression models were run using PROC GENMOD. A linear model was used to assess associations with each covariate and the continuous NDI. Logistic binomial models were fit to assess associations between the covariates and preterm birth status as well as with the main outcome, failing the math CRCT. Additionally, the relationships between the two exposures, preterm birth and NDI, were modeled with the outcome using a logistic binomial model. Log-likelihood chi-square statistics were used to assess the significance of each association.

Using PROC GENMOD, generalized estimating equation (GEE) models were used to obtain odds ratios approximating risk ratios for the exposures as adjusted for the covariates. A multivariable logistic binomial model with a compound symmetric correlation structure was used to model the odds for failure of the math CRCT. A repeated statement was used to account for correlation of subjects residing in the same neighborhood, defined as a census tract. This was important, as those living in the same area may have correlated outcomes. Typically, this violates the independence assumptions that are a part of many traditional regression strategies. However, the coefficients that result from the GEE model explain changes in the population mean given changes in the covariates, while accounting for non-independence that may be present within neighborhoods (101).

Six models were run using this method to assess the association of the two exposures, preterm birth and NDI, and probability of failing the CRCT. The first model contained only the two exposures. The second model included the two exposures and all demographic covariates including maternal age and marital status at child's birth, maternal race, and child sex. The third model included the two exposures and measures of individual socioeconomic status including payor status and maternal education at the time of child's birth. The fourth model included the two exposures and maternal smoking status during pregnancy. The fifth model included the two exposures and the Kotelchuck index to measure adequacy of prenatal care. The sixth, and final, model included the two exposures and all covariates. The same six models were run a second time using the same methods, but including an interaction term to assess for multiplicative interaction between preterm birth and neighborhood deprivation. Additionally, a subset of the interaction models were run stratified on race in order to consider a potential three-way interaction between preterm birth, neighborhood deprivation, and race.

While the GEE models account for the non-independence of subjects living in the same census tract, the resulting coefficients are assumed to be constant over space and there is no consideration of spatial variability, ultimately ignoring any spatial dependencies between variables (102). Ignoring space could result in biased results with an overstatement of associations. To explore potential spatial variability in the relationship between the exposures and the outcome when adjusted for all covariates, the R software package was used to employ the geographically weighted regression (GWR) modeling technique.

GWR assumes that the relationship between an exposure and an outcome may vary over space. Each observation point i gets its own set of local regression coefficients to allow for this variation (103, 104). The GWR model can be written as:

$$y_i = \beta_{i0}(u_i, v_i) + \sum_{k=1}^{p} \beta_{ik}(u_i, v_i) x_{ik} + \varepsilon_i \,, \; i = 1, \ldots, n$$

The intercept parameter at point i is represented by $\beta_{i0}(u_i,v_i)$. $\beta_{ik}(u_i,v_i)$ is the regression coefficient for the *kth* independent variable at point i and (u_i,v_i) are the coordinates of the point in the study area. In this analysis, these coordinates are the latitude and longitude coordinates of each mother's residence at the time of giving birth. The GWR method was applied to a subset of the final, complete, dataset used in all other models. The subset was taken as a random sample of 10,000. Using the quasibinomial distribution, the GWR provided odds ratios for each point in the sample.

The local regression coefficients for all points were estimated using the locally weighted likelihood for the quasibinomial-logistic model produced by weighting all observations according to their spatial proximity to each point *i*. Those observations closer to the point of interest have greater weight on the local regression coefficient. These weighting parameters can be calculated from this equation:

$$\hat{\beta}(u,v) = (X^T W(u,v)X)^{-1} X^T W(u,v)Y$$

$\hat{\beta}$ *(u,v)* is the unbiased estimated of β while *W(u,v)* is the weighting matrix that is used to appropriately weigh observations near point *i* based on the determined kernel function. The appropriate weight can be calculated using a Gaussian weighting kernel function form, as follows:

$$w_{ij} = \exp\left(\frac{-d_{ij}^2}{h^2}\right)$$

The distance between point *i* and another point is represented by d_{ij}^2 and the kernel bandwidth is represented by h^2. A kernel bandwidth is assigned to determine the point beyond which the weight of an observation is zero and can be either fixed or adaptive. The fixed kernel bandwidth remains constant over space while the adaptive kernel bandwidth varies over space, being larger where data are more sparse and smaller where data are denser. For this analysis, an adaptive bandwidth of 0.25 was used. This means that for each point *i*, those observations that were within the 25th percentile of distance from the point were weighted in the local regression coefficient and all other points were weighted as zero. The Emory Institutional Review Board approved this study.

Results

In this data of 97,747 children from the five core counties (Clayton, Cobb, DeKalb, Fulton, and Gwinnet) of Atlanta, 11.4% of children failed the math portion of the CRCT in first grade [Table 1]. Children born preterm (before 37 complete weeks of gestation) made up 9.6% of the sample. At the time of giving birth, 10.2% of the mothers in the sample were living in a census tract with an NDI greater than one standard deviation above the mean.

The highest proportion of mothers gave birth between the ages of 25 and 29 (26.5%), 30 and 34 years (24.7%), and 20 and 24 years (23.3%). The majority of mothers were non-Hispanic black (42.9%) while 36.6% were non-Hispanic white, 13.7% were Hispanic, and 6.79% were other races. At the time of giving birth, 20.6% mothers had not finished high school, 28.1% finished high school, 21.6% attended one to three years of school after high school, and 29.8% completed college. Also, 62.9% of mothers were married and 4.6% reported smoking during pregnancy.

The final dataset was compared with the overall dataset that included all observations with missing information and inaccurate geocoding. The distribution of all variables except for child sex was significantly different in the two datasets; however, there do not appear to be any clinically meaningful differences. The significance is likely due to the large sample size making even the slightest differences appear highly significant.

The descriptive statistics for the population that was born preterm or lived in a neighborhood with above average deprivation at time of birth are shown in Table 2. In this sample, there were 9,409 preterm births. Women living in higher than average deprivation had a higher proportion of preterm births than women living below deprivation (12.7% vs. 7.8%). Preterm births disproportionately affected women in the lowest and highest age groups (ages 15-19: 11.1% preterm, ages 40-44: 12.0%), those who are non-Hispanic Black (11.89%), and unmarried (11.68%).

In the sample, 10,455 women were living in above average deprivation at the time of giving birth. Younger women had a greater proportion of their population living in above average deprivation with 23.5% of 15 to 19 year olds and 17.5% of 20 to 24 year olds living in those areas. There was also a large disparity in race with 21.5% of non-Hispanic black women living in above average deprivation compared to 0.9% of non-Hispanic white women. Among unmarried women, 23.2% lived in above average deprivation. For women who completed less than high school, 22.9% lived in above average deprivation at the time of giving birth while only 1.4% of women who completed college did.

As shown in Table 3, there was a significant crude association between preterm birth and failure of the math CRCT in first grade (RR: 1.42, 95% confidence interval [CI]: 1.35, 1.49). There was also a significant crude association between NDI and failure of the math CRCT in first grade (RR: 1.38, 95% CI: 1.37, 1.30). All of the covariates (maternal age, maternal race, maternal marital status, child sex, payor status, maternal education, maternal smoking status, and the Kotelchuck index) were significantly associated with failing the math portion of the CRCT in first grade ($p<0.001$ for all). Additionally, all the covariates were significantly associated with preterm birth ($p<0.001$ for all) and all except for child sex were significantly associated with the NDI.

The results from the generalized estimated equation models [Table 4] that included both exposures, but are otherwise not adjusted for covariates (Model 1) show a significant independent association between both preterm birth (RR: 1.30 95% CI: 1.24, 1.36) and neighborhood deprivation (RR: 1.35 95% CI 1.30, 1.41) and the risk of failing the math CRCT. Adding demographic variables to the model (Model 2) attenuated the risk ratios of each, but maintained a significant association. Adding individual socioeconomic measures (Model 3) attenuated the risk ratios in a similar fashion. When adjusting for all covariates (Model 6), the risk ratios for the exposures remained significant although they were lower than the crude estimates. The adjusted risk ratio of failing for those born preterm versus term was 1.23 (95% CI: 1.17, 1.30) and the risk ratio for failing for those living in a neighborhood that had an NDI one standard deviation higher than the average was 1.04 (95% CI: 1.02, 1.06).

The results from the interaction models [Table 5] show a similar pattern and suggest that there is significant interaction between preterm birth and NDI when predicting failure in each model. In the crude model (Model 1), which contained only the exposures and the interaction term, preterm birth and NDI were independently associated with the risk of failing (RR: 1.32, 95% CI: 1.26, 1.39; RR: 1.37 95% CI: 1.31, 1.42, respectively). The interaction term was significant ($p=0.009$), indicating that among those born preterm, a one standard deviation increase in NDI increased risk of failing by 30% (RR=1.30, 95% CI: 1.24, 1.36) rather than the estimated 37% increase for term born children. Again, adding demographic variables (Model 2) or individual socioeconomic status (Model 3) variables to the model attenuated the effect of both exposures, although the exposures and interaction term remained significant. Adding smoking status during pregnancy (Model 4) or the quality of prenatal care (Model 5) increased the effect of both preterm birth and NDI on failure status. In the final model that controlled for all covariates (Model 6), the risk ratio for preterm and deprivation remained significant, although increased NDI had a very small effect. Additionally, the interaction term was significant ($p=0.016$). These results indicate that among those born preterm, there was no significant effect of NDI (aRR=1.00, 95% CI: 0.97, 1.04). Among children born at term, a change of one standard deviation of the NDI increased risk of failing math by 4% (RR=1.04, 95% CI: 1.02,1.06).

In an effort to understand how the demographic variables may explain some of the relationship between preterm birth, NDI, and failure status, Table 6 shows the results of the interaction models stratified by black and white race. Among non-Hispanic blacks, the fully adjusted (Model 6a) risk ratio for the relation between preterm and term births was 1.28 (95% CI: 1.20, 1.36) while the risk ratio for a one standard deviation increase in deprivation index was 1.03 (95% CI: 1.01, 1.05). There is evidence of interaction between preterm birth and NDI. Specifically, among blacks born preterm, there is no significant association between a change in deprivation and failure status (aRR: 0.98, 95% CI: 0.94, 1.02). On the other hand, among blacks born at term there is a small, but significant, effect of the change in NDI on failure status (aRR: 1.03, 95% CI: 1.01, 1.05). This is a similar pattern as seen in the fully adjusted model for the whole sample (Table 5, Model 6). Among non-Hispanic whites, when adjusted for all covariates (Model 6b), the effect of preterm birth is similar (aRR: 1.25, 95% CI: 1.04, 1.50). Among whites that were born preterm, the risk ratio for a one standard deviation increase of NDI is 1.22 (95% CI: 1.04, 1.44). Among whites born at term, the risk ratio for an increase in NDI is 1.27 (95% CI: 1.19, 1.36).

The results from the geographically weighted regression appear to show similar patterns. Figure 1 depicts the interaction between preterm birth and NDI when predicting failure status of the CRCT math test. The geographically weighted regression model depicted contains only preterm birth status, neighborhood deprivation, and the interaction between the two. The map on the left shows odds of failing math with a one standard deviation increase in NDI among all preterm births. The map on the right shows the same relationship for term births. These maps indicate that there is a difference in the interaction between preterm birth and deprivation based on residential location in the five core counties of Atlanta. Among preterm births, it appears that deprivation has the greatest effect in the northwest and eastern areas of the five-county region. The northeast area and middle-western area have the least effect of deprivation. Among term births, the greatest effect of deprivation is in the northeast area. Deprivation has the least effect in the southern half of the region.

Figure 2 shows the effect of deprivation on failing for preterm and terms births, but controls for all demographic variables, individual socioeconomic status, smoking status, and adequacy of prenatal care. The patterns are fairly similar to the patterns in Figure 1. Among preterm births, the influence of deprivation on failure status is greatest in the northwest and in the easternmost areas. In the northeast and center of the region there appears to be little, if any, effect of deprivation on failure. Among term births, deprivation has the greatest effect in the northeast and in small areas in the northwest and very south. There is little, if any, effect of deprivation in the central and mid-western areas of the region.

The numerical results of the GWR [Table 7] suggest a similar pattern as seen in the multivariable logistic regression. The medians and interquartile ranges offer insight in to the range of results of the odds ratios for each observation included in the analysis. In the model that included preterm birth, NDI, and the interaction between the two (Model 1), there appeared to be a consistent influence of both preterm birth and NDI on the odds of failing. When controlling for all the covariates in Model 6, the effect of preterm birth remained high while the effect of the NDI appeared to be attenuated.

Discussion

The results of this analysis indicate being born preterm versus term increases risk of failing the math portion of the CRCT in first grade when controlling for neighborhood deprivation, maternal age, maternal race, maternal marital status, child sex, insurance payor status, maternal education, maternal smoking status during pregnancy, and the quality of prenatal care. A one standard deviation increase in neighborhood deprivation also increases the risk of failing the math portion of the CRCT, but appears to have less of an effect than preterm birth when adjusting for the same covariates. Additionally, results of this analysis provide evidence that there is multiplicative interaction between preterm birth and neighborhood deprivation when predicting risk for poor cognitive development, as measured by first grade standardized test scores. The significance of the interaction term indicates that increased neighborhood deprivation increases the risk of failing the math CRCT in term births only. Among preterm births, there is no significant increase in risk with an increased level of neighborhood deprivation.

Although the significance of the coefficients from the geographically weighted regression are unknown, the results indicate that in addition to the interaction between preterm birth and neighborhood deprivation, there is also substantial spatial interaction. The effect of preterm birth, deprivation, and the interaction of the two appear to vary in different areas of the five core counties of Atlanta. Even after adjusting for demographic and individual socioeconomic variables, the spatial heterogeneity remained. This suggests that the relationship does differ by space, regardless of patterns of variables that are controlled for like maternal race and education level.

Of all covariates that were controlled for in the multivariable logistic regression models, maternal race and maternal education appear to have the greatest significant effect on the risk of failing the math CRCT in first grade. In the model that controlled for only the individual socioeconomic status and the full model controlling for all variables, there appeared to be a linear relationship between the years of school a mother had completed and the child's risk of failing.

Children of mothers with less education had a greater risk of failing. The effects were similar for both the full and reduced models, and in each the inclusion of maternal education in the model attenuated the risk of the exposures, especially neighborhood deprivation. There are several potential reasons that maternal education may appear to be so influential in these results. First off, maternal education is a proxy variable that is used for individual socioeconomic status. Individual socioeconomic status has been proven to be an important determinant of academic achievement and therefore is likely to be an important determinant of failing the math portion of the CRCT. Also, maternal education level may represent the IQ and other non-cognitive skills of a mother. There is potential that educational level is then accounting for some cognitive or non-cognitive characteristics that may be inherited by a child.

When only controlling for demographic information (maternal age, maternal race, child sex, and maternal martial statues), children with Hispanic mothers of any race had the highest risk of failing followed by non-Hispanic Black mothers. When adjusting for all covariates, children with non-Hispanic Black mothers had a higher risk of failing followed by those with Hispanic mothers. This suggests that the effect of the Hispanic race was accounted for by other variables included in the model, likely maternal education level.

The consistently significant effect of preterm birth on the risk of failing the math portion of the CRCT in first grade in this analysis is consistent with other studies that have used birth data and educational data to provide evidence of a significant association between gestational age at birth and educational attainment. A study by Lipkind et al. in New York City used birth data linked to educational data to determine that children born before 37 weeks of gestation had lower adjusted math and English scores than their peers (95). While they used a continuous measure of test scores rather than a dichotomous indicator of failure, the results are consistent with this analysis. Similarly, using data from the Early Childhood Longitudinal Study-Kindergarten Cohort (ECLS-K), Chyi et al. found that in the nationally representative sample of children who started kindergarten in 1998 and were born moderate preterm (defined as 32-33 weeks), late preterm (34 to 36 weeks), or full term (after 36 weeks) there were greater learning problems among those born late preterm when compared to term. Late preterm born children had a 22% increased odds for a below average math score when compared to term born children (96). The odds found by Chyi et al. are consistent with this analysis, where in the fully adjusted interaction model, there was a 25% increased risk of failing among children born preterm when compared to children born at term.

Resnick et al. linked school records to birth records in Florida to study the impact of perinatal and sociodemographic risk factors on educational attainment as measured by placement in a special education class or reports of academic problems. They found a significant association between both perinatal and sociodemographic risk factors. Perinatal risk factors had greater effects on more severe special education while sociodemographic factors were more indicative of a mild educational disability. Overall, they found that sociodemographic factors were more influential than the perinatal risk factors (105). These conclusions are generally consistent with the results of this analysis. Individual sociodemographic factors, especially maternal race and education, appear to have the greatest effect on the risk of failing. Preterm birth certainly has a significant effect, but it is not as large as those individual factors.

The independent effect of neighborhood deprivation on the risk of failing was significant, but small. The results of this analysis differ somewhat from other studies where researchers have found a greater association between deprivation (or other neighborhood level factors) and performance in school. For example, Sastry and Pebley used data from the 2000-2001 Los Angeles Family and Neighborhood Survey and found that one third of the variation in math performance was associated with differences in socioeconomic status. Further, using multi-level models, they found that neighborhood socioeconomic status has a larger impact on the inequality of test scores than coming from a low-income family (7). These results are opposite of what the results of this analysis suggest. Using the CRCT as an outcome, controlling for individual socioeconomic factors of insurance status and maternal education level attenuated the risk ratio of neighborhood deprivation in a way that suggested that the individual factors may be explaining more of the variation than the neighborhood level factor. These differences in results may be accounted for by regional differences or differences in measurement and controlling methods.

There are very few studies with the specific objective of assessing the combined effect of socioeconomic status and preterm birth on various measures of cognitive development. In a study of a cohort of births between 1992 and 1995, Andreias et al. used a multi level modeling technique that accounted for random effects of between-tract and within-tract variability to assess how a neighborhood may influence academic achievement of 8 year olds among those born with extremely low birth weight (<1,000 grams) and those born with normal birth weight. They found that those with extremely low birth weight had lower achievement scores then those born with normal birth weight. They also found that there was no significant interaction, so for both weight groups, neighborhood poverty was significantly associated with lower achievement, and this association was greater than individual and family level variables (106). Since birth weight and gestational age are often correlated, it is surprising that their results of interaction differ from the results in this paper. This may be attributable to the different exposure, the use of poverty rather than deprivation, different sample sizes, or the random effects modeling technique. Also, birth weight could very possibly be low for another reason besides gestational age. In that case, it is measuring something different, and should not be compared to results from an analysis using gestational age. Ultimately, the results of the analysis Andreias et al. and the results of this analysis cannot be directly compared, but offer insight in to future directions and modeling techniques for this type of research question.

There have been no analyses to assess the spatial heterogeneity of the effect of various early childhood and neighborhood level factors on academic achievement. The differences in space that were indicated by the geographically weighted regression could be the result of many factors. In areas of Atlanta where there is a higher concentration of deprivation, the effect of deprivation would likely be different, and perhaps more influential. Similarly, in areas that are composed of more suburban, middle class, residents, there may not be as great of an influence of deprivation. Also, these areas may have greater resources for early intervention services that may improve the likelihood that a child will meet or exceed standards in first grade. While the results of the geographically weighted regression appear to show spatial heterogeneity, there is much research that should be done to further assess the significance of the heterogeneity of the independent and combined effects of the exposures.

Strengths and Limitations

Considering the lack of research assessing the potential interaction between preterm birth and neighborhood deprivation, this analysis certainly adds to the body of research. This analysis suggests that there is not as large of an effect of neighborhood deprivation as one might expect, especially among children that were born preterm when controlling for demographic and individual level socioeconomic factors. There are several reasons that this may be the case. One explanation may be that there are additional factors that are unmeasured, but that confound the relationship. Another explanation is that level of neighborhood deprivation may be a cause of preterm birth and therefore would be an intermediary variable between preterm birth and failure of the math CRCT. In this case, the effect of deprivation would appear minimal among those born preterm as preterm birth status accounts for any variation. It is also possible that children born preterm in areas of greater deprivation may be recipients of services targeted to improve their development as a result of being born preterm and the associated morbidities. In this case, children born at term may not benefit from the same services because there were no alarming complications at birth. Finally, it is possible that none of these explanations are true and that there is truly no association.

In addition to adding to the very limited body of research on the combined effects of neighborhood deprivation and preterm birth on academic achievement in early elementary school, this analysis has additional strengths. The sample is large and population based. It follows an entire birth cohort (those born in years 1998 to 2002) through first grade. Although the dataset was created retrospectively, the outcomes were measured after the exposures. While there is potential for bias in the data collected from birth certificates and schools, there is little potential for any recall bias as children and their mothers are never directly interviewed regarding past exposures. Most importantly, this analysis is exploratory in nature, examining a new way of assessing place-based differences in significance, magnitude, and interaction of effects. Using geographically weighted regression, account is made for space and allows for consideration of spatial heterogeneity in a way that is not possible with other regression techniques.

There are several limitations of the data that was used for this analysis. Of the initial state-wide cohort, only 53% of observations were successfully linked to educational data. This could be due to several factors. First, there is potential of a child moving out of Georgia after being born but before entering first grade. Second, only public schools are mandated to do the CRCT testing in Georgia, so children that attend private schools or are homeschooled will not be successfully linked. Third, a small number of children may have died before starting school or have a disability that keeps them from attending school. Additionally, there could be errors in records that created an inability to correctly link the birth and education records. The linking process may potentially lead to selection bias in the sample. While this is a concern, previous analyses using this data have found that those who were successfully linked were demographically similar to those who were not linked.

For the records that were successfully linked, all information on mother and child, except for failure status of tests, came from the birth certificate. This is a potential concern for misclassification of exposure as the birth and first grade testing happened approximately 6 or 7 years apart. Of greatest concern is the potential for misclassification of residential status, as the Neighborhood Deprivation Index is derived from this. It is possible that a mother moved to a neighborhood early in a child's life that has a very different deprivation level than the neighborhood she was living in at the time of the child's birth. Mothers move a lot around the time of pregnancy, but it is assumed that they stay within areas with similar neighborhood level factors. Some research suggests that changes in neighborhood advantage are not linked to changes in children's achievement and that what matter most are the living conditions from very early life. One explanation is that neighborhood advantage sets children on a higher achievement course early and this early advantage is unchanged as children grow older, suggesting that neighborhood conditions may have a long-term impact on achievement (52). Additionally, there is potential for misclassification of several of the covariates including maternal education, marital status, and insurance status as they could have changed over time. Therefore the results can only reflect the consideration of these factors as they were at the time of the child's birth. In addition, we assume that the child in fact resides with their mother at time of birth and through early childhood. There is also potential that the relationship between the exposures and outcome may be explained by unmeasured variables.

Using the GWR method was helpful as an exploratory tool in understanding the spatial heterogeneity of the association and interaction between preterm birth and neighborhood deprivation on the risk of failing the first grade CRCT, however, there are limitations to the information it provides. First, the GWR provides the median, mean, and range of the coefficients of each individual point observation, but as implemented here does not allow for statistical testing of the average effect. Further work must be done to determine statistical significance. Also, the coefficients in the GWR are not necessarily comparable to the coefficients from the GEE models as the GEE are a global estimate and the GWR is not. In GWR, there is also potential for multicollinearity among the local estimates of the model. Finally, GWR may not adequately address spatial autocorrelation, although it does mitigate it.

In this analysis, CRCT scores are used as an indicator of a child's cognitive development at the end of first grade. While these scores do not directly test the cognitive development of a child, the thought is that they are representative of experiences and development that a child would have before entering school. First grade test scores are more indicative of early child development and external influences than test scores in later grades. While this academic performance is important when considering a child's development, interpretation of the results is limited to performance on these tests themselves as an indicator of development, rather than a direct measure of child development.

The cheating scandal in the Atlanta Public School system is important to mention. In 2011, educators in approximately thirty elementary and middle schools in Fulton County, Atlanta confessed to cheating on the Criterion-Referenced Competency Test (CRCT). A report from Governor Nathan Deal's office details evidence of cheating on the 2009 CRCT in 44 of 56 schools that were investigated within Fulton County (107). Investigators found evidence that cheating has been happening in the district since 2001, but from 2006 to 2009 there is strongest evidence of educators altering test answers. Of the 90 elementary and middle schools where the CRCT is given in Atlanta, 52 were flagged with having more than 20% of their classes greater than three standard deviations from the norm in an assessment of wrong-to-right erasures on the test. Most of the alleged cheating took place in Fulton County, the county with the greatest number of subjects for this study (28.3%). This study population attended first grade between 2004 and 2009 and therefore those attending school in Fulton County may have been influenced by the cheating scandal. The cheating scandal would decrease the amount of true failures of the math portion of the CRCT and would ultimately underestimate the true effect of both preterm birth and neighborhood deprivation on the risk of failing, biasing it toward the null.

Future Directions

While considering both the strengths and limitations of this analysis, there are recommendations for future research to impact potential future interventions. Further work using geographically weighted regression is important for understanding the significance of the results and determining if there are areas where preterm birth, neighborhood deprivation, or a combination of the two are disproportionately affecting the risk of failing to meet educational standards in the first grade. It would also be helpful to perform similar analyses using alternate measures of child development in order to directly assess cognition. Stratifying for race suggests some additional interaction, as the effect of deprivation was different among the blacks and whites in the study population. Further analysis should assess more interactions in order to find evidence of those populations that may benefit most from interventions.

The results of this exploratory analysis provide evidence of the importance of programs that aim to improve child development in vulnerable populations. Specifically, these results suggest that children born at term into areas of higher deprivation could benefit from early child development programs like Head Start. Those born preterm have a consistently higher risk of failing the math CRCT regardless of neighborhood deprivation, so there continuing evidence of a need for programs that help those who are born preterm to catch up to term born peers.

In conclusion, there is evidence of a significant effect of preterm birth and neighborhood deprivation on the potential for failure of the math portion of the CRCT in first grade. Additionally, there is strong evidence of multiplicative interaction between preterm birth and neighborhood deprivation. While for term births, an increase in neighborhood deprivation leads to an increased risk for failure, the effect is rather small. For preterm births, there is no effect of deprivation. In addition, there is evidence of the interactive relationship differing by space, suggesting that deprivation and preterm birth each have differing independent and combined effect on the odds of failing the math portion of the CRCT based on location within the five core counties of Atlanta.

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Tables

Table 1. Descriptive statistics of the birth to school cohort before and after excluding observations with missing variables

	Overall[a] N=111,150			Complete[b] N=97,747		
	n	%	Missing	n	%	p-value[c]
Outcome						
Fail Math CRCT	13,699	12.3	154	11,706	12.0	<0.001
Fail ELA[d] CRCT	17,589	15.9	185	14,963	15.32	<0.001
Fail Reading CRCT	10,825	9.8	131	9,146	9.4	<0.001
Exposures						
Gestational age			0			0.004
≤ 36 weeks	10,806	9.7		9,409	9.6	
> 36 weeks	100,344	90.3		88,338	90.4	
Deprivation Index[e]			1			<0.001
Below average deprivation	33,239	29.9		29,836	30.5	
Average	66,041	59.4		57,456	58.8	
Above average deprivation	11,869	10.7		10,455	10.7	
Characteristics						
Maternal age			0			<0.001
15-19 years	12,442	11.2		10,764	11.0	
20-24 years	26,231	23.6		22,660	23.2	
25-29 years	29,610	26.6		25,880	26.5	
30-34 years	27,010	24.3		24,118	24.7	
35-39 years	13,545	12.2		12,254	12.5	
40-44 years	2,312	2.1		2,071	2.1	
Maternal race			0			<0.001
Non-Hispanic white	38,870	35.0		35,788	36.6	
Non-Hispanic black	47,319	42.6		41,952	42.9	
Hispanic	16,941	15.2		13,367	13.7	
Other	8,020	7.2		6,640	6.8	
Marital status			2			<0.001
Married	69,707	62.7		61,463	62.9	
Unmarried	41,441	37.3		36,284	37.1	
Child sex			0			0.304
Male	56,219	50.6		49,384	50.5	
Female	54,931	49.4		48,363	49.5	
Birth year			0			<0.001
1998	23,598	21.2		20,856	21.3	
1999	24,295	21.9		20,898	21.4	
2000	26,025	23.4		22,939	23.5	
2001	22,868	20.6		19,941	20.4	
2002	14,364	12.9		13,113	13.4	
Payor			0			<0.001
Medicaid	42,867	38.6		37,419	38.3	

Unknown	68,283	61.4		60,328	61.7	
Education			2,988			<0.001
Less than high school	22,973	21.2		20,105	20.6	
Completed high school	30,628	28.3		27,472	28.1	
1-3 years of college	23,026	21.3		21,063	21.6	
Finished college	31,535	29.2		29,107	29.8	
Smoked during pregnancy	4,976	4.5	0	4,450	4.6	0.001
Kotelchuck Index			5,804			<0.001
Inadequate	8,229	7.4		7,614	7.8	
Intermediate	9,821	8.8		9,070	9.3	
Adequate	52,026	46.8		48,326	49.4	
Adequate plus	35,270	31.7		32,737	33.5	
County			0			<0.001
Clayton	11,140	10.0		9,151	9.4	
Cobb	23,059	20.8		20,926	21.4	
DeKalb	23,909	21.5		21,281	21.8	
Fulton	31,529	28.4		27,625	28.3	
Gwinnett	21,513	19.4		18,764	19.2	
Quality of Geocoding						
Street level match	101,984	91.8		94,277	96.5	<0.001
Block level match	3,738	3.4		3,470	3.4	
Tract level match	508	0.5		-	-	
Missing/County level	4,920	4.4		-	-	

[a] Includes observations >500g birth weight, >24 weeks gestation age, maternal age between 15-14

[b] Excludes all observations with missing data for failing math CRCT, NDI, maternal marital status, maternal education level, and Kotelchuck index, and includes those with a street or block level geocode

[c] p-value from chi-square test assessing significant differences between overall and complete datasets

[d] ELA = English Language Arts

[e] Below average deprivation = < -1 standard deviation from the average; Average = between -1 and 1 standard deviation from the average; Above average = > 1 standard deviation from the average

Table 2. Descriptive statistics by preterm and deprivation status

	Preterm[a] N=9,409		**"Deprived"** [b] N=10,455	
	n	%[c]	n	%[c]
Outcome				
% Fail Math	1,536	13.1	2,225	19.0
% Fail ELA	1,884	12.6	2,548	17.0
% Fail Reading	1,181	12.9	1,715	18.8
Exposures				
Gestational Age				
≤ 36 weeks	-	-	1,325	14.1
> 36 weeks	-	-	9,130	10.3
Neighborhood Deprivation Index[d]				
Below average deprivation	2,335	7.8	-	-
Average deprivation	5,749	10.0	-	-
Above average deprivation	1,325	12.7	-	-
Characteristics				
Maternal age				
15-19 years	1,193	11.1	2,527	23.5
20-24 years	2,240	9.9	3,963	17.5
25-29 years	2,285	8.8	2,232	8.6
30-34 years	2,166	9.0	1,098	4.6
35-39 years	1,276	10.4	511	4.2
40-44 years	249	12.0	124	6.0
Maternal race				
Non-Hispanic white	2,856	8.0	313	0.9
Non-Hispanic black	4,987	12.0	9,033	21.5
Hispanic	1,021	7.6	889	6.7
Other	545	8.2	210	3.2
Marital status				
Married	5,170	8.4	2,057	3.4
Unmarried	4,239	11.7	8,398	23.2
Child sex				
Male	4,979	10.1	5,320	10.8
Female	4,430	9.2	5,135	10.6
Birth year				
1998	1,975	9.5	2,517	12.1
1999	2,019	9.7	2,365	11.3
2000	2,088	9.1	2,577	11.2
2001	2,042	10.2	1,890	9.5
2002	1,285	9.8	1,106	8.4
Payor				
Medicaid	3,913	10.5	7,232	19.3
Unknown	5,496	9.1	3,223	5.3
Education				
Less than high school	2,092	10.4	4,600	22.9

Completed high school	2,902	10.6	4,088	14.9
1-3 years of college	2,117	10.1	1,374	6.5
Finished college	2,298	8.0	393	1.4
Smoked during pregnancy	608	13.7	841	19.0
Kotelchuck Index[e]				
Inadequate	994	13.1	1,952	25.6
Intermediate	366	4.0	1,239	13.7
Adequate	1,290	2.7	3,876	8.0
Adequate plus	6,759	20.7	3,388	10.4

ELA=English language arts

[a] Preterm is a birth before 36 weeks gestation

[b] "Deprived" is those with neighborhood deprivation index of greater than 1 standard deviation from the average

[c] Proportion of the overall population (Table 1) with a preterm birth or above average neighborhood deprivation

[d] Below average deprivation = < -1 standard deviation from the average; Average = between -1 and 1 standard deviation from the average; Above average = > 1 standard deviation from the average

[e] Measure of quality and quantity of prenatal care

Table 3. Bivariate associations of all variables with outcome and exposures

	Fail Math CRCT				Preterm birth				Neighborhood Deprivation Index			
	OR	95% CI		p-value	OR	95% CI		p-value	beta	95% CI		p-value
Exposures												
Preterm vs. Term	1.42	1.35	1.49	<0.001								
Neighborhood Deprivation Index	1.38	1.37	1.40	<0.001								
Characteristics												
Maternal age												
15-19 years	1.80	1.71	1.90	<0.001	1.26	1.17	1.34	<0.001	0.67	0.65	0.69	<0.001
20-24 years	1.57	1.50	1.64		1.12	1.06	1.18		0.46	0.44	0.48	
25-29 years	1.00	-	-		1.00	-	-		0.00	-	-	
30-34 years	0.70	0.66	0.74		1.02	0.96	1.08		-0.33	-0.34	-0.31	
35-39 years	0.73	0.68	0.78		1.18	1.11	1.26		-0.39	-0.41	-0.37	
40-44 years	0.80	0.69	0.92		1.36	1.20	1.54		-0.32	-0.37	-0.28	
New race				<0.001				<0.001				<0.001
Non-hispanic white	1.00	-	-		1.00	-	-		0.0	-	-	
Non-hispanic black	3.54	3.37	3.72		1.49	1.43	1.56		1.23	1.22	1.25	
Hispanic	3.61	3.41	3.83		0.96	0.89	1.03		0.74	0.72	0.76	
Other	1.18	1.06	1.31		1.03	0.94	1.12		0.33	0.31	0.36	
Marital status				<0.001				<0.001				<0.001
Married	1.00	-	-		1.00	-	-		0.0	-	-	
Unmarried	2.44	2.36	2.53		1.39	1.34	1.44		1.00	0.98	1.01	
Child sex				<0.001				<0.001				0.911
Male	1.30	1.25	1.34		1.10	1.06	1.14		0.00	-0.01	0.01	
Female	1.00	-	-		1.00	-	-		0	-	-	
Payor				<0.001				<0.001				<0.001
Medicaid	2.34	2.26	2.42		1.15	1.10	1.19		0.81	0.79	0.82	

Unknown	1.00	-	-		1.00	-	-		0.00	-	-	
Education				<0.001				<0.001				<0.001
Less than high school	6.25	5.86	6.68		1.32	1.25	1.39		1.24	1.23	1.26	
Completed high school	4.43	4.15	4.74		1.34	1.27	1.41		0.89	0.88	0.91	
1-3 years of college	2.80	2.61	3.02		1.27	1.20	1.35		0.50	0.49	0.52	
Finished college	1.00	-	-		1.00	-	-		0.00	-	-	
Smoking vs non-smoking	1.40	1.31	1.50	<0.001	1.45	1.34	1.56	<0.001	0.32	0.29	0.35	<0.001
Kotelchuck Index				<0.001				<0.001				<0.001
Inadequate	1.90	1.80	2.00		4.89	4.52	5.29		0.79	0.77	0.82	
Intermediate	1.20	1.13	1.28		1.51	1.35	1.69		0.28	0.25	0.30	
Adequate	1	-	-		1.00	-	-		0.00	-	-	
Adequate plus	1.05	1.01	1.09		7.73	7.30	8.20		0.09	0.07	0.10	

CI=Confidence interval

Table 4. No-interaction multivariable logistic regression models of risk of failing the math portion of the CRCT in first grade

	Model 1			Model 2			Model 3			Model 4			Model 5			Model 6		
	RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI	
Preterm birth	1.30	1.24	1.36	1.26	1.20	1.33	1.28	1.22	1.34	1.29	1.23	1.36	1.30	1.24	1.37	1.23	1.17	1.30
Neighborhood Deprivation Index	1.35	1.30	1.41	1.13	1.10	1.16	1.16	1.13	1.19	1.34	1.29	1.40	1.32	1.27	1.37	1.04	1.02	1.06
Demographics																		
Maternal age																		
15-19 years				1.17	1.11	1.24										0.89	0.84	0.94
20-24 years				1.16	1.10	1.21										1.02	0.97	1.07
25-29 years				1.00	-	-										1.00	-	-
30-34 years				0.92	0.87	0.97										1.00	0.95	1.06
35-39 years				0.99	0.93	1.07										1.08	1.01	1.16
40-44 years				1.03	0.90	1.18										1.10	0.96	1.26
Maternal race																		
Non-Hispanic white				1.00	-	-										1.00	-	-
Non-Hispanic black				2.01	1.85	2.17										2.01	1.88	2.16
Hispanic				2.44	2.23	2.67										1.77	1.63	1.92
Other				1.07	0.95	1.20										1.00	0.89	1.13
Marital status																		
Married				1.00	-	-										1.00	-	-
Unmarried				1.46	1.39	1.53										1.21	1.15	1.26
Child sex																		
Male				1.30	1.25	1.34										1.29	1.25	1.34
Female				1.00	-	-										1.00	-	-
Individual Socioeconomic status																		
Payor																		

Medicaid							1.29	1.24	1.35							1.18	1.13	1.23
Unknown							1.00	-	-							1.00	-	-
Education																		
Less than high school							3.56	3.27	3.87							3.27	3.00	3.56
Completed high school							2.76	2.56	2.98							2.50	2.32	2.70
1-3 years of college							1.98	1.84	2.15							1.80	1.66	1.94
Finished college							1.00	-	-							1.00	-	-
Smoking during pregnancy																		
Smoker										1.20	1.12	1.29				1.13	1.06	1.22
Non-Smoker										1.00	-	-				1.00	-	-
Kotelchuck Index																		
Inadequate													1.34	1.27	1.42	1.11	1.05	1.17
Intermediate													1.06	1.00	1.13	1.00	0.95	1.06
Adequate													1.00	-	-	1.00	-	-
Adequate plus													0.96	0.92	1.00		0.95	1.03

CI = Confidence Interval

Table 5. Interaction multivariable logistic regression models of risk of failing the math portion of the CRCT in first grade

	Model 1			Model 2			Model 3			Model 4			Model 5			Model 6		
	RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI	
Preterm birth	1.32	1.26	1.39	1.28	1.22	1.35	1.30	1.24	1.37	1.32	1.25	1.39	1.34	1.27	1.41	1.25	1.19	1.32
Neighborhood Deprivation Index	1.37	1.31	1.42	1.14	1.11	1.17	1.17	1.13	1.20	1.36	1.31	1.41	1.34	1.29	1.39	1.04	1.02	1.06
Interactions																		
Preterm: 1 SD increase in NDI	1.30	1.24	1.36	1.09	1.05	1.13	1.11	1.07	1.15	1.29	1.23	1.36	1.26	1.20	1.32	1.00	0.97	1.04
Term: 1 SD increase in NDI	1.37	1.31	1.42	1.14	1.11	1.17	1.17	1.13	1.20	1.36	1.31	1.41	1.34	1.29	1.39	1.04	1.02	1.06
Demographics																		
Maternal age																		
15-19 years				1.17	1.11	1.24										0.89	0.84	0.94
20-24 years				1.16	1.10	1.21										1.02	0.97	1.07
25-29 years				1.00	-	-										1.00	-	-
30-34 years				0.92	0.87	0.97										1.00	0.95	1.06
35-39 years				0.99	0.93	1.07										1.08	1.01	1.16
40-44 years				1.03	0.90	1.18										1.10	0.96	1.26
Maternal race																		
Non-Hispanic white				1.00	-	-										1.00	-	-
Non-Hispanic black				2.01	1.85	2.17										2.01	1.88	2.16
Hispanic				2.44	2.23	2.67										1.77	1.63	1.92
Other				1.07	0.95	1.20										1.00	0.89	1.13
Marital status																		
Married				1.00	-	-										1.00	-	-
Unmarried				1.46	1.39	1.53										1.21	1.15	1.26
Child sex																		
Male				1.30	1.25	1.34										1.29	1.25	1.34
Female				1.00	-	-										1.00	-	-
Individual Socioeconomic status																		

Payor														
Medicaid			1.29	1.24	1.35							1.18	1.13	1.23
Unknown			1.00	-	-							1.00	-	-
Education														
Less than high school			3.56	3.27	3.88							3.26	2.99	3.56
Completed high school			2.76	2.56	2.98							2.50	2.32	2.70
1-3 years of college			1.98	1.84	2.15							1.80	1.66	1.94
Finished college			1.00	-	-							1.00	-	-
Smoking during pregnancy														
Smoking						1.21	1.12	1.30				1.14	1.06	1.22
Non-smoker						1.00	-	-						
Kotelchuck Index														
Inadequate									1.35	1.27	1.42	1.11	1.05	1.17
Intermediate									1.06	1.00	1.12	1.00	0.94	1.06
Adequate									1.00	-	-	1.00	-	-
Adequate plus									0.96	0.92	1.00	0.99	0.95	1.03

CI = Confidence Interval

Table 6. Interaction multivariable logistic regression models stratified by race

	Non-Hispanic Black						Non-Hispanic White					
	Model 1a			Model 6a			Model 1b*			Model 6b		
	RR	95% CI		RR	95% CI		RR	95% CI		RR	95% CI	
Preterm birth	1.31	1.24	1.39	1.28	1.20	1.36	Did not converge			1.25	1.04	1.50
Neighborhood Deprivation Index	1.18	1.15	1.21	1.03	1.01	1.05				1.27	1.19	1.36
Interactions												
Preterm: 1 unit increase in NDI	1.12	1.08	1.17	0.98	0.94	1.02				1.22	1.04	1.44
Term: 1 unit increase in NDI	1.18	1.15	1.21	1.03	1.01	1.05				1.27	1.19	1.36
Demographics												
Maternal age												
15-19 years				0.85	0.79	0.91				0.95	0.80	1.13
20-24 years				1.00	0.95	1.06				0.99	0.86	1.15
25-29 years				1.00	-	-				1.00	-	
30-34 years				1.04	0.97	1.11				1.03	0.90	1.18
35-39 years				1.09	1.00	1.20				1.03	0.87	1.22
40-44 years				1.22	1.15	1.30				1.22	0.89	1.67
Marital status												
Married				1.00	-	-				1.00	-	-
Unmarried				1.22	1.15	1.30				1.07	0.94	1.21
Child sex												
Male				1.33	1.27	1.39				1.35	1.24	1.47
Female				1.00	-	-				1.00	-	-
Individual Socioeconomic status												
Payor												
Medicaid				1.16	1.11	1.22				1.53	1.34	1.73
Unknown				1.00	-	-				1.00	-	-

Education						
Less than high school	2.71	2.44	3.02	5.55	4.61	6.68
Completed high school	2.05	1.88	2.25	3.94	3.37	4.61
1-3 years of college	1.53	1.39	1.68	2.27	1.95	2.65
Finished college	1.00	-	-	1.00	-	-
Smoking during pregnancy						
Smoking	1.09	1.00	1.19	1.04	0.92	1.19
Non-smoker	1.00	-	-	1.00	-	-
Kotelchuck Index						
Inadequate	1.07	1.00	1.14	1.34	1.11	1.61
Intermediate	0.99	0.92	1.06	0.95	0.79	1.15
Adequate	1.00	-	-	1.00	-	-
Adequate plus	0.97	0.92	1.01	1.03	0.93	1.15

CI = Confidence Interval

Table 7. Results of geographically weighted regression. Median and interquartile range of odds ratios for failing the math portion of the CRCT

	Model 1 Median [IQR]	Model 2 Median [IQR]	Model 3 Median [IQR]	Model 4 Median [IQR]	Model 5 Median [IQR]	Model 6 Median [IQR]
Preterm birth	1.58 [1.06, 1.93]	1.45 [1.09, 1.80]	1.49 [1.07, 1.88]	1.58 [1.08, 1.92]	1.73 [1.12, 2.05]	1.52 [1.02, 1.86]
Neighborhood Deprivation Index	1.65 [1.28, 2.76]	1.23 [1.13, 1.84]	1.26 [1.09, 1.77]	1.64 [1.26, 2.76]	1.62 [1.26, 2.65]	1.07 [1.01, 1.60]
Interactions						
Preterm: 1 unit increase in NDI	1.39 [1.11, 2.08]	1.13 [0.90, 1.50]	1.1 [0.85, 1.56]	1.38 [1.11, 2.06]	1.36 [1.06, 2.00]	1.01 [0.80, 1.33]
Term: 1 unit increase in NDI	1.65 [1.28, 2.76]	1.23 [1.13, 1.84]	1.26 [1.09, 1.77]	1.64 [1.26, 2.76]	1.62 [1.26, 2.65]	1.07 [1.01, 1.60]
Demographics						
Maternal age						
15-19 years		1.28 [1.07, 1.50]				0.92 [0.78, 1.11]
20-24 years		1.41 [1.17, 1.70]				1.21 [1.06, 1.44]
25-29 years		Reference				Reference
30-34 years		1.02 [0.83, 1.19]				1.15 [0.92, 1.32]
35-39 years		1.00 [0.75, 1.24]				1.09 [0.87, 1.39]
40-44 years		0.99 [0.76, 1.11]				0.99 [0.78, 1.20]
New race						
Non-Hispanic white		Reference				Reference
Non-Hispanic black		1.73 [1.39, 2.91]				2.08 [1.51, 2.65]
Hispanic		2.64 [1.82, 3.67]				1.72 [1.26, 2.11]
Other		0.95 [0.66, 1.37]				0.87 [0.69, 1.15]
Marital status						
Married		Reference				Reference
Unmarried		1.33 [1.12, 1.61]				1.11 [0.86, 1.34]
Child sex						
Male		1.35 [1.25, 1.46]				1.35 [1.26, 1.47]
Female		Reference				Reference
Individual Socioeconomic Status						

Payor	1.21 [1.08, 1.34]			1.12 [0.98, 1.24]
Medicaid	Reference			Reference
Unknown				
Education				
Less than high school	5.48 [3.64, 7.80]			4.45 [3.90, 5.20]
Completed high school	3.38 [2.89, 4.55]			3.09 [2.68, 3.69]
1-3 years of college	2.49 [1.84, 3.23]			2.18 [1.55, 2.69]
Finished college	Reference			Reference
Smoking during pregnancy				
Smoker		1.39 [0.89, 1.81]		1.30 [0.91, 1.78]
Non-smoker		Reference		Reference
Kotelchuck Index				
Inadequate			1.64 [1.18, 2.41]	1.26 [0.90, 1.87]
Intermediate			0.93 [0.86, 1.22]	0.88 [0.78, 1.04]
Adequate			Reference	Reference
Adequate plus			0.80 [0.69, 0.95]	0.86 [0.70, 1.05]

IQR = Interquartile Range, NDI = Neighborhood Deprivation Index

Figures

Figure 1. Median odds ratios of failing the math CRCT in first grade for a one standard deviation increase in neighborhood deprivation index among preterm births (left) and term births (right)

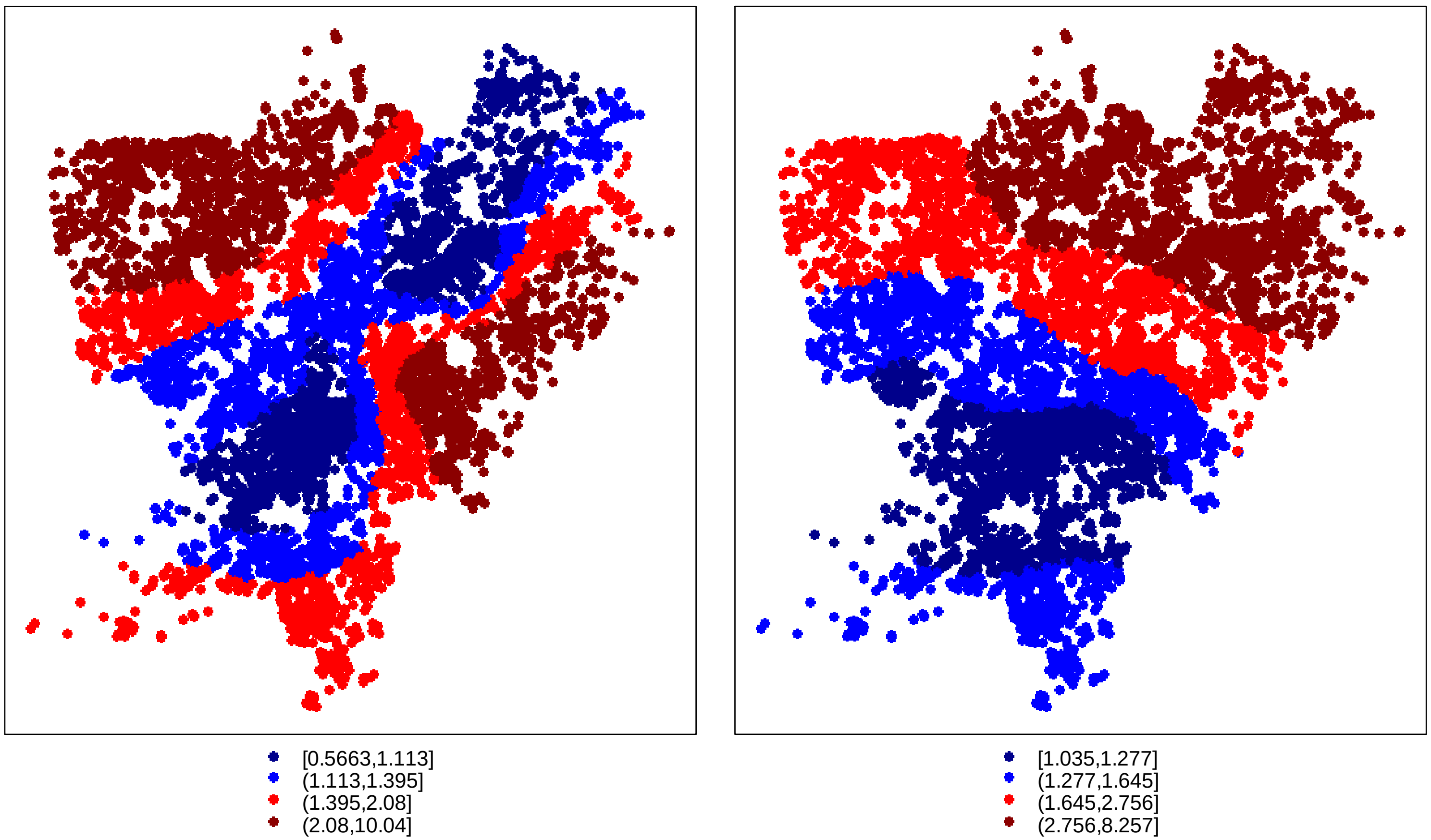
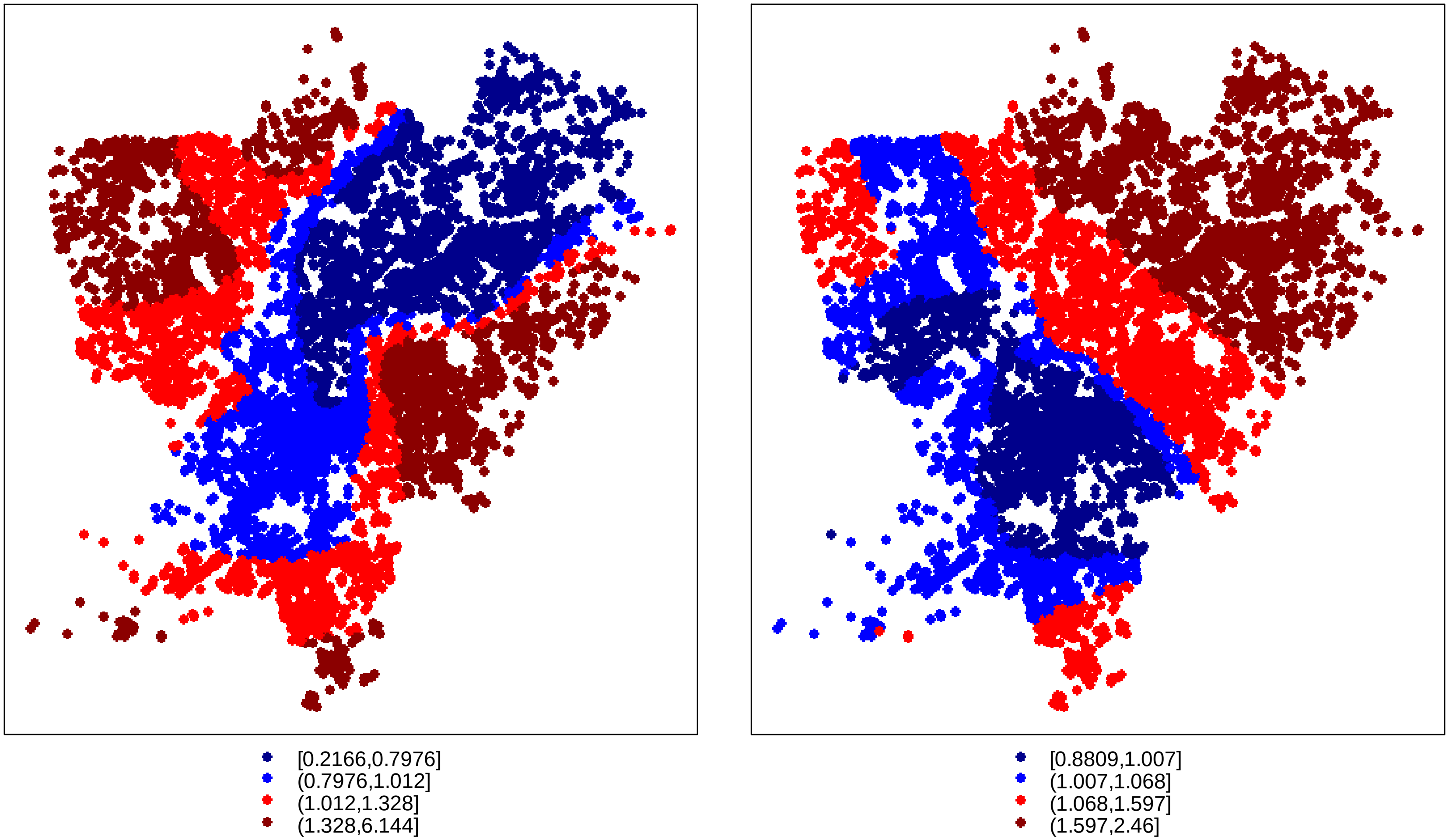


Figure 2. Median odds ratios of failing the math CRCT in first grade for a one standard deviation increase in neighborhood deprivation index among preterm births (left) and term births (right), adjusted for maternal age, maternal race, maternal marital status, child sex, maternal education, insurance status, smoking status during pregnancy, and Kotelchuck index



Appendix

IRB Letter

EMORY UNIVERSITY | Institutional Review Board

TO: Bryan Williams, MD Principal Investigator SOM: F&P PREV MED
DATE: 12/18/2012

RE: **Continuing Review Expedited Approval**

CR2_IRB00044043

IRB00044043

Late Term Prematurity and Early School Performance

Thank you for submitting a renewal application for this protocol. The Emory IRB reviewed it by the expedited process on DATE, per 45 CFR 46.110, the Federal Register expeditable category F(5), and/or 21 CFR 56.110. This reapproval is effective from **12/15/2012** through **12/14/2013.** Thereafter, continuation of human subjects research activities requires the submission of another renewal application, which must be reviewed and approved by the IRB prior to the expiration date noted above.

Any reportable events (e.g., unanticipated problems involving risk to subjects or others, noncompliance, breaches of confidentiality, HIPAA violations, protocol deviations) must be reported to the IRB according to our Policies & Procedures at www.irb.emory.edu, immediately, promptly, or periodically. Be sure to check the reporting guidance and contact us if you have questions. Terms and conditions of sponsors, if any, also apply to reporting.

Before implementing any change to this protocol (including but not limited to sample size, informed consent, study design, you must submit an amendment request and secure IRB approval.

In future correspondence about this matter, please refer to the IRB file ID, name of the Principal Investigator, and study title. Thank you.

Sincerely,

Michael Arenson, MA Analyst Assistant

CC: Dunlop Anne SOM: F&P PREV MED
Jain Lucky Neonatolog
Kramer Michael Epidemiology