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Assessing the joint impacts of preterm birth and socioeconomic status on children's early cognitive outcomes

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Abstract

Assessing the joint impacts of preterm birth and socioeconomic status on children's early cognitive outcomes
By Jennifer L. Richards

Being born preterm and being raised in poverty are each linked with worse cognitive and academic outcomes. While socioeconomic status (SES) has often been treated as a confounding factor in studies of the developmental impacts of preterm birth, it has also been hypothesized that SES acts as an effect modifier of the relationship between preterm birth and cognitive and academic outcomes. Since preterm children may be more vulnerable to the adverse developmental impacts of growing up in disadvantaged households, it is plausible that lower SES exacerbates the adverse impacts of preterm birth. Conversely, it is also possible that childhood poverty exerts such profound effects on cognitive outcomes that being born early does not contribute additional substantial risk. This dissertation investigated whether SES modifies the effect of preterm birth on children's cognitive and academic outcomes in early childhood through entry into school with an explicit focus on assessment of additive interaction. Data sources were the Early Childhood Longitudinal Study-Birth Cohort (ECLS-B) and the Millennium Cohort Study (MCS). The ECLS-B and MCS were longitudinal birth cohorts that enrolled 10,700 children in the US and 18,818 children in the UK, respectively, in 2001 and followed them through childhood with prospective measurement of cognitive development. The first goal was to better understand patterns of cognitive outcomes with each additional gestational week (**Aim 1**). In ECLS-B, those born early preterm, moderate preterm, or late preterm scored worse than term children on cognitive ability tests at two years old and reading and mathematics tests at kindergarten but there were no significant differences observed for other gestational ages. The second goal was to assess the presence of additive interaction between preterm or early term birth and household SES in their effects on cognitive scores in ECLS-B (**Aim 2**) and MCS (**Aim 3**). In ECLS-B, adjusted deficits were 0.4-0.6 standard deviations (SD) for early preterm, 0.2-0.3 SD for moderate preterm, and 0.1 SD for late preterm compared with term, and 0.6-0.9 SD comparing highest versus lowest SES quintiles on cognitive ability tests at two years old and reading and mathematics tests at kindergarten. In MCS, adjusted deficits were 0.2-0.3 SD for early or moderate preterm, 0.1 SD for late preterm, and 0.05 SD for early term compared with term, and 0.3-0.4 SD for children living in poverty compared with those not living in poverty on cognitive assessments at three, five, and seven years old. In both studies, there was no evidence of additive interaction between the two risk factors; household SES did not modify the relationship between gestational age and cognitive outcomes. Findings underscore the important adverse impacts of both being born preterm and being raised in more disadvantaged households on children's cognitive outcomes. The estimated joint effects were additive with doubly exposed children performing the worst, suggesting the need for targeting of early childhood interventions to these high-risk children.

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Chapter 1. Introduction

Children's cognitive development and performance in academics are influenced by a myriad of factors such as health status and nutrition, household resources, parental stress, environmental stimuli, and genetics. Among these factors, being born preterm and being raised in poverty are each known to be linked with adverse cognitive outcomes among children. Socioeconomic status has been hypothesized to act as a modifier of the effect of preterm birth on children's cognitive outcomes. Since preterm children may be more vulnerable to the adverse developmental impacts of growing up in disadvantaged households, it is plausible that lower socioeconomic status may exacerbate the adverse impacts of preterm and early term birth. Conversely, it is also possible that the impacts of poverty on children's cognitive development are so profound that the apparent additional effect of preterm birth may be diminished—in other words, there may be a threshold to the effects of being doubly exposed.

This dissertation seeks to understand the joint impacts of preterm birth and socioeconomic status on children's cognitive and academic outcomes from early to mid-childhood. In Chapter 2 of this dissertation, we review background literature related to the independent and joint impacts of these risk factors on children's cognitive and academic outcomes. Our data sources were two nationally representative, prospective birth cohort studies of children in the United States (Early Childhood Longitudinal Study-Birth Cohort, ECLS-B) and the United Kingdom (Millennium Cohort Study, MCS). The ECLS-B enrolled a nationally representative sample of US children born in 2001 and collected data from them and their families at 9 months, 2 years, preschool age, and kindergarten age. The MCS enrolled a nationally representative sample of UK children born in 2000-2002 and collected data from them and their families at 9 months, 3 years, 5 years, 7 years, 11 years, and 14 years. In this dissertation, we used data from the first four data collection time points. Chapter 3 describes each of these data sources in detail.

The first study of this dissertation (Aim 1; Chapter 4) investigated the shapes of the relationships between gestational age at birth and cognitive ability at two years old and academic achievement at kindergarten age using data from the ECLS-B. Few studies of the cognitive and academic outcomes of preterm birth have evaluated outcomes along the entire range of gestational age within the same analytic population. Given recent evidence of adverse impacts of even mild prematurity, we sought to understand the impacts of each additional week spent *in utero* on cognitive scores at two years old and academic scores at kindergarten age. These analyses compared multiple methods for defining gestational age—using linear and quadratic terms based on continuous gestational age, categories for each gestational week, and categories from the American College of Obstetricians and Gynecologists for early preterm, moderate preterm, late preterm, early term, full term, late term, and post-term.

The second and third studies of this dissertation investigated whether the effects of preterm and early term birth on children's cognitive and academic outcomes vary by socioeconomic status by explicitly testing additive interaction between the two risk factors in both the ECLS-B and the MCS. In the second study (Aim 2; Chapter 5), we used data from the ECLS-B to investigate whether the estimated effects of preterm and early term birth on children's cognitive ability at two years old and academic achievement at kindergarten age vary by household socioeconomic status. In the third study (Aim 3; Chapter 6), we used data from the MCS to investigate whether the estimated effects of preterm and early term birth on children's cognitive scores at three, five, and seven years old vary by household socioeconomic status. Cross-cohort comparisons testing similar hypotheses in different cohorts with potentially different confounding structures can be informative in terms of strengthening arguments for or against the presence of causal relationships based on similarities or differences in findings. In these studies, we investigated similar questions but operationalized measures of gestational age, socioeconomic status, and covariates in slightly different ways depending on the availability and measurement of variables in the two datasets. Further, in the third study, we extended our analyses to include a later time point of cognitive measurement after children had entered school.

The final chapter of this dissertation discusses the collective findings of the three studies as well as public health implications and future directions of this research. Both preterm birth and childhood poverty are important public health problems in the United States and the United Kingdom, as well as worldwide. In the US and UK, about 8-10% of children are born preterm, 20-25% are born early term,[1,2] and 25-30% of children live in poverty.[3,4] These factors likely overlap in distribution compared with if they were randomly distributed through the population because lower socioeconomic status is an important risk factor for preterm birth.[5,6] From an etiologic standpoint, it is important to understand how the cognitive development of an individual child may be affected by being doubly exposed to both preterm birth and being raised in a more disadvantaged environment. From a public health standpoint, gaining a better understanding of the impacts of being doubly exposed and whether preterm birth exerts different impacts across socioeconomic strata may help to inform the targeting of early childhood interventions.

Chapter 2. Background

2.1 Introduction

Children's cognitive development and performance in academics are influenced by a myriad of factors such as health status and nutrition, household resources, parental stress, environmental stimuli, and genetics. Among these, preterm and early term birth and childhood poverty are each known to adversely impact children's cognitive and academic outcomes. Both of these factors impact a substantial proportion of children in the United States and the United Kingdom. Further, they may be likely to co-occur due to the well-documented association between lower socioeconomic status and higher risk of preterm birth. This dissertation focuses on the independent and joint effects of preterm birth and socioeconomic status on children's cognitive and academic outcomes, and explicitly tests whether socioeconomic status acts as a modifier of the relationship between preterm birth and these outcomes. This chapter reviews background literature relevant for understanding preterm birth, socioeconomic status, and the relationships between each of preterm birth and socioeconomic status with children's cognitive development. It also reviews the existing literature on modification of the effect of preterm birth on cognitive and academic outcomes by socioeconomic status, and discusses epidemiologic methods for assessing interaction for continuous outcomes.

2.2 Effects of preterm and early term birth on cognitive and academic outcomes

Definition and epidemiology of preterm and early term birth

Preterm births are live births occurring before 37 completed weeks of gestation. Preterm birth is a complex syndrome with multiple causes, which may occur spontaneously or be initiated by medical providers. About 65-70% of preterm births occur spontaneously after early onset of labor or premature rupture of membranes.[7] Risk factors for spontaneous preterm birth are multi-factorial including multiple pregnancy resulting in uterine over-distension, maternal factors (e.g., young or advanced age, short inter-pregnancy intervals, low maternal body mass index), infection (e.g., chorioamnionitis, bacterial vaginosis) and inflammation, underlying maternal chronic conditions (e.g., diabetes, hypertension, anemia), social stress and socioeconomic status, maternal race/ethnicity, and genetics.[6,8,9] The remaining 30-35% of preterm births are provider-initiated via early labor induction or Cesarean section due to maternal or fetal indications such as preeclampsia or fetal distress or due to non-medical reasons such as elective Cesarean section.[7,8]

In studies of preterm birth, it is critical to understand that this group of live births represents substantial heterogeneity in terms of developmental maturity and risk of adverse neonatal outcomes. Clinical and epidemiologic studies typically specify the exact range of gestational age and/or birth weight in which investigators are interested. Preterm births are often categorized in some way to reflect degree of prematurity and differentiate among risk groups. For example, sub-groups for early preterm (<28 weeks), moderate preterm (28-33 weeks), and late preterm (34-36 weeks) have been used in the United States.[10] Further, while the definition of “preterm” birth includes only births up to 37 weeks, it is now recognized that optimal timing of delivery is at 39-41 weeks and that “early term” births at 37-38 weeks are also a risk group of concern. Until recently, births delivered at 37 to 42 completed weeks were defined as term deliveries and considered to be relatively homogenous in terms of neonatal outcomes. In 2013, the American College of Obstetricians and Gynecologists (ACOG) defined new sub-groups of “term” deliveries for early term (37-38 weeks), full term (39-40 weeks), late term (41 weeks), and post-term (42 weeks and beyond) based on evidence of non-uniformity of neonatal outcomes within this group.[11]

Preterm birth affected 11% of live births or roughly 15 million infants worldwide in 2010.[8,12] About 70% of preterm births occur during the late preterm period.[1] The burden of preterm birth increased over the period of 1990 to 2010 in most high-income countries.[13] Slight decreases have been observed in the United States since 2006 and some European countries have maintained or slightly reduced preterm birth rates over past decades.[8,14–16] Due to recent recognition of the higher risks of adverse neonatal and later outcomes among children born at early term, multi-national comparisons of early term birth rates have also become of interest. A recent analysis of data from 34 European countries, the United States, Canada, Japan, and Australia found that early term birth rates in these countries ranged from 13% to 27% (median 18%) in 1996 and from 16% to 31% (median 22%) in 2010 (Delnord et al., under review). Preterm and early term births remain an important public health concern in both the United States and the United Kingdom. In the United States, 2014 national data showed that 9.6% of births were preterm and another 24.8% were early term.[17] In the United Kingdom, 2015 national data showed that 7.6% of births were preterm and another 20.8% were early term.[2]

Impacts of preterm birth on brain development and injury

Preterm delivery results in developmental immaturity of numerous organ systems at birth including the brain and central nervous system.[18] Brain growth and development involves both prenatal and postnatal processes of proliferation, migration, differentiation, and regression of neurons and glia, which are cells that support and protect neurons. Neural development begins in the first month of gestation with the formation of the neural plate. By the sixth week of fetal development, the brain is formed and divided into the sub-regions that will make up the mature adult brain. Neurons and glial support cells proliferate and are nearly all created by 24 weeks, with peak proliferation occurring between the second and fourth months. Mass migration of neurons to their specific locations in the brain—known as neuronal migration—occurs between the third and fifth months. Neurons differentiate to take on specific functions and form synapses—or connections—with each other to communicate and store information. Neuronal differentiation and myelination as well as formation of complex networks of synapses and neuronal circuits occurs starting around the sixth month of gestation and continues into childhood.[18,19]

After birth, a child's immature brain continues to undergo major changes as he or she grows, learns to move, encounters new experiences, and is exposed to sensory inputs. Early in development, neuronal synapses proliferate as the child encounters stimulating experiences, and continued triggering of those connections fosters their growth, such as the early stimulation of visual acuity. This process of proliferation is accompanied by selective pruning of synapses that are under-used in order to enhance the efficiency of brain functioning.[18,19]

Preterm delivery interrupts normal *in utero* processes of brain growth and development resulting in the birth of a child with a developmentally immature brain. When a child is born preterm, the brain has not had sufficient time to achieve optimal size and neuronal development. At the lower limit of live birth viability—or about 20 weeks—the brain weighs 10% of its weight at full term. During the gestational period of 20-40 weeks, there is relatively linear growth in brain weight,[20] and even at 34 weeks during the late preterm period, the maturing brain is only at 65% of its potential full-term weight.[21] During the last several weeks of gestation, there is substantial growth of gyri and sulci, the ridges and depressions on the cerebral cortex that give the human brain its folded appearance; creation of synapses; and dendritic arborization, the growth and branching of dendrites.[21] In a systematic review by Keunen et al. (2012), it was noted that brain volumes of preterm infants were smaller at term-equivalent age (the week after conception at which a preterm child would have been born if born at term) compared with healthy term-born controls.[22] Brain tissue volumes were smaller in cortical gray matter, subcortical gray matter, and myelinated white matter as well as in specific brain regions. The most pronounced deficits were seen in the most premature infants. These deficits may persist later in childhood and into adolescence. A recent meta-analysis of 15 studies reported that adolescents who had been born very preterm (≤32 weeks) and very low birth weight (≤1500 g) had roughly half standard deviation deficits in total brain, white matter, and gray matter volumes compared with term-born controls; they also had similar reductions in the specific brain regions of the cerebellum, hippocampus, and corpus callosum.[23] Brain volume deficits in preterm children have been associated with worse neurodevelopmental outcomes such as lower Mental Development Index scores on the Bayley Scales of Infant Development-II at 2 years old[22,24] and lower intellectual quotient (IQ) scores and specific deficits in language, memory, motor skills, and executive functioning in adolescence.[23]

Preterm children are also more vulnerable to injuries to the central nervous system and brain both due to brain immaturity at birth and due to processes such as infection and inflammation that contribute to the preterm deliveries.[25] The most common central nervous system injuries observed in preterm children include intraventricular hemorrhage, intraparenchymal hemorrhage, and white matter injury including periventricular leukomalacia. These severe brain injuries increase in prevalence and severity with decreasing gestational age and birth weight.[18] Central nervous system injuries are associated with higher prevalence of neurodevelopmental disabilities. For example, an estimated 20-75% of preterm children with intraventricular hemorrhage (bleeding into the germinal matrix) experience neurodevelopmental disabilities, with prevalence of disabilities varying by location and size of the hemorrhage.[18] Children with periventricular leukomalacia (cystic necrotic lesions in white matter) are at higher risk of cerebral palsy, neurodevelopmental disability, cognitive impairment, and visual impairment, with severity of complications varying by extensiveness of the injury.[18] Among preterm children, those with central nervous system injuries experience worse cognitive and academic outcomes.[26–31] While late preterm children have often been considered to be free of risk of substantial brain injuries, Kinney (2006) noted that neurological risk is not restricted to very preterm infants and that elevated risk of injuries such as periventricular leukomalacia persists up through late preterm delivery.[21]

Impacts of preterm birth on cognitive and academic outcomes

Children who are born preterm, especially those born at very early gestational ages, are at higher risk of severe neurologic and neurosensory impairments such as cerebral palsy, mental retardation, microcephaly, blindness, and deafness.[32,33] These severe outcomes represent only a subset of the neurodevelopmental consequences of prematurity. Preterm children are also more likely to experience subtler deficits in cognitive ability, motor skills, visual-motor skills, language, executive function, behavior, and academic achievement.[32,34–41]

Many early studies of cognitive impairment experienced by preterm children used IQ as their primary outcome. Preterm children score worse on IQ tests such as the Stanford-Binet Intelligence Scale and Wechsler Intelligence Scale for Children and are more likely to be classified as having borderline (IQ 70-84) or abnormal (IQ <70) cognitive function. Mean cognitive scores tend to decline with lower gestational age and birth weight.[18,42] In a meta-analysis of 17 case-control studies comparing cognitive scores between preterm children and term-born controls born in 1975-1988, Bhutta et al. (2002) found a 10.9 (95% CI: 9.2-12.5) point deficit in IQ for preterm children; this deficit was slightly attenuated to 10.2 (95% CI: 9.0-11.5) points after exclusion of severely neurologically impaired children.[42] A similar, updated meta-analysis by Kerr-Wilson et al. (2012) of studies including children born in 1980-2009 reported an 11.9 (95% CI: 10.5-13.4) point deficit in IQ comparing preterm with term children, and the authors noted no improvement in the association between preterm birth and IQ over the 30-year period covered by their study.[43] Among children born <33 weeks, Johnson (2007) estimated a 1.7 (95% CI: 0.81-2.55) point decline in IQ with each earlier gestational week.[44]

More recently, the limitations of IQ scores as a global measure of “intelligence” have been recognized and studies have turned to other tests of cognitive ability and/or learning achievement. In a recent comprehensive review of U.S. preterm birth research, Behrman et al. (2007) commented that "intelligence is not one skill but a composite of multiple cognitive processes, including visual and auditory memory, abstract reasoning, complex language processing, understanding of syntax, visual perception, visual motor integration, and visual spatial processing."[18] Preterm children exhibit, along with lower mean cognitive scores, deficits in a number of specific cognitive processes and domains such as visual perception, visual motor integration, attention, and vocabulary.[33,45,46] Even when samples are restricted to children with IQ scores in the normal range, very low birth weight children have been shown to have specific deficits in areas such as attention, executive function, memory, and language.[18] Further, evidence from longitudinal studies of preterm children suggests that cognitive test scores for individual children may not remain consistent as children get older. For example, among 200 extremely low birth weight children born in 1992-1995, cognitive scores on the Bayley Scales of Infant Development, Second Edition at 20 months were not predictive of children's performance on the Kaufman Assessment Battery for Children at 8 years old. At 20 months, 39% of the children were classified as cognitively impaired whereas only 16% were classified as cognitively impaired at 8 years old.[47] Possible explanations included the use of different tests at different ages and upward drift in IQ scores over time with longer time elapsed since test standardization.[18]

Noting the limitations of IQ scores, numerous studies have turned to assessment of specific cognitive processes and domains, in addition to or instead of measuring global IQ. Other tests of cognitive ability and/or learning achievement that have been used include the Woodcock-Johnson tests of cognitive abilities and/or achievement, Kaufman

Assessment Battery for Children (K-ABC), Wide Range Achievement Test, and McCarthy Scales of Children's Abilities. Preterm as compared with term children score worse on academic achievement tests in reading, mathematics, and spelling, with evidence suggesting that these deficits exist not only among extremely preterm[48] and very preterm[35] children, but also those born moderate to late preterm.[49] For example, a recent review by de Jong et al. (2012) noted that children born moderate to late preterm (i.e., 32-36 weeks) scored worse on reading, spelling, and mathematics tests at 5-10 years, and had more reading and spelling difficulties at 9-11 years.[49]

Preterm children are also more likely to experience school problems such as learning disabilities, grade repetition, and requiring special education. These outcomes came to be of interest to researchers as they attempted to elucidate the longer-term functional impairments of earlier cognitive difficulties, particularly how preterm children deal with the demands of school. Several recent reviews have noted that preterm children are more likely to have learning disabilities, repeating a school grade, attending a non-mainstream school, and requiring special education, with evidence that these problems may be more severe among the earliest born but persist even up to early term (i.e., 37-38 weeks) births.[32,33,35,50–54] Academic problems associated with prematurity may persist beyond childhood. There is some evidence to suggest that late adolescent and adult survivors of extremely preterm birth[55] and very low birth weight[56] score worse on academic achievement tests, are more likely to repeat grades, and are less likely to complete high school and pursue postsecondary education.[32,55,56]

Methodological issues

A few methodological issues in neurodevelopmental outcome studies of preterm birth must be considered when interpreting the large literature on this subject. First, definitions of prematurity vary across studies, impacting estimated prevalence of adverse neurodevelopmental outcomes.[18] Much of the formative literature on low birth weight and/or preterm birth and neurodevelopmental outcomes focused on the extremes of both ranges (e.g., <1000 g or extremely low birth weight, <1500 g or very low birth weight, <28 weeks or very preterm), although more recent studies have investigated outcomes of children born closer to term (e.g., moderate preterm, late preterm, early term). Due to the fact that investigators choose different sub-sets of preterm birth for study, prevalence estimates for adverse outcomes are highly heterogeneous across studies. For example, early outcome studies of prematurity often enrolled only extremely or very preterm children and often set inclusion criteria based on birth weight rather than gestational age. Therefore, prevalence estimates from these studies must be interpreted recognizing that they reflect outcomes of infants at the highest medical risk who would be expected to have the most extreme outcomes.

Second, studies are heterogeneous in terms of specific outcomes studied, how investigators measured those outcomes, and the ages at which children were assessed.[18] For example, focusing specifically on cognitive and academic consequences of preterm birth, investigators have assessed a range of outcomes such as cognitive test scores (e.g., global IQ, specific cognitive domains), academic achievement test scores, and school problems (e.g., requirement for special education, grade repetition). Even within these broader outcome categories, studies have used a variety of assessments to measure similar competencies. For example, global cognitive ability has been assessed using IQ scores and developmental quotient (DQ) scores, and academic achievement has been tested using a variety of assessments such as the Woodcock-Johnson Psycho-Educational Battery and the K-ABC. Likewise, “school problems” have been measured by special education placement, learning disabilities, and teachers’ assessment of children’s performance in certain subjects, among other outcomes. Variation in outcome selection and measurement makes it challenging to make direct comparisons across studies.

Third, methodological differences across studies such as selection factors (e.g., gestational age and/or birth weight criteria, specific hospitals, neonatal intensive care graduates); outcome diagnosis and age at ascertainment; and length of follow-up and sample attrition are likely contributors to variation in findings.[18] Furthermore, secular trends in neonatal care over the past several decades including improvements in clinical practice (e.g., introduction of surfactant therapy) and in neonatal intensive care have likely contributed to increases in both the survival of preterm children and the prevalence of adverse neurodevelopmental outcomes. Studies of the long-term neurodevelopmental consequences of preterm birth are delayed by the lag time required from birth to assessment of childhood and adolescent outcomes. For example, studies published in the 1990s focused mostly on cohorts born in the 1980s. Changes in clinical practice over time make it necessary to continue contemporary research on the long-term consequences of prematurity.

An important gap in this literature is that few studies have examined children’s outcomes along the entire range of gestational age within the same analytic population. It is increasingly being recognized that child outcomes vary by individual gestational week.

Examples include ACOG's recent introduction of new sub-categories of term births in response to evidence of non-uniformity of neonatal outcomes even among infants born at or after 37 weeks,[11] as well as recent interest in estimating the effects of specific sub-categories of early births (e.g., late preterm, early term) on cognitive and academic outcomes.[52,57] Risk of requiring special education has been observed to follow a J-shaped curve across the full distribution of gestational age (i.e., 24-43 weeks) with a nadir at 40-41 weeks.[58] Even among children born at "term", variation in scores by individual gestational week has been shown for IQ scores at 6.5 years[59] and performance on standardized reading and mathematics tests in third grade.[60] Among children born earlier than 33 weeks, IQ scores have been observed to decline by 1.7 points for each earlier gestational week.[44] The first study of this dissertation used US population-based data to describe cognitive outcomes in early childhood and academic outcomes at kindergarten age across the full range of gestational age at birth.

2.3 Effects of socioeconomic status on cognitive and academic outcomes

Childhood poverty is a critical societal problem in both the United States and the United Kingdom. In the United States, 25% of children under age 6 lived in poor families (under the federal poverty level), and 49% lived in low-income families (under 200% of the federal poverty level) in 2011.[3] In the United Kingdom, 29% of children lived in low-income households (or under the median national income) in 2015.[4]

Children who are raised in poverty are more likely to experience developmental delays and learning disabilities; to have worse indicators of cognitive status such as lower scores on IQ, verbal ability, and achievement tests; and to have more school problems such as being more likely to repeat grades or drop out of high school.[61] When children enter school for the first time, there are already socioeconomic disparities in their cognitive abilities.[62] Childhood poverty is hypothesized to influence cognitive and academic outcomes through pathways such as the home environment (e.g., access to opportunities for learning, reading materials); parents' interactions with their children (e.g., warmth and consistency versus harshness in parenting style); parental mental health (e.g., irritability and depression); neighborhood conditions (e.g., access to resources such as playgrounds, parks, and high-quality preschool education); nutrition; and environmental exposures.[61,63] Cognitive ability in early childhood and being ready to enter school are important predictors of children's later social and academic achievement as well as life course socioeconomic and health trajectories into adulthood.[64–66]

Following on the earlier discussion of the influence of preterm birth on interrupting prenatal processes of brain growth and development, we now consider how early life environments influence those processes. While prenatal development establishes functional areas and early cortical patterning of the brain, postnatal experiences are crucial to brain development and growth.[63,67] Neuronal growth (or neurogenesis) occurs mostly during the prenatal period; neurons migrate, differentiate, and develop neuronal processes involving axons and dendrites form synapses for communicating with other neurons in information processing networks. Along with neuronal proliferation, prenatal neurodevelopment also involves programmed cell death processes wherein large proportions of these neurons will die off. Postnatally, glial cells continue to proliferate, migrate, and differentiate. Differentiation and maturation of both neurons and glia continue to occur over the course of childhood. Similar to prenatal cell death processes that occur mostly in neurons, glial cells undergo similar processes postnatally. Over the course of childhood and adolescence, there is exuberant growth of neural connections in the developing brain coupled with selective pruning based on usage of the pathways. Specific brain regions differ in the timing of periods of rapid brain development and sensitive periods when they exhibit the most plasticity or susceptibility to environmental influences.[63,67]

These postnatal processes of brain growth and development are influenced by children’s experiences of sensory enrichment—such as exposure to more and higher quality words and conversations spoken in the home—and deprivation—such as lower quality parental engagement and infant attachment—in their environments.[67] Operationally, Johnson et al. (2016) theorized that socioeconomic status influences brain growth and development through material deprivation, exposure to higher levels of stress, and greater exposure to environmental toxins in neighborhoods.[63] Material deprivation may be marked by lower exposure to cognitively stimulating experiences such as book reading, exposure to spoken words, and engagement in complex conversations, as well as by nutritional deprivation. Early exposure to “toxic stress” in the home—such as through parental emotional distress that affects their functioning and how they interact with their children—may lead to changes in areas of the brain that govern stress responses.[63] A growing body of neuroimaging literature suggests that the impacts of poverty on children’s cognitive and academic outcomes may be manifest through volume deficits and atypical development in the brain. For example, a recent cross-sectional study of 1,099 children aged 3 to 20 years found that more parental education and family income were associated with higher volume in brain surface areas.[68] Another recent study found that the association between low SES and academic achievement deficits was mediated in part through reduced gray matter volume and atypical development in the frontal lobe, temporal lobe, and hippocampus, regions that are known to be relatively less influenced by heritability and more by the postnatal environment.[69]

The concept of socioeconomic status involves numerous potentially interrelated measures and constructs such as income and occupational status, family structure and stability, educational attainment, racial/ethnicity minority status, and social capital.[70] Composite indices measuring household income, parental educational attainment, and parental occupation have frequently been used to assess the effect of family-based SES on children's cognitive and academic outcomes.[71] It has also been argued that specific components of socioeconomic status—such as income, education, occupational status—should be examined separately because they affect children's upbringing and development in distinct ways and also differ in terms of manipulability through policy and interventions.[72,73] For example, income may be reflective of families' material or financial capital, whereas education is more reflective of human capital (e.g., knowledge and skills).[72] Further, Duncan and Magnuson (2015) argue that intervention upon a composite concept of "socioeconomic status" is vague while improvements in specific components such as increasing income are theoretically more practicable.[73] Complicating the measurement of childhood poverty is the fact that its timing and persistence over the course of early childhood matters for how it influences cognitive development. Childhood poverty may have a more profound effect on cognitive and academic outcomes when experienced earlier and/or more persistently.[61,74–76]

2.4 Interaction between preterm birth and socioeconomic status in the effects on cognitive and academic outcomes

Children's development is a transactional process wherein children grow and respond to stimuli in their environments, which in turn fosters further learning.[19] This process is influenced jointly by biological factors such as preterm birth and social factors such as socioeconomic adversity, the home environment, and parenting factors.[77] Developmental studies have long supported the idea of the "cumulative risks" of adverse biological and environmental conditions on children's vulnerability to poorer developmental outcomes.[78] In many studies of the cognitive outcomes of preterm birth, SES has been treated as a confounding factor. When mutually adjusted, both preterm birth and lower SES serve as strong risk factors for poorer cognitive outcomes.[79–81] Recognizing that both factors play key roles in influencing children's developmental trajectories, there has been interest in whether socioeconomic conditions modify the relationships between preterm birth and children's cognitive outcomes. From an etiologic standpoint, it is important to understand the joint impacts of being doubly exposed to both preterm birth and being raised in a more disadvantaged environment for an individual child. From a public health standpoint, understanding the impacts of being doubly exposed may help to inform the targeting of early childhood interventions, especially since a higher-than-expected proportion of children may be doubly exposed due to socioeconomic disparities in the occurrence of preterm birth compared with if the two factors were randomly distributed through the population.

It is plausible that being raised in worse socioeconomic conditions exacerbates the effects of preterm birth on children's cognitive development. Preterm delivery interrupts the normal processes of brain maturation, and postnatal brain development after early delivery may be adversely affected by neonatal illness, medical treatment, and social environments (e.g., neonatal care, caregiver interactions).[82,83] Preterm children who are raised in higher social risk settings may be more susceptible to the influences of family and social environments in terms of providing the experiences and resources necessary for cognitive growth and academic success.[26,61,84–88] Among preterm-born children, being raised in more advantaged environments is associated with better development outcomes.[30,95,96] This suggests that enriching environments may buffer the adverse developmental effects of preterm birth.[26,77,78] For example, Weisglas-Kuperus et al. (1993) found that a stimulating home environment could buffer against cognitive deficit in preschool among very low birth weight children.[26] Brooks-Gunn et al. (1992) found that early developmental interventions for preterm and low birth weight children were most effective among families with lower parental educational attainment.[89] Since preterm children may be more vulnerable to early environmental conditions in terms of providing resources supportive of cognitive development, it is plausible that deficits between preterm and term children may be larger in lower socioeconomic circumstances.

On the other hand, it is also plausible that the adverse developmental impacts of poverty are so profound that experiencing that additional biological insult of preterm birth may not add substantial risk for children living in poverty.[90] Some studies have found smaller cognitive deficits for very low birth weight[91] or small for gestational age[92] children among lower SES groups compared with higher SES groups. Evidence from twin studies suggests that the cognitive outcomes of lower SES children are influenced more by socioeconomic factors and comparatively less by biological risks. Among twins enrolled in the National Collaborative Perinatal Project, Turkheimer et al. (2003) found that environmental factors explained 60% of variance in IQ at seven years old among low SES children with genetics playing a negligible role, whereas genetics played a larger role and environmental factors were less important among high SES children.[93] Koeppen-Shomerus et al. (2000) examined modification of gene-environment effects by gestational age, finding that environmental factors explained most of the variance in verbal and non-verbal cognitive scores at 2 years among very preterm (<32 weeks), with genetics playing a negligible role. In contrast, genetic effects explained 18-33% of variance among children born at 32-33 weeks, or >33 weeks, with environmental factors playing a lesser, but still important role.[80] Due to the twin study design, these analyses investigated relative effects of genetics and environment after conditioning upon preterm birth since twins necessarily share the same gestational age.

Some early follow-up studies of the outcomes of extremely preterm or low birth weight infants in the 1980s and 1990s tested interaction between prematurity and social class by testing variation in group-wise differences between low birth weight infants and term controls using two-way analysis of variance, or inclusion of interaction terms between birth weight group and SES in regression models. Findings were mixed with some finding that deficits between premature children and term controls were greater at lower SES compared with higher SES,[26,94,95] others finding no interaction,[91,96–98] and some finding a smaller deficit at lower SES.[91,95] These studies suffered from a number of limitations such as small sample sizes, highly selected populations (e.g., extremely preterm survivors of the neonatal intensive care unit), inadequate confounding control, lack of comparison groups, and limited statistical methods. In most of these studies, investigators did not purposively evaluate additive or multiplicative interaction; instead, the scale on which they assessed interaction was a function of how the outcome was defined (e.g., binary, continuous). Since many of these early studies were focused on extremely preterm or low birth weight children, the question of interaction between gestational age and socioeconomic status remained largely unexplored for less severely preterm and early term groups.

More recently, several larger population-based studies have explicitly tested the hypothesis that socioeconomic status modifies the effect of preterm birth on children's cognitive and academic outcomes. We review these studies in Appendix Table A.1, and highlight the most relevant studies here. These studies vary in terms of specific outcomes, exposure definitions both in terms of gestational ages included and measurement of socioeconomic status, and assessment of additive or multiplicative interaction.

In an earlier study, we investigated whether neighborhood deprivation modified the estimated effect of early preterm (<28 weeks), moderate preterm (28-33 weeks), and late preterm (34-36 weeks) birth on children's first grade standardized test performance, among about 330,000 children born in the state of Georgia in 1998-2002 who took the end-of-year Georgia Criterion-Reference Competency Tests (CRCT) in mathematics, reading, and English/language arts in first grade.[99] Neighborhood deprivation was operationalized as the Neighborhood Deprivation Index of the census tract in which each child's mother resided at the time of birth. We found that both preterm birth and higher neighborhood deprivation were associated with higher risk of test failure. For the mathematics assessment, the main effect of preterm birth increased children's risk of test failure by 15.9% (95% CI: 13.3-18.5%) for early, 5.0% (95% CI: 4.1-5.9%) for moderate, and 1.3% (95% CI: 0.9-1.7%) for late preterm. Each 1 standard deviation increase in neighborhood deprivation was associated with 0.6% increased risk of test failure. There was positive additive interaction between the two exposures such that doubly exposed children experienced even higher risk of test failure than predicted from the sum of the effects of preterm birth and neighborhood deprivation (an additional 4.8% for early preterm, 1.5% for moderate preterm, and 0.8% for late preterm, with a 1 SD increase in NDI).

Brown et al. (2014) investigated whether proximal social factors modified the effect of late preterm (34-36 weeks) and early term (37-38 weeks) birth on developmental delay at age 2-3 years and receptive vocabulary delay at age 4-5 years, among about 15,000 children born in 1996-2005 and enrolled in the Canadian National Longitudinal Survey of Children and Youth (NLSCY).[100] Proximal social factors were operationalized as quality of parenting interactions, effectiveness, and consistency. The authors found that after adjustment for perinatal, child, and family variables, neither late preterm nor early term birth significantly increased risk of the outcomes, compared with being born at term (39-41 weeks). Further, no evidence of additive interaction was found in analyses using relative excess risk due to interaction (RERI) calculations to assess additive interaction between preterm birth category and each individual parenting factor (i.e., a total of 6 RERI computations for each outcomes). This is the only study to have evaluated whether parenting factors modify the effect of preterm birth on developmental outcomes, and to have purposively assessed additive interaction.

Two similar studies of interaction between preterm birth and parental education in their effects on adolescent academic performance were conducted in Taiwan and Sweden. In Sweden, Gisselman et al. (2010) evaluated whether cognitive environment modified the effect of preterm birth (<37 weeks) on grades in Swedish at the end of compulsory schooling at age 15-16 years, among 10,742 children born in 1973-1981.[84] Children's cognitive environment was measured by parental educational attainment. In adjusted ordinal logistic models, preterm birth was associated with significantly lower odds of achieving higher grades in Swedish (adjusted odds ratio (aOR) = 0.81, 95% CI: 0.66-0.98); higher parental education was associated with better performance (aOR for concordantly high education = 4.59, 95% CI: 4.13-5.09; aOR for discordant high/low education = 1.94, 95% CI: 1.77-2.13). Multiplicative interaction was assessed by including an interaction term between preterm birth and parental education. Interaction was significant, suggesting that the adverse effect of preterm birth was confined to children whose parents both had low educational attainment (aOR = 0.59, 95% CI: 0.33-0.79). For the other categories of parental educational attainment, there was no longer an association between preterm birth and grades in Swedish.

The Taiwanese study by Wang et al. (2008) had a similar objective, to assess whether social class modified the effect of prematurity on adolescents' performance on the Basic Competence Tests (BCT) in Mandarin, mathematics, and science at age 15-16 years, among 163,008 children born in 1985-1989.[85] The authors used a different definition for prematurity, comparing three categories based on gestational age and birth weight (term low birth weight, preterm normal birth weight, and preterm low birth weight) with term normal birth weight. In adjusted linear regression models, being in any of the premature categories and having lower paternal education were each independently associated with lower BCT scores in all three subjects. Additive interaction was assessed by including interaction terms between premature birth category and parental education in linear regression models. Interaction was significant for all three outcomes; the trend toward greater deficits among preterm children with lower paternal education was most apparent for Mandarin test scores.

Another Swedish study by Ekeus et al. (2010) assessed whether childhood SES modified the effect of gestational age on intelligence test performance in logical, spatial, verbal, and technical capabilities at age 18 years, among 119,124 boys born in 1973-1975 who were assessed at the time of their mandatory military conscription.[101] Gestational age was categorized into 24-28 weeks, 29-32 weeks, 33-34 weeks, 35-36 weeks, 37-38 years, and 39-41 weeks. SES was defined dichotomously as high or low based on parents' occupation, level of education, type of production, and the job category of the head of household. In adjusted linear regression models, the authors found that both lower gestational age and low SES were associated with lower intellectual test scores. Additive interaction was assessed by including interaction terms between gestational age and SES, and the term for the interaction of birth at 33-36 weeks and SES was significant. However, the authors incorrectly concluded that they had found evidence of multiplicative interaction based on this assessment.

Potijk et al. (2013) assessed multiplicative interaction between family SES and moderate preterm birth (32-35 weeks) in their effects on developmental delay at 4 years, among 926 moderate preterm and 544 term-born children enrolled in the Dutch

Longitudinal Preterm Outcome Project.[102] Children were assigned a standardized composite SES score based on parental education, parental occupation, and family income. Developmental delay was assessed using the Ages and Stages Questionnaire, with domain scores in fine motor, gross motor, problem-solving, and personal-social skills. In adjusted logistic regression models, both decreasing gestational age and decreasing SES were associated with abnormal scores in each developmental domain. Multiplicative interaction was tested by including interaction terms between standardized gestational age and SES. Significant negative interaction was observed for communication skills, while no significant interaction was observed for other outcomes. However, these findings should be interpreted with caution because the authors assigned each child a standardized value for gestational age based on his or her relative positioning within the sample distribution of gestational age. This categorization is not clinically meaningful because the sample did not reflect actual prevalence of moderate preterm birth; the sample was selected to have fewer term controls than moderate preterm cases.

2.5 Assessing interaction in epidemiologic studies

In epidemiologic studies, interaction between two exposures (A and B) in their effects on an outcome of interest (D) refers to a situation in which the effect of one exposure (A) varies across strata of the other exposure (B), and vice versa. When interaction is present, exposures A and B are not independent in their effects on D.[103,104] Statistical interaction is scale-dependent, corresponding with departure from additivity or multiplicativity of estimated effects.[103,105] Assessment of statistical interaction may be considered to be an assessment of effect measure modification under the assumption of no uncontrolled bias.[105]

Statistical interaction is present on the additive scale when there is departure from additivity of effects (i.e., the combined effect of exposures A and B on outcome D is less than or greater than the sum of their individual effects). For binary outcomes, this corresponds to heterogeneity of risk differences whereas for continuous outcomes, this corresponds to heterogeneity in estimated betas derived from linear regression models. In a linear binomial (binary) or linear regression (continuous) model, the regression coefficient for a product term between two exposures directly estimates departure from additivity. Statistical interaction is present on the multiplicative scale when there is departure from multiplicativity of effects (i.e., the combined effect of exposures A and B on outcome D is less than or greater than the product of their individual effects). For binary outcomes, this corresponds to heterogeneity of risk ratios whereas for continuous outcomes, this corresponds to heterogeneity in estimated betas derived from log-linear models. In logistic, log-binomial, or Poisson with log-link (binary) or log-linear (continuous) models, the regression coefficient for the product term directly estimates departure from multiplicativity. Considering both additive and multiplicative scales of interaction, it is possible for interaction to be present on one scale but absent on the other. It is also possible to simultaneously observe greater than additive (i.e., positive or supra-additive) and less than multiplicative interaction (i.e., negative or sub-multiplicative).[103]

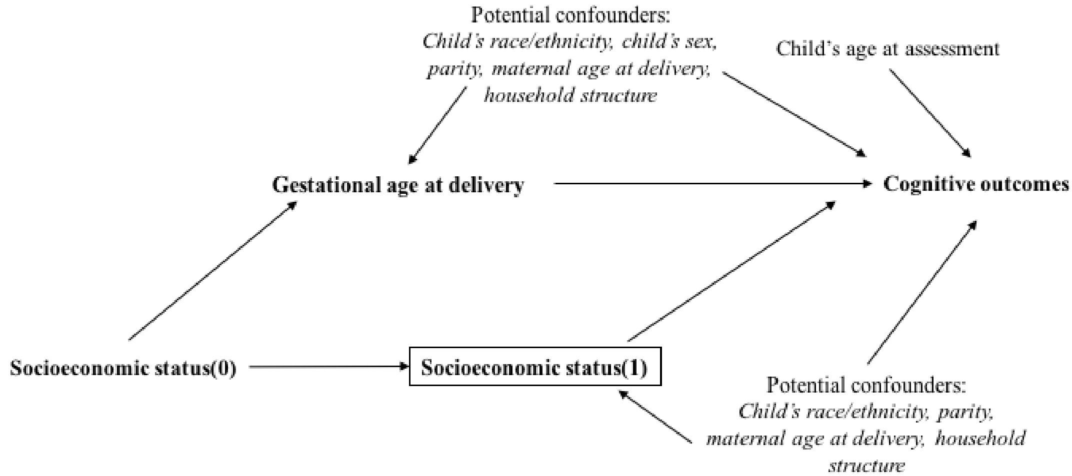
In general, for binary outcomes, assessment of additive interaction is considered to be the more appropriate scale for assessing causal interaction compared with assessment of multiplicative interaction.[103,105] Departure from additivity (e.g., heterogeneity of risk differences, interaction contrast > 0) corresponds with the presence of interactive potential outcome response types.[105,106] It is also informative from a public health perspective because it directly estimates strata-specific risk differences and thus provides information to identify high-risk sub-groups and estimate the absolute risk reductions those groups would experience if the exposure were removed.[103,105] Using the multiplicative scale does not provide information on absolute changes in risk because risk ratios or odds ratios may be operating on different baseline risks within sub-groups (e.g., an RR of 2 will result in a greater absolute increase in risk for a sub-group with baseline risk of 10% versus 1%).[103] For continuous outcomes like those studied in this dissertation, the presence of additive interaction is directly estimated using linear regression.[103] Assessment of additive interaction for continuous outcomes has not been shown to give insight into the presence of causal interaction between two risk factors, however it may be informative in terms of estimating strata-specific absolute differences in the outcome.[103]

In this dissertation, we aim to test the presence of additive interaction between gestational age at delivery and socioeconomic status in their effects on children's cognitive outcomes, measured as continuous outcome variables. Socioeconomic status is treated as a potential effect modifier of the relationship between gestational age at delivery and children's cognitive outcomes. In the absence of effect modification, the estimated effects of preterm birth would be constant across socioeconomic strata. If there were supra-additive interaction, the estimated effects of preterm birth (i.e., cognitive score deficit) would be larger among children of lower socioeconomic status; conversely if there were sub-additive interaction, the estimated effects of preterm birth would be smaller among children of lower socioeconomic status.

2.6 Proposed causal diagram

Figure 2.1 displays our theorized directed acyclic graph (DAG) representing relationships between gestational age at delivery (exposure), socioeconomic status (potential effect modifier), and cognitive outcomes (outcomes), as well as potential confounders. This representation of potential effect modification by socioeconomic status is based on guidance from VanderWeele and Robins (2007).[104] Socioeconomic status is represented both as a potential confounder and effect modifier of the relationship between gestational age at delivery and cognitive outcomes. Socioeconomic status at time 0 represents a family's socioeconomic status prior to a child's birth, which may influence the gestational age at delivery for that child and influences the socioeconomic status of the family during the child's early life at time 1. Based on guidance from VanderWeele and Robins (2007), we use a box around socioeconomic status at time 1 (the available measurement of the potential effect modifier) to indicate that effect modification may be present if, after conditioning on the effect modifier, the relationship between exposure and outcome is not constant across levels of the effect modifier. Potential confounders of both the exposure-outcome and modifier-outcome relationships are child's race/ethnicity, child's sex, parity, maternal age at delivery, and household structure. Child's age at assessment is also included as a covariate due to the rapid pace of development during childhood with children's cognitive scores on any given assessment increasing with age.

Figure 2.1. Directed acyclic graph representing effect modification by family socioeconomic status of the relationship between preterm birth and children's cognitive and academic outcomes.



2.7 Conclusions

Children's cognitive development and academic performance are linked to both fetal and early childhood factors, including being born preterm and growing up in a family with lower SES. Some susceptible children are likely to be at higher-than-expected risk of the "double jeopardy" of experiencing both exposures due to socioeconomic disparities in the occurrence of preterm birth. This dissertation sought to better understand how gestational age and SES jointly influence cognitive and academic outcomes in early childhood and at school age by assessing additive interaction between the two risk factors.

Chapter 3. Data Sources

3.1 Early Childhood Longitudinal Study-Birth Cohort

The Early Childhood Longitudinal Study-Birth Cohort (ECLS-B) was a nationally representative longitudinal study of children born in the United States in 2001 and followed through kindergarten. The ECLS-B was sponsored primarily by the U.S. Department of Education, National Center of Education Statistics (NCES). The purpose of ECLS-B was to investigate children's cognitive, social, emotional, and physical development over early childhood; health care, nutrition, and physical well-being; preparation for school; and experiences in early care and education programs and kindergarten.[107]

The ECLS-B sampled children from the 2001 U.S. birth cohort using a complex sample design, employing stratification and clustering as well as oversampling of low birth weight, very low birth weight, twins, American Indian/Alaska Native, Chinese, and other Asian/Pacific Islander groups. The target population for the ECLS-B was children who were born in the United States in 2001 to mothers aged 15 years old or older and who did not die, move abroad, or get adopted prior to the 9-month data collection. The sampling frame was all U.S. birth certificates for live births in 2001. Births were sampled within 96 primary sampling units (PSU). In order to achieve oversampling of American Indian/Alaska Native children, an additional 18 PSUs were sampled from a sampling frame including areas with higher proportions of American Indian/Alaska Native births (located mainly in the western United States). PSUs were constructed from contiguous counties, using metropolitan statistical areas and National Center for Health Statistics

(NCHS) health service areas.[108] About 14,000 birth certificates were included in the initial sample, and about 10,700 children enrolled in the study at 9 months old.

Data were abstracted from birth certificates and prospectively collected in 5 waves of data collection at 9 months (Wave 1), 2 years (Wave 2), preschool age (Wave 3), and kindergarten age (Waves 4 and 5). The kindergarten assessment was split into two waves in order to assess children when they entered kindergarten. For each subsequent round of data collection, children were eligible to participate if they had a completed parent interview in the previous round (with the exception of American Indian/Alaska Native children for the kindergarten 2006 wave). Children could be excluded at any time after the 9-month wave if they died or moved permanently outside of the United States. In order to reduce study field costs, the kindergarten waves followed an 85% sub-sample of children eligible to participate in that wave (except for American Indian/Alaska Native children, who were included if they had responded at the 9-month wave as well as the 2-year wave and/or the preschool wave). The prospective waves of data collection involved direct testing of the children as well as surveys of the primary responding parent/guardian (which in >90% of cases was the child's mother or female guardian), resident and non-resident fathers, early care and education providers, wrap-around early care and education providers, and teachers.

3.1.1 ECLS-B data used in this dissertation

Gestational age at delivery: Gestational age data were obtained from birth certificates. Since the study children were all born in 2001, all births were reported on the 1989 version of the U.S. Certificate of Live Birth. Gestational age was recorded on this birth certificate version by two definitions: (1) estimated gestational age based on last reported menstrual period, and (2) clinical estimate of gestation based on a medical provider assessment.

Family socioeconomic status: The ECLS-B constructed a composite variable to describe household socioeconomic status based on father/male guardian's education, mother/female guardian's education, father/male guardian's occupation, mother/female guardian's occupation, and household income. Parental education was recorded using three variables: highest level of education for the child's parents who reside in the household, father's highest level of education, and mother's highest level of education. Highest level of education was defined using the following categories: 8th grade or below, 9th to 12th grades, high school diploma/equivalent, vocational/technical program, some college, bachelor's degree, graduate professional school/no degree, master's degree, and doctorate or professional degree. Occupation categories were defined using 23 aggregated categories based on the federal Office of Management and Budget's *Standard Occupational Classification Manual* (2000).[109] The ECLS-B dataset includes a variable for the mother's and father's occupational category, and the average of the 1989 General Social Survey prestige score associated with that occupational category. Annual household income was recorded in multiple ways: broad-range household income (≤$25,000 versus >$25,000) and detailed-range household income (≤$5,000; $5,001 to 10,000; $10,001 to $15,000; $15,001 to $20,000; $20,001 to $25,000; $25,001 to $30,000; $30,001 to $35,000; $35,001 to $40,000; $40,001 to $50,000; $50,001 to $75,000; $75,001 to $100,000; $100,001 to $200,000; $200,001 or more). In constructing the composite SES variable, the median of the detailed income range was used.

Missing data on components of the SES composite variable were handled using hot deck methodology to impute values for subjects who were missing component variables. Imputed values were assigned based on data available from subjects with similar characteristics. The composite SES variable was constructed in two steps. First, each component variable was standardized to a N(0,1) distribution, accounting for sample weighting; each subject was assigned a z-score for each component. The z-score for income was calculated using the logarithm of the median of the detailed income range. Second, the non-missing z-scores for each subject were averaged to compute the composite SES variable. The composite SES variable is recorded as a continuous measure, as well as a categorical variable for five quintiles of composite SES (quintile 1 = lowest SES category, quintile 5 = highest SES category). When there were missing components (e.g., single parent family), the composite SES variable was calculated by taking the average of the available components. In addition to using the composite variable to measure SES, we also used individual component variables including maternal education, household income, and household poverty (relative to the Federal poverty level).

Other demographics: Potential confounders were child's race/ethnicity, child's sex, parity, maternal marital status, and maternal age at delivery. These data were taken from birth certificates or Wave 1.

Cognitive ability scores at two years old: Children's cognitive ability in early childhood was measured at Wave 2 using the Bayley Short Form-Research Edition (BSF-R) Mental Scale. The BSF-R was designed specifically for the ECLS-B based on a subset of questions from the Bayley Scales of Infant Development-Second Edition (BSID-II).[110]

The BSF-R Mental Scale consisted of 33 items. Of these, a core set of 19 items was administered to all children. Based on their performance on these items, some children were routed to basal or ceiling items. If a child answered 0-4 of the 19 core items correctly, he or she was administered an additional 5 basal items. If a child answered 14 or more of the 19 core items correctly, he or she was administered an additional 9 ceiling items. On each item, interviewers scored children as credit (C) or no credit (NC). BSF-R Mental Scale scores were not computed if fewer than two-thirds of items were scored.[110]

Scale scores and standardized t-scores were computed for the BSF-R Mental scale assessment. Scale scores reflect the item response theory (IRT) model-based estimate of a child's raw score on the full BSID-II based on his/her score on the BSF-R Mental Scale, and hypothetically range from 0-178. Since the BSF-R was a reduced version of the full BSID-II and did not include items testing at the lowest and highest developmental ages, the actual range of scores among ECLS-B children was narrower from 92.35-174.14.[110] Since scale scores reflect "measures of overall mental … ability" representing a child's absolute position along the developmental spectrum, not accounting for difference in age, analyses utilizing scale scores must be adjusted for age at testing.[110] In contrast, standardized t-scores reflect a child's relative positioning within his or her age-reference population (i.e., children at the same chronological age, corrected for prematurity). For children born more than 3 weeks early, age was corrected for prematurity by subtracting the number of days he or she was born early from the chronological age at which he or she was assessed (e.g., if a child was born 4 weeks early and assessed at age 24 months, his or her 'corrected' age at assessment was 23 months). Scores were norm-referenced within age groups to a N(50,10) distribution.[110]

Reading and mathematics achievement scores at kindergarten age: Children's kindergarten-age early reading and early mathematics achievement were assessed at Waves 4 and 5 using ECLS-B-designed kindergarten assessments in reading and mathematics. The same assessments were used in both Waves 4 and 5. These assessments were designed to be a broad test of knowledge and skills across several domains, with consideration of key developmental milestones at preschool and kindergarten age as well as knowledge and skills that are important for school readiness and early school success.[108] The assessments drew upon existing items from standardized instruments and assessment batteries for preschool- and kindergarten-aged children, such as the Peabody Picture Vocabulary Test and PreLAS® 2000.[111] Further, the design of the kindergarten assessments took into account logistical concerns related to the amount of training and experience required for field staff, appropriateness for implementation in a home environment, assessment length, accommodation of children with varying levels of ability, and inclusion of children with limited English fluency.[108] Each of the assessments had a two-stage design consisting of a routing test administered to all children as well as a second-stage test of low, medium, or high difficulty that was selected based on children's performance on the routing test. Discontinue rules were used during test administration to stop the administration of items that were too difficult for a particular child.

The early reading assessment covered the following content areas: basic skills (53 items covering including letter recognition in receptive and expressive modes, letter sounds, early reading—recognition of simple words, phonological awareness, knowledge of print conventions, and word matching); initial understanding (10 items testing early readers on their initial impression or global understanding of what they have read); developing interpretation (2 items testing early readers on extending their initial impressions to a more complete understanding of what they have read); demonstrating a critical stance (2 items testing early readers on demonstrating an understanding of the story they have read); and vocabulary (7 items covering receptive and expressive vocabulary). The early reading routing test consisted of 24 items, and the low, medium, and high difficulty second-stage tests consisted of 16, 21, and 27 items, respectively. Children who answered <8 items correctly on the routing test received the low difficulty (basal) second-stage test; those who answered 8-13 items correctly on the routing test received the medium difficulty second-stage test; and those who answered ≥14 items correctly on the routing test receiving the high difficulty (ceiling) second-stage test.[112]

The early mathematics assessment covered the following content areas: number sense, properties, and operations (41 items); measurement (3 items); geometry and spatial sense (4 items); data analysis, statistics, and probability (3 items); and patterns, algebra, and functions (7 items). The early mathematics routing test consisted of 17 items, and the low, medium, and high difficulty second-stage tests consisted of 16, 20, and 25 items, respectively. Children who answered ≤5 items correctly on the routing test received the low difficulty second-stage test; those who answered 6-12 items correctly on the routing test received the medium difficulty second-stage test; and those who answered ≥13 items correctly on the routing test received the high difficulty second-stage test.[112]

Scale scores and theta scores were computed for the early reading and mathematics assessments. Scale scores reflect the estimated number of items in a content domain that a child would have answered correctly, if they had been asked all of the scored questions. These scores were calculated using item response theory (IRT) procedures, which allow for different subsets of questions to be administered to different children. Therefore, scores can be compared across children regardless of the actual subset of questions that the individual children received.[108] Scores were equal to the sum of probabilities of answering each question correctly, and range from 0 to the total number of assessment questions in a given content domain but are not restricted to integer values. Theta scores reflect estimated ability in a particular domain. Theta is used to calculate the overall scale score, because it informs the probability that a child will answer a particular question correctly. Theta scores are more normally distributed than scale scores, because the probability of answering a question correctly also depends on characteristics of the question (e.g., discrimination, difficulty, guessing). If there are high difficulty items, overall scale scores may be left-skewed because of the low probability of answering these questions correctly.[108]

3.2 Millennium Cohort Study

The Millennium Cohort Study (MCS) is a nationally representative longitudinal study of children born in the United Kingdom in 2000-2002, with follow-up continuing to the present day. The MCS is administered by the Centre for Longitudinal Studies at the Institute of Education, University of London and is funded by the Economic and Social Research Council as well as by the United Kingdom, Welsh, Scottish, and Northern Ireland governments. The purpose of the MCS was to follow the lives of UK children through childhood and adolescence into adulthood, with focus on how early family contexts impact development and outcomes across these life periods.[113]

The MCS sampled children using Child Benefit records from the Department of Social Security using a stratified, geographically clustered sample design. Children were oversampled in Wales, Scotland, and Northern Ireland; areas of England with high proportions of ethnic minorities; and areas of high child poverty. In England and Wales, children were sampled between September 2000 and August 2001. In Scotland and Northern Ireland, children were sampled between November 2000 and January 2002. Child Benefit records were used to sample children rather than birth records because the benefit coverage is nearly universal and families were asked to opt-out of providing a postal mail address to the benefits office rather than opt-in as is done with birth records. Less than 3% of children were removed from the eligible sample if they died or were adopted, or if the family was investigated for benefit fraud. Another 40 children were removed from eligibility because their families had already taken part in the National Centre for Social Research's Families and Children Survey.[114] A total of 18,552 families including 18,818 children enrolled in the MCS at 9 months old.

To date, data have been prospectively collected in 6 sweeps at 9 months (Sweep 1), 3 years (Sweep 2), 5 years (Sweep 3), 7 years (Sweep 4), 11 years (Sweep 5), and 14 years (Sweep 6). This dissertation uses data collected in the first 3 sweeps covering children's early childhood and entry into school. Families were eligible to participate in each sweep of data collection regardless of whether they had completed the previous sweep, with the exception of those who became ineligible due to death, emigration, permanent refusal, being permanently untraceable, or sensitive family circumstances. Each data collection sweep consisted of direct testing of children as well as surveys of the primary respondent (usually the natural mother) and partner. At some waves, there were teacher surveys, linkage to school records, and linkage to geographic data.

3.2.1. MCS data used in this dissertation

Gestational age at delivery: Primary respondents were asked to report the study child's due date and actual birth date at Sweep 1. These dates were used to estimate a gestational age at delivery in days. In a validation study, Poulsen et al. (2011) linked 50% of MCS singleton births with hospital records, and found that maternal self-reported due date agreed with hospital gestational age data within 1 week in 94.5% (95% CI: 93.8-95.1) of births.[115] Agreement was poor, however, for post-term births; these births are excluded from analyses in this dissertation. Since agreement between self-reported data at Wave 1 and hospital reports was only 72.2% (95% CI: 70.4-73.9) for exact number of gestational weeks, the authors suggested that these data were most reliable when used for categorizing gestational ages into groups; agreement when categorizing into <32 weeks, 32-36 weeks, and 37+ weeks was 98% (95% CI: 97.7-98.3).[115]

Socioeconomic status: Although the MCS did not calculate a composite measure of SES similar to the ECLS-B, multiple indicators of socioeconomic status were measured in the MCS. These measures include employment status for the primary respondent and partner, family income band (£0 to less than £3100, = £3100 to less than £10400, £10400 to less than £20800, £20800 to less than £31200, = £31200 to less than £52000, £52000 and above), household income equivalized for household size, income quintile, poverty status relative to the UK poverty threshold (60% of median equivalized household income), highest educational attainment of the primary respondent and partner, and occupation level based on the National Statistics Socio-economic Classification (NS-SEC) of the primary respondent and partner.[114]

Other demographics: Potential confounders were child's race/ethnicity, child's sex, number of siblings, household type (two-parent versus single mother), and maternal age at delivery. These data were taken from Sweep 1.

Cognitive scores at three years old: At Sweep 2, MCS children completed the Bracken School Readiness Assessment-Revised (BSRA-R) and the naming vocabulary scale of the British Ability Scales II (BAS II). The Bracken Basic Concept Scale – Revised (BBCS-R) measures basic concept development among children aged 2 years 6 months to 7 years 11 months using 11 sub-tests covering 308 educational concepts. MCS children completed the first 6 sub-tests comprising the BSRA-R, covering colors, letters, numbers/counting, sizes, comparisons, and shapes. All MCS children completed the same items. Raw scores for each BSRA-R sub-test were computed by summing the number of items answered correctly, and sub-test raw scores were summed to compute a composite raw score. Composite raw scores were age-adjusted to produce a standardized score with mean of 100 and standard deviation of 15, which can be used to compare BSRA-R scores across children of different ages. Standardization was done using look-up tables for transforming raw to age-standardized scores based on a norming sample of 1,100 children representative of the US population in 1995, with age normed within 3-month age groups.[116]

The naming vocabulary scale measures expressive language ability, by asking children to name the objects pictured in a testing booklet. Competencies that may be reflected by naming vocabulary scores are: “expressive language skills, vocabulary knowledge of nouns, ability to attach verbal labels to pictures, general knowledge, general language development, retrieval of names from long-term memory, [and] level of language stimulation”.[114] A weakness of the naming vocabulary scale is that low scores may be reflective of children being reluctant to speak or not knowing what the presented object is (although the pictures are selected to be generally known by young children). The naming vocabulary scale consists of an initial routing test administered to all children, after which children may progress to a set of more difficult items or more simple items depending on their performance on the routing set. Since not all children complete the same set of items, raw scores are converted into ability scores and t-scores. Item response theory methods were used to convert raw scores into ability scores, taking item difficulty into account; the MCS used look-up tables to convert raw to ability scores. The analytic challenge of comparing ability scores across children is that they are not measured on a truly continuous scale. Ability scores were age-adjusted to provide t-scores with mean of 50 and standard deviation of 15, which can be used to compare naming vocabulary test scores across children. Standardization was done used look-up tables for transforming ability to age-standardized t-scores based on a norming sample of 1,689 children representative of the UK population 1995, with age normed within 3-month age groups. Analytically, t-scores represent children’s performance relative to children of their same age.[116]

Cognitive scores at five years old: At Sweep 3, MCS children completed the BAS II naming vocabulary, picture similarity, and pattern construction scales. The naming vocabulary scale was repeated from Sweep 2. The pattern construction scale tested spatial problem solving by asking children to repeat a design using flat squares or solid cubes, and the picture similarities scale tested non-verbal reasoning or problem solving by showing children a row of four pictures and asking them to identify a fifth picture that is most similar to the others.[114] Scoring procedures for all three tests repeated those used for the naming vocabulary test at Sweep 2.[116]

Cognitive and achievement scores at seven years old: At Sweep 5, MCS children completed the BAS II pattern construction and word reading scales and the National Foundation for Education Research (NFER) Number Skills assessment. The pattern construction scale was repeated from Sweep 3.[114]

The word reading scale tested English reading ability by asking children to read aloud a series of words. There were 90 words total presented in 9 blocks of 10 words; the number of blocks administered to each child depending on his or her performance. Scoring procedures were similar to the other BAS II scales administered at the previous sweeps, except that standardized scores were normed to a mean of 100 and standard deviation of 100.[114]

The NFER Number Skills assessment was adapted from the NFER Progress in Maths (PiM) test, which was developed and standardized to the national UK population in 2004. The assessment had a two-stage design in which all children completed an initial routing test and then an additional section of easier, medium, or harder difficulty. Since not all children completed the same set of items, item response theory methods were used to convert raw scores to estimated raw scores on the full PiM test.[114] Standardized age-adjusted scores were computed based on comparing with the PiM norming sample. These standardized scores allow for direct comparison among children of different ages.[116]

Chapter 4. Describing the shape of the relationship between gestational age at birth and cognitive development in a nationally representative U.S. birth cohort

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Abstract

Background: Preterm children face higher risk of cognitive and academic deficits compared with their full-term peers. The objective of this study was to describe early childhood cognitive ability and kindergarten academic achievement across gestational age at birth in a population-based longitudinal cohort.

Methods: The study population included singletons born at 24-42 weeks GA enrolled in the Early Childhood Longitudinal Study-Birth Cohort (n=6,150 for 2-year outcome, n=4,450 for kindergarten outcome). Home-based assessments measured cognitive ability at 2 years and reading and mathematics achievement at kindergarten age. Linear regression models estimated the association between gestational age and cognitive and academic scores using four different ways of modeling gestational age: continuous variable in linear and quadratic terms; categories for individual weeks; and clinical categories for early preterm, moderate preterm, late preterm, early term, full term, late term, and post-term.

Results: Children born at early preterm (24-27 weeks), moderate preterm (28-33 weeks), and late preterm (34-36 weeks) scored significantly worse than full-term (39-40 weeks) peers on 2-year and kindergarten assessments; however, no deficits were observed for early term (37-38 weeks). These categories were a clinically useful and parsimonious approach to stratifying risk of adverse cognitive and academic outcomes.

Conclusions: This study estimated the relative performance of children born at 24-42 weeks in a population-based birth cohort using multiple approaches to modeling gestational age, providing a more rigorous understanding of the relationships between the

full spectrum of gestational age and cognitive and academic outcomes in early childhood and at school age.

Introduction

Children who are born preterm are more likely to experience cognitive and academic deficits as well as learning disabilities and problems in school.[18,32] Preterm delivery interrupts *in utero* brain growth and development; children are born with developmentally immature brains before they have had sufficient time to achieve optimal size and neuronal development. Preterm children may have smaller brain volumes[24,117] and experience central nervous system injuries[30,31], both of which are associated with worsened neurodevelopmental outcomes in childhood. Children born at the earliest gestational ages and lowest birth weights have the most severe consequences; however, even children born nearer to term—i.e., at late preterm or early term—may have worsened cognitive and academic outcomes compared those born at full term or at 39 weeks or later.[118–121]

Numerous studies have evaluated children's outcomes following preterm or early term birth but few have examined outcomes along the entire range of gestational age within the same analytic population. Given evidence of the adverse impacts of even mild prematurity, we wanted to understand the impacts of each additional week spent *in utero* on cognitive scores or school outcomes without limiting our analyses by using a single reference group (e.g., ≥37 weeks). Variation in cognitive test scores by each additional gestational week has been found among children born earlier than 33 weeks[44] and among infants born at 37-41 weeks.[59,60,122] Two studies examined the relationship between the full range of gestational age and academic problems, focusing on special education provisions in Scotland[123] and completion of basic schooling requirements in Denmark.[124] The objective of this study was to describe cognitive and academic outcomes at 2 years and kindergarten age across the full spectrum of gestational age at birth among children enrolled in a U.S. population-based longitudinal cohort study.

Methods

This study used data from the Early Childhood Longitudinal Study-Birth Cohort (ECLS-B), a population-based longitudinal study that sampled children from 2001 U.S. births and followed them through kindergarten. Its design and data collection procedures have been described extensively.[108] Briefly, more than 14,000 children were selected in a stratified, clustered sample of 2001 birth certificates with oversampling of twins, low birth weight, very low birth weight, and certain racial/ethnic groups. About 10,700 children including 8,850 singletons enrolled in the study at 9 months old. Data were also collected at 2 years, preschool age, and kindergarten age. Kindergarten data collection was split across two waves starting in fall 2006 and fall 2007 in order to assess children at kindergarten entry, which typically differed based on birth date; we used data from children's first entry into kindergarten. The kindergarten waves followed an 85% sub-sample (n=7,700; 6,250 singletons) of children who had completed the preschool wave (n=9,000; 7,400 singletons). To be eligible for follow-up in each subsequent wave, children needed to have a completed parent interview at the previous wave.

There were 7,250 singletons born at 24-42 completed weeks who were eligible for this study. Children were excluded if part of a multiple birth (n=1,800), missing clinical estimate of gestational age (n=1,450) or birth weight (n=150), or reported birth weight was implausible for gestational age (n<50).[125] Nearly all (97%) of children missing clinical estimate of gestational age were California births, where the clinical estimate was not reported on birth certificates until adoption of the 2003 revised birth certificate.[126]

Gestational age at delivery was defined using the clinical estimate of gestation reported on the birth certificate. Gestational age was modeled using four methods spanning three general approaches: continuous (linear and quadratic terms); using each gestational age week as its own category; and using categories defined by the American Congress of Obstetricians and Gynecologists (ACOG) for early preterm (24-27 weeks), moderate preterm (28-33 weeks), late preterm (34-36 weeks), early term (37-38 weeks), term (39-40 weeks), late term (41 weeks), and post-term (42 weeks).[11]

Cognitive ability at 2 years old was measured using the Bayley Short Form-Research Edition (BSF-R) Mental Scale, an abbreviated version of the Bayley Scales of Infant Development-Second Edition (BSID-II) developed for the ECLS-B.[110] The BSID-II comprises 178 items organized into age sets; individual test takers receive different sets of items based on their assessment age (corrected for prematurity). In contrast, ECLS-B children were all administered the same set of up to 33 items—including 19 core items, 5 basal items, and 9 ceiling items—selected based on psychometric properties to validly test cognitive ability for 22-26 month old children. Our analyses used children's scale scores, which represented the item response theory (IRT)-based estimate of raw score on the full BSID-II.[127] Some children completed the BSF-R Mental Scale outside of the target age range of 22-26 months; therefore we restricted to children in this age range in a sensitivity analysis.

Reading and mathematics achievement at kindergarten age was measured using ECLS-B-designed assessments of knowledge and skills in reading and mathematics.[108] These assessments used existing items from standardized instruments and assessment batteries for preschool- and kindergarten-aged children (e.g., Peabody Picture Vocabulary Test, PreLAS® 2000), as well as ECLS-B-developed items.[111] There was a two-stage design consisting of a routing test administered to all children and a second-stage test of low, medium, or high difficulty selected based on routing test performance. Our analyses used children's scale scores, which represented the IRT-based estimate of the number of items that a child would have answered correctly if they had been asked all of the scored questions.

Covariates of interest were child's race/ethnicity (American Indian or Alaska Native, Asian, non-Hispanic black, Hispanic, multi-racial, Native Hawaiian or other Pacific Islander, non-Hispanic white), maternal educational attainment (less than high school, completed high school, some college, bachelor's degree or higher), household poverty adjusted for household size (<130% of the federal poverty threshold [FPL], 130% to <185% of FPL, and ≥185% of FPL), child's sex, parity (first-born, second or third born, fourth-born or above), and maternal age at delivery (categorized as 15-17, 18-19, 20-24, 25-29, 30-34, 35-39, and 40 years or older). Covariates were ascertained from birth certificates (child's sex, parity, maternal age at delivery) or parent interviews at 9 months (child's race/ethnicity, maternal educational attainment, household poverty for 2-year analyses) and 2 years (household poverty for kindergarten analyses).

Statistical analysis

Descriptive statistics included frequencies by gestational age and covariates as well as unadjusted mean outcome scores by categories of gestational age and covariates. Multivariable analyses with generalized estimating equations (GEE) based on the normal distribution estimated mean differences in outcome scores at each time point, accounting for clustering of subjects by ECLS-B designed sample clusters. Sampling weights were not applied in the primary analyses because the objective was to obtain internally valid estimates of the relationship between gestational age and outcome scores among study participants rather than to ensure that findings were representative of 2001 U.S. births.

In order to describe the shape of the relationship between gestational age and each outcome, four methods of modeling gestational age were compared: (1) categories for each week comparing to a 40-week referent category, (2) ACOG categories comparing to a full term (39-40 weeks) referent category, (3) continuous (linear model), and (4) continuous adding a quadratic term (i.e., squared gestational age). Model fit was compared using quasi-likelihood under the independence model (QIC) statistics analogous to Akaike information criterion (AIC) statistics for generalized estimating equations. Cubic terms were also considered but dropped from final analyses due to limited statistical power especially in the smaller gestational age categories and because they did not offer superior model fit compared to quadratic models. To graphically compare across gestational age definitions, predicted scores for each week of gestation were plotted at covariate reference values.

All analyses were adjusted for child's assessment age. Clinical recommendations suggest correcting for prematurity until two or three years of age; therefore we used corrected age for the primary 2-year analyses. Correcting for prematurity means that a child's degree of prematurity (e.g., 3 weeks premature) is subtracted from his or her chronological age measured from birth date in order to arrive at a "testing age" for developmental assessments—effectively resulting in a premature child being compared with term-born children of higher chronological age. Typical practice is to subtract the number of weeks born early (compared with 37 weeks) from the child's chronological age.[128] Given recent evidence of the impacts of mild prematurity on cognitive outcomes, however, we corrected children's testing ages to a referent of 40 weeks, and we applied the correction for all children born earlier than 40 weeks. For example, a child born at 36 weeks and tested at 24 months chronological age was assigned a correcting age of 23 months. Sensitivity analyses were conducted using chronological age for the BSF-R Mental Scale outcome, and using prematurity-corrected age for the kindergarten outcomes. Analyses were also adjusted for child's race/ethnicity, maternal educational attainment, household poverty, child's sex, parity, and maternal age at delivery.

About 8% (n = 550) of eligible children who completed the 2-year wave were missing BSF-R Mental Scale scores. In a sensitivity analysis, missing BSF-R scores were multiply imputed using multivariate imputation by chained equations.[129] One-third of the eligible sample was lost to follow up between the 2-year and kindergarten waves. In a sensitivity analysis, the possibility of selection bias influencing the kindergarten results was evaluated using inverse probability of censorship weighting (IPCW) and marginal structural models.[130,131] Among eligible children who completed the 2-year wave (n=6,700), logistic regression was used to obtain predicted probabilities of participating in the kindergarten wave based on baseline covariates. In weighted GEE models for the kindergarten outcomes, non-censored children were assigned stabilized inverse probability weights, effectively up-weighting subjects who were less likely to complete the kindergarten wave.

Analyses were conducted using SAS v9.3 (Cary, NC) and R 3.1 (R Foundation for Statistical Computing, Vienna, Austria). This study was approved by the Emory Institutional Review Board. Unweighted frequencies are rounded to the nearest 50 per National Center for Education Statistics guidelines.

Results

A total of 6,150 children were included in 2-year analyses and 4,450 were included in kindergarten analyses (Supplemental Table 4.1). Due to oversampling of low birth weight children, about 18% were born before 37 weeks (Table 4.1). Children included in our analyses were racially and socioeconomically diverse: 57% were racial/ethnic minorities, 50% lived under 185% of the FPL, and 50% had mothers who had completed a high school degree or less. The mean BSF-R Mental Scale score was 126.1 (SD=11.0, range 92.4-174.1). Mean scores on the kindergarten reading and mathematics assessments were 44.4 (SD=14.8, range 12.4-82.5) and 43.9 (SD=10.5, range 11.2-69.7) respectively.

Children born at 24-39 weeks performed worse compared with children born at 40 weeks, although estimated deficits were not statistically significant for those born at 31 or 35-39 weeks after covariate adjustment (Table 4.2; Figure 4.1a). Using ACOG categories, significant deficits were observed for the early preterm (-6.6, 95% CI: -8.1, -5.0), moderate preterm (-2.9, 95% CI: -4.0, -1.8), and late preterm (-1.3, 95% CI: -2.3, -0.4) groups. Using a linear term for continuous gestational age suggested a significant, positive relationship between gestational age and BSF-R Mental Scale score. The quadratic function of continuous gestational age was significant but very small in magnitude. There was little difference in QIC statistics across adjusted models. When models were instead adjusted for chronological age at assessment, estimated deficits were stronger (Supplemental Table 4.1). Significant deficits were observed for the early preterm (-12.9, 95% CI: -14.2, -11.5), moderate preterm (-7.2, 95% CI: -8.2, -6.3), late preterm (-3.3, 95% CI: -4.2, -2.5), as well as early term (-1.1, 95% CI: -1.7, -0.5) groups.

Children born at late preterm or earlier scored significantly worse on the kindergarten reading and mathematics assessments compared to those born at term (Tables 4.3-4.4, Figures 4.1b-4.1c). Using individual week categories, most groups under 37 weeks exhibited significant deficits in reading and mathematics scale scores compared to children born at 40 weeks. Using ACOG categories, significant reading deficits were observed for early preterm (-5.1, 95% CI: -7.2, -3.0), moderate preterm (-3.0, 95% CI: -4.3, -1.8), and late preterm (-1.8, 95% CI: -3.3, -0.4). On the mathematics assessment, significant deficits were observed for early preterm (-6.7, 95% CI: -8.5, -4.9), moderate preterm (-3.6, 95% CI: -4.6, -2.7), and late preterm (-1.6, 95% CI: -2.6, -0.6). For both outcomes, we found that only the linear term was significant in models operationalizing gestational age as a continuous variable; quadratic terms were not significant. There was little difference in QIC comparing across adjusted models for each of the kindergarten outcomes. When adjusted for corrected age, estimated deficits for preterm and early term children on both the reading and mathematics assessments were attenuated (Supplemental Tables 4.2-4.3). For reading, estimated deficits were no longer significant for early preterm, moderate preterm, or late preterm compared with term births. For mathematics, significant deficits remained for early preterm (-4.4, 95% CI: -6.2, -2.6) and moderate preterm (-2.0, 95% CI: -3.0, -1.1).

Factors associated with missing 2-year scores were early preterm and moderate preterm delivery, household poverty, hospital stays due to medical problems after birth, receipt of early intervention or other support services for special needs at 9 months or 2 years, and having a parent-reported health problem or impairment that limited ability to walk, run, or play. Rates of chromosomal anomalies or birth defects were similar across children with and without 2-year scores. Results were similar when missing 2-year scores (n=550) were multiply imputed (Supplemental Table 4.4). When 2-year analyses were restricted to children tested at 22-26 months of age, results were similar in models adjusting for chronological age (Supplemental Table 4.5). In models adjusting for corrected age, estimated deficits for early preterm and moderate preterm children were slightly attenuated. Larger proportions of these groups were excluded based on the 22-26 month criterion after correcting children's ages for prematurity.

About half of those lost to follow up between the 2-year and kindergarten waves were part of the planned 85% sample size reduction between the preschool and kindergarten waves (Supplemental Figure 4.1). These children were more likely to be non-Hispanic white, be preterm, live in poverty, and have younger and less educated mothers, but did not differ in terms of 2-year scores. Applying IPCW stabilized weights to account for potential selection bias did not meaningfully change results for the kindergarten outcomes (Supplemental Tables 4.6-4.7).

Comment

Children born at early preterm, moderate preterm, and late preterm had deficits in cognitive ability at 2 years old and reading and mathematics achievement scores at kindergarten age compared with their peers born at full term. Magnitude of deficits increased with decreasing gestational age.

Our examination of the relationship between gestational age at delivery and cognitive and academic outcomes in early childhood using multiple approaches to modeling the full continuum of gestational age contributes to the extant literature that often dichotomizes or coarsely categorizes preterm births in some way (e.g., <32 weeks, 34-36 weeks) and uses 37 weeks or later as a reference group. The consequence of these categorical schemes is that children with different risk may be inappropriately pooled into common groups—our objective was to formally test the assumption that such categories adequately describe outcome risks. These analyses of multiple methods for modeling gestational age support the use of ACOG categories—which were developed primarily to capture differences in neonatal medical outcomes—as a useful, parsimonious approach to capturing overall patterns in cognitive and academic outcomes by gestational age. Similar fit statistics across models suggested that none of the methods for operationalizing gestational age resulted in a model that clearly had comparatively superior predictive power. For all three outcomes, the use of ACOG categories adequately described the shape of the relationship between gestational age and cognitive/academic score within our study cohort and did so with clinically meaningful cut-points.

This study benefitted from the use of data from a large birth cohort with rigorous prospective data collection and direct assessment of children's cognitive and academic outcomes. The population-based design of the study, however, comes with some inherent limitations, namely that even with over-sampling of low birth weight infants and a large overall sample, numbers of children at earlier gestational weeks, especially below 32 weeks, were still relatively small. There may have been low power to detect associations and identify non-linear relationships when categorizing gestational age by individual week and using continuous functions of gestational age, particularly in very preterm range where non-linearities might be observed. Being able to potentially delineate differences in outcomes within the early ACOG categories (e.g., very preterm spanning 24-27 weeks and moderate preterm spanning 28-33 weeks), with comparison to outcomes along the full spectrum of gestational age as we have done in this study, may be useful for neonatologists and pediatricians as well as for parents and families of very and moderately preterm children. Additional studies with larger sample sizes at extreme gestational weeks is needed to estimate week-by-week differences, and we suggest that these studies use a similar approach to ours analyzing the full spectrum of gestational age to better understand the distribution of outcomes rather than restricting to pre-specified reference groups.

Further, a limitation of using population-based secondary data—in contrast to, for example, follow up of hospital-based populations—is potential underrepresentation of children with severe disabilities that preclude them and their families from agreeing to participate. In this study, we did find that children with parent-reported impairments or who received early intervention services were slightly less likely to complete the 2-year assessment. Our results should be interpreted with the caveat that they may be representative of the group of preterm and early term children who are well-functioning enough to participate in a longitudinal study and to complete standard cognitive and academic assessments.

The extant literature suggests that higher risk of cognitive and academic problems and educational problems persists up through early term births,[52,132] but we found a significant deficit for ECLS-B children born at early term only on the BSF-R Mental Scale when adjusting for chronological instead of corrected age. It is possible that this was driven by correcting for prematurity for all children born earlier than 40 weeks rather than the more common clinical practice of applying the correction if born earlier than 37 weeks. Further examination of the appropriate gestational age cut-off for applying a “prematurity” correction is needed in light of more recent findings of cognitive and academic deficits nearer to term.

It is also interesting to note that adjusting for corrected age for the kindergarten outcomes substantially attenuated estimated deficits for preterm children. This may suggest—in line with several recent studies[133–135]—that correction for prematurity may be warranted beyond two or three years of age, an issue that remains under debate. Use of a prematurity correction relies on an assumption that developmental outcomes of preterm children temporarily lag behind full-term children due to their early delivery and therefore shorter time since conception for central nervous system maturation. Clinical recommendations to correct for prematurity through two or three years old are based on the notion that preterm children are expected to eventually catch up with their term peers as the pace of developmental growth slows. The use of chronological age is supported by the rationale that environmental factors such as the home environment, medical care, and parent-child interactions also play an important role in post-birth development.[136] In practical terms, chronological age may be used in screening for early intervention services and becomes even more relevant as children enter school based on their birth date. A recent survey of pediatric health care providers in a primary care network in Pennsylvania, New Jersey, and Delaware, showed that chronological age was used in developmental surveillance in 71% of visits for children born <32 weeks[137] suggesting the importance of understanding potential differences in observed outcomes when using corrected versus chronological age.

A few additional limitations should be mentioned. Our analyses used the clinical estimate of gestational age due to measurement concerns related to using LMP dating[138] and therefore excluded California births; results were similar, however, when analyses were repeated using gestational age based on LMP dating. Measurement error in gestational age reported on the birth certificate is possible and may potentially vary with factors such as socioeconomic status and timing of entry into prenatal care. Further, the analytic sample dropped by about 30% between Wave 2 and the kindergarten waves raising concerns about potential selection bias. There was little change in our findings when IPCW weights were applied to account for differential probabilities of loss to follow up. Longitudinal trajectories of cognitive and academic scores were not studied because the BSF-R Mental Scale used at age 2 years and the ECLS-B kindergarten reading and mathematics were not designed to be comparable assessments.

A large body of literature demonstrates that preterm and early term children are at higher risk of cognitive deficits and worsened academic outcomes in childhood. This study contributes to that literature by estimating the relative performance of children at all gestational ages in a population-based birth cohort using multiple approaches to modeling gestational age, providing a more rigorous understanding of the relationships between the full spectrum of gestational age and cognitive and academic outcomes in early childhood and at school age.

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Table 4.1. Characteristics of the analytic cohorts.

	2-year cognitive scores				Kindergarten scores					
			BSF-R Mental Scale				Reading		Mathematics	
	N	(%)	Mean	SD	N	(%)	Mean	SD	Mean	SD
Total	6,150		126.1	11.0	4,450		44.4	14.8	43.9	10.5
Gestational age (weeks)										
24	50	(0.4)	113.5	10.1	*	(0.4)	38.2	13.4	35.2	11.3
25	50	(0.5)	110.9	11.6	*	(0.5)	40.9	16.8	37.6	11.5
26	50	(0.8)	115.7	8.4	50	(0.8)	37.7	13.6	35.4	10.8
27	100	(1.4)	114.4	9.5	50	(1.3)	42.4	15.3	41.1	9.8
28	100	(1.5)	117.5	10.2	50	(1.5)	40.9	13.7	39.9	9.2
29	100	(1.2)	118.5	10.2	50	(1.4)	38.0	13.5	38.1	9.2
30	100	(1.4)	119.0	10.6	50	(1.3)	41.7	16.2	39.9	11.7
31	50	(1.1)	122.9	8.6	50	(1.1)	44.1	13.1	41.6	10.1
32	50	(0.9)	120.3	11.2	50	(0.8)	42.3	13.2	40.6	10.9
33	100	(1.2)	121.2	9.5	50	(1.3)	44.4	14.4	43.7	9.6
34	100	(1.8)	121.0	9.9	50	(1.5)	42.9	14.2	42.4	10.5
35	150	(2.1)	125.4	11.9	100	(1.9)	42.5	14.9	41.7	10.1
36	250	(4.1)	124.5	9.7	150	(3.8)	42.0	14.4	42.3	10.6
37	450	(7.6)	125.5	11.7	350	(7.7)	44.1	14.7	43.9	10.5
38	1,000	(16.2)	126.6	10.4	750	(16.6)	44.3	15.0	44.1	10.7
39	1,450	(23.7)	127.4	10.6	1,050	(23.9)	45.1	14.9	44.8	10.3
40	1,550	(25.2)	128.2	10.5	1,150	(25.7)	45.9	14.8	44.9	10.2
41	500	(7.7)	128.0	10.3	350	(7.7)	44.0	14.6	44.5	10.7
42	50	(0.9)	127.3	9.5	50	(0.8)	45.5	15.2	45.4	8.8)
Child's race/ethnicity										
Black or African American, non-Hispanic	1,100	(17.8)	123.0	10.5	800	(18.5)	41.3	14.2	40.2	9.9
Hispanic	1,050	(17.4)	122.6	10.5	800	(17.6)	39.9	14.2	40.6	9.7
Asian	550	(9.1)	126.4	11.6	450	(10.6)	54.0	16.3	50.3	10.3

Native Hawaiian or other Pacific Islander	50	(0.5)	121.9	10.3	*	(0.3)	35.9	9.8	36.5	6.9
American Indian or Alaska Native	200	(2.9)	124.9	9.1	150	(3.6)	38.7	12.9	39.9	9.7
More than 1 race, non-Hispanic	550	(8.8)	127.2	10.7	400	(9.2)	45.3	14.8	45.3	10.7
White, non-Hispanic	2,650	(43.3)	128.6	10.7	1,750	(40.0)	45.7	13.8	45.6	9.9
Missing	*	(0.2)			*	(0.3)				
Assessment age (months), mean (SD)	24.5	(1.3)			68.3	(4.2)				
Corrected assessment age (months), mean (SD)	23.9	(1.6)			67.8	(4.3)				
Child's sex										
Female	3,000	(48.8)	127.9	10.6	2,200	(49.4)	45.5	14.2	44.2	10.0
Male	3,150	(51.2)	124.3	11.0	2,250	(50.6)	43.3	15.3	43.7	10.9
Maternal age at birth (years)										
15-17	250	(4.3)	123.7	10.1	200	(3.9)	37.4	12.6	38.3	9.4
18-19	500	(8.5)	123.9	10.1	350	(8.1)	38.6	13.8	39.8	10.0
20-24	1,650	(26.7)	125.0	10.3	1,150	(26.1)	41.9	14.2	41.8	10.2
25-29	1,500	(24.3)	126.6	11.1	1,100	(24.4)	45.4	14.6	44.6	10.2
30-34	1,400	(22.6)	127.5	11.6	1,050	(23.7)	47.6	15.2	46.5	10.3
35-39	700	(11.1)	127.0	11.1	500	(11.2)	47.7	14.6	46.5	10.6
≥40	150	(2.6)	127.1	11.9	100	(2.6)	46.8	13.4	46.7	9.3
Parity										
Nulliparous	2,550	(41.6)	126.5	11.2	1,850	(42.3)	45.7	15.1	44.3	10.5
1-2 previous live births	2,950	(48.3)	126.4	10.8	2,150	(48.0)	44.5	14.5	44.3	10.3
3+ previous live births	600	(9.7)	123.1	10.5	400	(9.4)	38.4	14.5	40.3	10.8
Missing	50	(0.4)			*	(0.3)				
Maternal education										
Less than high school	1,150	(18.6)	122.6	9.9	800	(17.7)	36.4	13.5	38.0	10.1
Completed high school	1,900	(31.2)	124.5	10.7	1,350	(30.5)	41.1	13.6	41.4	9.7
Some college	1,500	(24.6)	126.5	10.9	1,100	(24.6)	44.9	13.4	44.6	9.6
Bachelor's degree or higher	1,550	(25.5)	130.2	10.9	1,200	(27.1)	53.0	14.0	50.1	8.9
Missing	*	(0.1)			*	(0.1)				

Household poverty at 9 months										
<130% of federal poverty level	2,250	(36.8)	123.2	10.3						
130 to <185% of federal poverty level	800	(12.7)	124.8	10.8						
≥185% of federal poverty level	3,100	(50.4)	128.5	10.9						
Household poverty at 2 years										
<130% of federal poverty level					1,500	(33.9)	38.6	14.0	39.5	10.4
130 to <185% of federal poverty level					550	(12.4)	41.7	13.3	42.5	9.3
≥185% of federal poverty level					2,400	(53.7)	48.7	14.3	47.1	9.7

NOTE: Unweighted sample sizes are rounded to the nearest 50 per National Center for Education Statistics guidelines. Frequencies denoted * round to zero. SD = standard deviation.

Table 4.2. Association between gestational age and Bayley Short Form-Research Edition (BSF-R) Mental Scale score at 2 years old.

Gestational age	Adjusted for corrected age	Fully adjusted*
	β (95% CI)	β (95% CI)
Categorical (1-week categories)		
24	-7.9 (-11.9, -4.0)	-5.8 (-9.6, -2.1)
25	-10.5 (-14.0, -7.0)	-8.8 (-11.9, -5.7)
26	-6.9 (-9.0, -4.8)	-5.4 (-7.5, -3.2)
27	-8.4 (-10.3, -6.4)	-7.1 (-8.9, -5.3)
28	-5.2 (-7.2, -3.2)	-3.8 (-5.7, -1.8)
29	-5.2 (-7.6, -2.8)	-4.0 (-6.1, -1.8)
30	-4.9 (-7.3, -2.6)	-3.8 (-5.8, -1.8)
31	-1.7 (-3.5, 0.1)	-0.6 (-2.5, 1.2)
32	-4.5 (-7.6, -1.4)	-3.4 (-6.6, -0.2)
33	-3.7 (-5.9, -1.5)	-2.8 (-4.9, -0.6)
34	-4.5 (-6.5, -2.6)	-3.6 (-5.4, -1.9)
35	-0.6 (-2.7, 1.4)	-0.3 (-2.3, 1.6)
36	-2.0 (-3.4, -0.6)	-1.1 (-2.5, 0.2)
37	-1.3 (-2.4, -0.2)	-0.8 (-1.9, 0.2)
38	-0.5 (-1.3, 0.3)	-0.1 (-0.8, 0.7)
39	-0.4 (-1.0, 0.2)	-0.3 (-0.9, 0.4)
40	0.0 (Reference)	0.0 (Reference)
41	-0.1 (-1.3, 1.0)	0.0 (-1.0, 1.0)
42	-1.2 (-3.7, 1.2)	-0.2 (-2.4, 2.0)
ACOG categories		
Early preterm (22-27 weeks)	-8.0 (-9.5, -6.4)	-6.6 (-8.1, -5.0)
Moderate preterm (28-33 weeks)	-4.0 (-5.1, -2.9)	-2.9 (-4.0, -1.8)
Late preterm (34-36 weeks)	-2.0 (-3.0, -0.9)	-1.3 (-2.3, -0.4)
Early term (37-38 weeks)	-0.5 (-1.2, 0.1)	-0.2 (-0.8, 0.4)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	0.0 (-1.0, 1.1)	0.1 (-0.9, 1.1)
Post term (42 weeks)	-1.1 (-3.5, 1.4)	-0.1 (-2.2, 2.0)
Continuous: Linear model		
1 week increase in GA	0.5 (0.4, 0.6)	0.4 (0.3, 0.5)
Continuous: Quadratic model		
1 week increase in GA	1.9 (0.7, 3.1)	1.8 (0.7, 3.0)
Squared term	-0.02 (-0.04, 0.00)	-0.02 (-0.04, 0.00)

n = 6,150. Mean (SD) score on the BSF-R Mental Scale was 126.1 (11.0). β estimates change in BSF-R Mental Scale score. *Adjusted for child’s corrected age at assessment, child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Table 4.3. Association between gestational age and kindergarten reading scale score.

Gestational age	Adjusted for chronological age	Fully adjusted*
	β (95% CI)	β (95% CI)
Categorical (1-week categories)		
24	-9.8 (-15.6, -4.0)	-7.5 (-13.7, -1.3)
25	-7.2 (-11.8, -2.5)	-7.8 (-12.4, -3.2)
26	-9.5 (-13.4, -5.7)	-7.0 (-10.0, -4.0)
27	-4.6 (-8.1, -1.1)	-3.2 (-6.6, 0.1)
28	-6.4 (-9.2, -3.5)	-4.4 (-6.9, -1.8)
29	-8.9 (-12.2, -5.6)	-7.3 (-10.0, -4.5)
30	-4.7 (-8.0, -1.4)	-2.6 (-5.7, 0.5)
31	-2.3 (-6.2, 1.5)	-1.7 (-5.2, 1.9)
32	-4.9 (-9.0, -0.7)	-3.4 (-6.8, 0.1)
33	-2.2 (-5.7, 1.3)	-0.8 (-3.9, 2.4)
34	-3.1 (-6.1, -0.1)	-1.5 (-4.3, 1.3)
35	-4.0 (-6.8, -1.2)	-2.8 (-5.5, -0.2)
36	-4.2 (-6.5, -2.0)	-2.3 (-4.1, -0.5)
37	-1.5 (-3.1, 0.1)	-1.4 (-2.8, 0.0)
38	-1.2 (-2.6, 0.2)	-0.8 (-2.0, 0.3)
39	-1.1 (-2.3, 0.0)	-0.9 (-2.0, 0.1)
40	0.0 (Reference)	0.0 (Reference)
41	-0.6 (-2.5, 1.2)	-0.2 (-1.7, 1.3)
42	0.0 (-4.7, 4.8)	0.9 (-3.3, 5.2)
ACOG categories		
Early preterm (22-27 weeks)	-6.5 (-8.8, -4.3)	-5.1 (-7.2, -3.0)
Moderate preterm (28-33 weeks)	-4.5 (-5.9, -3.1)	-3.0 (-4.3, -1.8)
Late preterm (34-36 weeks)	-3.4 (-5.0, -1.8)	-1.8 (-3.2, -0.4)
Early term (37-38 weeks)	-0.8 (-1.9, 0.3)	-0.5 (-1.5, 0.4)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	-0.1 (-1.9, 1.7)	0.2 (-1.2, 1.7)
Post term (42 weeks)	0.6 (-4.2, 5.4)	1.4 (-2.9, 5.6)
Continuous: Linear model		
1 week increase in GA	0.5 (0.4, 0.6)	0.4 (0.3, 0.5)
Continuous: Quadratic model		
1 week increase in GA	0.6 (-1.3, 2.6)	0.8 (-0.8, 2.4)
Squared term	0.00 (-0.03, 0.03)	-0.01 (-0.03, 0.02)

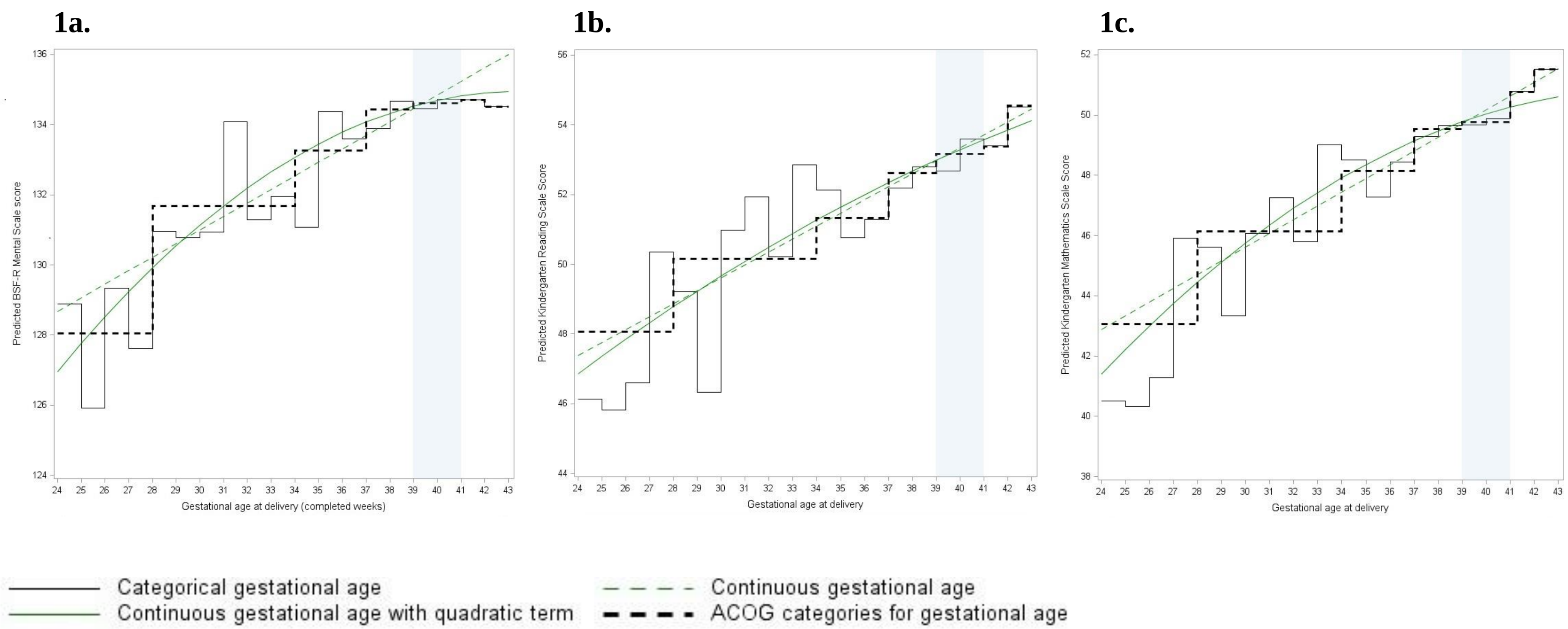
n = 4,450. Mean (SD) scale score on kindergarten reading assessment was 44.4 (14.8). β estimates change in kindergarten reading scale score. *Adjusted for child's chronological age at assessment, child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Table 4.4. Association between gestational age and kindergarten mathematics scale score.

Gestational age	Adjusted for chronological age β (95% CI)	Fully adjusted* β (95% CI)
Categorical (1-week categories)		
24	-10.8 (-16.0, -5.7)	-9.4 (-14.9, -3.8)
25	-9.4 (-13.2, -5.7)	-9.5 (-13.8, -5.3)
26	-10.1 (-13.3, -6.9)	-8.6 (-11.4, -5.8)
27	-4.8 (-7.2, -2.5)	-4.0 (-6.4, -1.6)
28	-5.9 (-8.0, -3.9)	-4.3 (-6.3, -2.3)
29	-7.7 (-9.8, -5.6)	-6.5 (-8.6, -4.5)
30	-5.2 (-7.8, -2.6)	-3.8 (-6.2, -1.4)
31	-3.5 (-6.3, -0.6)	-2.6 (-5.2, 0.0)
32	-5.1 (-8.4, -1.7)	-4.1 (-6.9, -1.2)
33	-1.9 (-4.3, 0.5)	-0.9 (-2.9, 1.2)
34	-2.7 (-4.9, -0.4)	-1.4 (-3.6, 0.8)
35	-3.4 (-5.4, -1.3)	-2.6 (-4.5, -0.7)
36	-2.7 (-4.2, -1.2)	-1.4 (-2.7, -0.1)
37	-0.7 (-1.8, 0.4)	-0.6 (-1.6, 0.4)
38	-0.5 (-1.3, 0.4)	-0.2 (-1.0, 0.5)
39	-0.3 (-1.0, 0.5)	-0.2 (-0.9, 0.4)
40	0.0 (Reference)	0.0 (Reference)
41	0.5 (-0.8, 1.9)	0.9 (-0.2, 2.0)
42	1.1 (-1.7, 3.9)	1.6 (-0.9, 4.2)
ACOG categories		
Early preterm (22-27 weeks)	-7.7 (-9.5, -5.9)	-6.7 (-8.5, -4.9)
Moderate preterm (28-33 weeks)	-4.8 (-5.8, -3.8)	-3.6 (-4.6, -2.7)
Late preterm (34-36 weeks)	-2.8 (-3.9, -1.6)	-1.6 (-2.6, -0.6)
Early term (37-38 weeks)	-0.4 (-1.1, 0.3)	-0.2 (-0.9, 0.4)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	0.6 (-0.6, 1.9)	1.0 (0.0, 2.1)
Post term (42 weeks)	1.3 (-1.5, 4.0)	1.8 (-0.8, 4.3)
Continuous: Linear model		
1 week increase in GA	0.6 (0.5, 0.6)	0.5 (0.4, 0.5)
Continuous: Quadratic model		
1 week increase in GA	1.7 (0.3, 3.1)	1.7 (0.5, 3.0)
Squared term	-0.02 (-0.04, 0.00)	-0.02 (-0.04, 0.00)

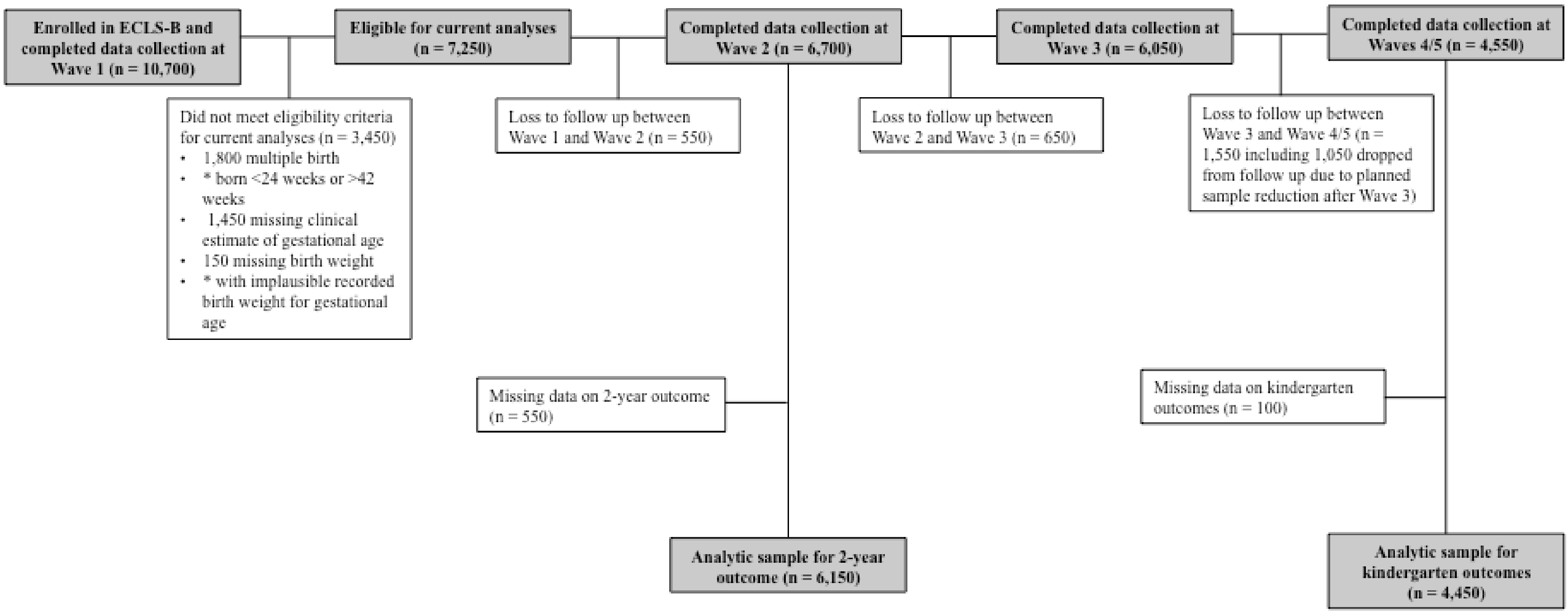
n = 4,450. Mean (SD) scale score on kindergarten mathematics assessment was 43.9 (10.5). β estimates change in kindergarten mathematics scale score. *Adjusted for child's chronological age at assessment, child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Figure 4.1. (a–c) Model-predicted Bayley Short Form-Research Edition (BSF-R) Mental Scale scores at age 2 years (a), kindergarten reading scale scores (b), and kindergarten mathematics scale scores (c), by gestational age.



Predicted scores are for a hypothetical individual at covariate reference values (child race/ethnicity = non-Hispanic white, maternal education = bachelor's degree or higher, household poverty = ≥185 percent of federal poverty level, child's gender = female, parity = nulliparous, maternal age at birth = 25–29 years) taking each assessment at the median age of testing (corrected 24 months for 2-year outcome, 68 months for kindergarten outcomes). Shaded region of figure denotes full term referent group (39–40 weeks).

Supplemental Figure 4.1. Definition of analytic cohorts.



Unweighted sample sizes are rounded to the nearest 50. Frequencies denoted * round to zero.

Supplemental Table 4.1. Association between gestational age and Bayley Short Form-Research Edition (BSF-R) Mental Scale score at 2 years old, adjusting for chronological age.

Gestational age	Adjusted for chronological age	Fully adjusted*
	β (95% CI)	β (95% CI)
Categorical (1-week categories)		
24	-14.6 (-18.4, -10.9)	-13.2 (-16.8, -9.6)
25	-16.9 (-20.4, -13.4)	-15.8 (-18.9, -12.7)
26	-12.7 (-14.6, -10.8)	-11.8 (-13.7, -9.8)
27	-13.8 (-15.7, -12.0)	-13.1 (-14.8, -11.4)
28	-10.3 (-12.2, -8.3)	-9.3 (-11.2, -7.5)
29	-9.8 (-12.0, -7.5)	-8.9 (-10.9, -7.0)
30	-9.1 (-11.3, -6.9)	-8.4 (-10.2, -6.5)
31	-5.6 (-7.3, -3.8)	-4.8 (-6.6, -3.0)
32	-7.8 (-10.9, -4.6)	-7.0 (-10.2, -3.8)
33	-6.6 (-8.7, -4.5)	-6.0 (-8.1, -3.9)
34	-7.1 (-9.0, -5.2)	-6.4 (-8.1, -4.7)
35	-2.8 (-4.8, -0.8)	-2.7 (-4.6, -0.9)
36	-3.6 (-5.0, -2.3)	-2.9 (-4.2, -1.6)
37	-2.6 (-3.7, -1.5)	-2.2 (-3.3, -1.2)
38	-1.4 (-2.2, -0.6)	-1.1 (-1.8, -0.3)
39	-0.8 (-1.4, -0.1)	-0.7 (-1.3, 0.0)
40	0.0 (Reference)	0.0 (Reference)
41	-0.1 (-1.3, 1.0)	0.0 (-1.0, 1.0)
42	-1.2 (-3.7, 1.2)	-0.2 (-2.4, 2.0)
ACOG categories		
Early preterm (22-27 weeks)	-13.8 (-15.1, -12.4)	-12.9 (-14.2, -11.5)
Moderate preterm (28-33 weeks)	-8.0 (-8.9, -7.0)	-7.2 (-8.2, -6.3)
Late preterm (34-36 weeks)	-3.8 (-4.8, -2.8)	-3.3 (-4.2, -2.5)
Early term (37-38 weeks)	-1.4 (-2.0, -0.8)	-1.1 (-1.7, -0.5)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	0.2 (-0.9, 1.3)	0.3 (-0.7, 1.3)
Post term (42 weeks)	-0.9 (-3.3, 1.5)	0.1 (-2.0, 2.2)
Continuous: Linear model		
1 week increase in GA	0.9 (0.8, 1.0)	0.8 (0.8, 0.9)
Continuous: Quadratic model		
1 week increase in GA	2.6 (1.4, 3.8)	2.6 (1.4, 3.7)
Squared term	-0.02 (-0.04, -0.01)	-0.03 (-0.04, -0.01)

N = 6,150. Mean (SD) score on the BSF-R Mental Scale was 126.1 (11.0). β estimates change in BSF-R Mental Scale score.
* Adjusted for child's chronological age at assessment, child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Supplemental Table 4.2. Association between gestational age and kindergarten reading scale score, adjusting for corrected age.

Gestational age	Adjusted for corrected age	Fully adjusted*
	β (95% CI)	β (95% CI)
Categorical (1-week categories)		
24	-6.3 (-12.2, -0.5)	-3.8 (-10.0, 2.5)
25	-3.9 (-8.5, 0.8)	-4.3 (-8.9, 0.3)
26	-6.5 (-10.4, -2.6)	-3.8 (-6.8, -0.8)
27	-1.7 (-5.2, 1.8)	-0.3 (-3.6, 3.1)
28	-3.7 (-6.6, -0.8)	-1.6 (-4.2, 1.0)
29	-6.5 (-9.8, -3.2)	-4.8 (-7.5, -2.0)
30	-2.5 (-5.9, 0.8)	-0.3 (-3.4, 2.7)
31	-0.3 (-4.2, 3.5)	0.4 (-3.1, 4.0)
32	-3.2 (-7.3, 1.0)	-1.6 (-5.0, 1.9)
33	-0.7 (-4.3, 2.8)	0.8 (-2.3, 4.0)
34	-1.8 (-4.8, 1.2)	-0.1 (-2.9, 2.7)
35	-2.9 (-5.7, 0.0)	-1.7 (-4.3, 1.0)
36	-3.4 (-5.6, -1.1)	-1.4 (-3.2, 0.4)
37	-0.9 (-2.5, 0.7)	-0.7 (-2.1, 0.7)
38	-0.8 (-2.2, 0.6)	-0.3 (-1.5, 0.8)
39	-0.9 (-2.1, 0.2)	-0.7 (-1.8, 0.3)
40	0.0 (Reference)	0.0 (Reference)
41	-0.6 (-2.5, 1.2)	-0.2 (-1.7, 1.3)
42	0.0 (-4.7, 4.8)	0.9 (-3.3, 5.2)
ACOG categories		
Early preterm (22-27 weeks)	-3.6 (-5.8, -1.3)	-2.0 (-4.1, 0.1)
Moderate preterm (28-33 weeks)	-2.5 (-4.0, -1.0)	-0.9 (-2.1, 0.4)
Late preterm (34-36 weeks)	-2.5 (-4.1, -0.8)	-0.8 (-2.3, 0.6)
Early term (37-38 weeks)	-0.3 (-1.5, 0.8)	-0.1 (-1.0, 0.9)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	-0.2 (-1.9, 1.6)	0.1 (-1.3, 1.6)
Post term (42 weeks)	0.5 (-4.3, 5.3)	1.3 (-3.0, 5.5)
Continuous: Linear model		
1 week increase in GA	0.3 (0.2, 0.4)	0.1 (0.0, 0.2)
Continuous: Quadratic model		
1 week increase in GA	0.3 (-1.6, 2.2)	0.5 (-1.2, 2.1)
Squared term	0.00 (-0.03, 0.03)	0.0 (-0.03, 0.02)

N = 4,450. Mean (SD) scale score on kindergarten reading assessment was 44.4 (14.8).
β estimates change in kindergarten reading scale score.
* Adjusted for child's corrected age at assessment, child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Supplemental Table 4.3. Association between gestational age and kindergarten mathematics scale score, adjusting for corrected age.

Gestational age	Adjusted for corrected age β (95% CI)	Fully adjusted* β (95% CI)
Categorical (1-week categories)		
24	-8.2 (-13.4, -3.0)	-6.6 (-12.2, -1.1)
25	-6.9 (-10.7, -3.1)	-7.0 (-11.2, -2.7)
26	-7.8 (-11.1, -4.5)	-6.2 (-9.0, -3.4)
27	-2.7 (-5.1, -0.3)	-1.8 (-4.2, 0.7)
28	-3.9 (-6.0, -1.9)	-2.2 (-4.2, -0.2)
29	-5.9 (-8.0, -3.8)	4.7 (-6.7, -2.7)
30	-3.6 (-6.2, -1.0)	-2.1 (-4.5, 0.3)
31	-1.9 (-4.8, 0.9)	-1.1 (-3.7, 1.5)
32	-3.8 (-7.1, -0.4)	-2.7 (-5.6, 0.1)
33	-0.7 (-3.1, 1.7)	0.3 (-1.7, 2.4)
34	-1.6 (-3.9, 0.6)	-0.3 (-2.5, 1.9)
35	-2.5 (-4.6, -0.4)	-1.7 (-3.6, 0.2)
36	-2.1 (-3.6, -0.6)	-0.8 (-2.0, 0.5)
37	-0.2 (-1.3, 0.9)	-0.1 (-1.1, 0.9)
38	-0.1 (-1.0, 0.8)	0.1 (-0.6, 0.9)
39	-0.1 (-0.8, 0.6)	-0.1 (-0.7, 0.6)
40	0.0 (Reference)	0.0 (Reference)
41	0.5 (-0.8, 1.9)	0.9 (-0.2, 2.0)
42	1.1 (-1.7, 3.9)	1.6 (-0.9, 4.2)
ACOG categories		
Early preterm (22-27 weeks)	-5.5 (-7.3, -3.6)	-4.4 (-6.2, -2.6)
Moderate preterm (28-33 weeks)	-3.3 (-4.3, -2.2)	-2.0 (-3.0, -1.1)
Late preterm (34-36 weeks)	-2.0 (-3.2, -0.9)	-0.9 (-1.9, 0.1)
Early term (37-38 weeks)	-0.1 (-0.8, 0.7)	0.1 (-0.5, 0.7)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	0.6 (-0.7, 1.9)	0.9 (-0.1, 2.0)
Post term (42 weeks)	1.2 (-1.6, 3.9)	1.7 (-0.9, 4.2)
Continuous: Linear model		
1 week increase in GA	0.4 (0.3, 0.5)	0.3 (0.2, 0.4)
Continuous: Quadratic model		
1 week increase in GA	1.4 (0.1, 2.8)	1.5 (0.2, 2.7)
Squared term	-0.02 (-0.04, 0.01)	-0.02 (-0.04, 0.00)

N = 4,450. Mean (SD) scale score on kindergarten mathematics assessment was 43.9 (10.5). β estimates change in kindergarten mathematics scale score.
* Adjusted for child's corrected age at assessment, child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Supplemental Table 4.4. Association between gestational age and Bayley Short Form-Research Edition (BSF-R) Mental Scale score at 2 years old, after multiple imputation of missing BSF-R scores.

Gestational age	Adjusted for corrected age	Fully adjusted*
	β (95% CI)	β (95% CI)
Categorical (1-week categories)		
24	-9.2 (-13.1, -5.3)	-7.2 (-10.9, -3.5)
25	-11.1 (-14.3, -7.8)	-9.4 (-12.5, -6.4)
26	-9.0 (-11.4, -6.6)	-7.3 (-9.7, -4.9)
27	-9.1 (-11.0, -7.1)	-8.2 (-10.0, -6.3)
28	-6.6 (-9.0, -4.2)	-5.2 (-7.6, -2.8)
29	-6.5 (-8.9, -4.2)	-5.5 (-7.7, -3.3)
30	-6.3 (-8.9, -3.7)	-5.4 (-7.6, -3.2)
31	-2.8 (-4.7, -0.9)	-1.6 (-3.4, 0.3)
32	-5.9 (-9.4, -2.4)	-4.6 (-8.1, -1.1)
33	-4.2 (-6.5, -1.9)	-3.5 (-5.7, -1.3)
34	-5.3 (-7.3, -3.3)	-4.3 (-6.0, -2.6)
35	-1.1 (-3.2, 1.0)	-1.0 (-3.0, 1.0)
36	-2.4 (-3.9, -0.9)	-1.5 (-2.9, 0.0)
37	-2.0 (-3.1, -1.0)	-1.7 (-2.7, -0.7)
38	-0.8 (-1.6, 0.1)	-0.4 (-1.2, 0.4)
39	-0.6 (-1.3, 0.1)	-0.4 (-1.1, 0.2)
40	0.0 (Reference)	0.0 (Reference)
41	0.0 (-1.2, 1.1)	0.0 (-1.1, 1.0)
42	-1.2 (-3.8, 1.4)	-0.1 (-2.6, 2.4)
ACOG categories		
Early preterm (22-27 weeks)	-9.1 (-10.5, -7.7)	-7.8 (-9.2, -6.3)
Moderate preterm (28-33 weeks)	-5.1 (-6.3, -3.9)	-4.1 (-5.3, -2.9)
Late preterm (34-36 weeks)	-2.3 (-3.4, -1.3)	-1.7 (-2.7, -0.7)
Early term (37-38 weeks)	-0.9 (-1.6, -0.2)	-0.6 (-1.2, 0.0)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	0.2 (-0.9, 1.4)	0.2 (-0.8, 1.2)
Post term (42 weeks)	-0.9 (-3.4, 1.6)	0.1 (-2.3, 2.5)
Continuous: Linear model		
1 week increase in GA	0.6 (0.5, 0.7)	0.5 (0.4, 0.6)
Continuous: Quadratic model		
1 week increase in GA	1.7 (0.5, 3.0)	1.6 (0.5, 2.8)
Squared term	-0.02 (-0.03, 0.00)	-0.02 (-0.03, 0.00)

N = 6,700. Mean (standard error of mean) score on the BSF-R Mental Scale across 5 imputed datasets was 126.0 (0.1). β estimates change in BSF-R Mental Scale score.
* Adjusted for child's corrected age at assessment, child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Supplemental Table 4.5. Association between gestational age and Bayley Short Form-Research Edition (BSF-R) Mental Scale score at 2 years old, after restricting to children who completed BSF-R assessment at 22-26 months corrected or chronological age.

Gestational age	**Adjusted for corrected age and covariates (N = 5,600)**	**Adjusted for chronological age and covariates (N = 5,900)**
	β (95% CI)	**β (95% CI)**
Categorical (1-week categories)		
24	-10.6 (-18.0, -3.2)	-13.2 (-17.0, -9.3)
25	-7.0 (-17.7, 3.8)	-16.8 (-19.8, -13.9)
26	-2.0 (-4.9, 0.9)	-11.8 (-13.8, -9.8)
27	-5.5 (-10.2, -0.8)	-13.2 (-14.8, -11.5)
28	-3.3 (-6.0, -0.6)	-9.9 (12.0, -7.7)
29	-3.9 (-6.6, -1.2)	-8.9 (-11.0, -6.9)
30	-3.1 (-6.0, -0.2)	-8.7 (-10.6, -6.8)
31	-0.5 (-3.1, 2.1)	-4.9 (-6.8, -3.0)
32	-3.3 (-6.7, 0.2)	-7.4 (-10.5, -4.3)
33	-2.0 (-4.4, 0.3)	-6.4 (-8.5, -4.3)
34	-3.7 (-5.6, -1.9)	-6.4 (-8.1, -4.6)
35	-0.4 (-2.3, 1.4)	-3.0 (-4.9, -1.1)
36	-0.9 (-2.3, 0.4)	-3.0 (-4.3, -1.7)
37	-0.7 (-1.8, 0.3)	-2.4 (-3.4, -1.3)
38	-0.1 (-0.8, 0.7)	-1.2 (-2.0, -0.5)
39	-0.3 (-1.0, 0.3)	-0.8 (-1.5, -0.2)
40	0.0 (Reference)	0.0 (Reference)
41	-0.2 (-1.2, 0.8)	-0.2 (-1.2, 0.9)
42	-0.3 (-2.5, 2.0)	-0.2 (-2.5, 2.0)
ACOG categories		
Early preterm (22-27 weeks)	-5.2 (-8.9, -1.5)	-13.0 (-14.3, -11.7)
Moderate preterm (28-33 weeks)	-2.4 (-3.6, -1.2)	-7.5 (-8.5, -6.4)
Late preterm (34-36 weeks)	-1.2 (-2.2, -0.3)	-3.4 (-4.3, -2.4)
Early term (37-38 weeks)	-0.1 (-0.7, 0.5)	-1.2 (-1.8, -0.6)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	-0.1 (-1.0, 0.9)	0.2 (-0.8, 1.2)
Post term (42 weeks)	-0.1 (-2.3, 2.0)	0.2 (-2.0, 2.3)
Continuous: Linear model		
1 week increase in GA	0.3 (0.2, 0.4)	0.9 (0.8, 0.9)
Continuous: Quadratic model		
1 week increase in GA	1.6 (0.0, 3.3)	2.5 (1.4, 3.7)
Squared term	-0.02 (-0.04, 0.00)	-0.02 (-0.04, -0.01)

Mean (SD) score on the BSF-R Mental Scale was 126.5 (10.6) in analyses adjusting for corrected age, and 125.8 (10.8) in analyses adjusted for chronological age. β estimates change in BSF-R Mental Scale score.

All models adjusted for child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Supplemental Table 4.6. Association between gestational age and kindergarten reading scale score, applying inverse probability of censoring weights to account for potential selection bias between wave 2 and kindergarten data waves.

Gestational age	Unadjusted	Adjusted*
	β (95% CI)	β (95% CI)
Categorical (1-week categories)		
24	-9.7 (-15.7, -3.7)	-6.8 (-13.1, -0.5)
25	-2.7 (-10.7, 5.4)	-3.2 (-10.4, 3.9)
26	-7.1 (-11.3, -2.9)	-5.2 (-8.6, -1.8)
27	-4.3 (-8.0, -0.5)	-2.7 (-6.3, 0.9)
28	-6.9 (-10.0, -3.8)	-4.6 (-7.3, -1.9)
29	-7.8 (-11.4, -4.2)	-6.3 (-9.5, -3.2)
30	-5.5 (-8.9, -2.0)	-3.3 (-6.4, -0.1)
31	-1.6 (-6.0, 2.7)	-1.0 (-5.0, 3.0)
32	-5.1 (-9.3, -1.0)	-2.8 (-6.0, 0.5)
33	-3.7 (-7.1, -0.3)	-1.4 (-4.5, 1.7)
34	-3.4 (-6.6, -0.1)	-1.8 (-5.0, 1.3)
35	-3.6 (-7.0, -0.1)	-1.9 (-5.2, 1.4)
36	-4.1 (-6.7, -1.6)	-2.2 (-4.2, -0.2)
37	-1.9 (-3.6, -0.2)	-1.7 (-3.3, -0.2)
38	-1.2 (-2.8, 0.3)	-0.8 (-2.0, 0.4)
39	-1.1 (-2.3, 0.1)	-0.8 (-1.9, 0.3)
40	0.0 (Reference)	0.0 (Reference)
41	-0.4 (-2.3, 1.6)	0.0 (-1.5, 1.6)
42	0.0 (-4.8, 4.8)	1.5 (-2.7, 5.6)
ACOG categories		
Early preterm (22-27 weeks)	-5.1 (-7.4, -2.7)	-3.6 (-5.9, -1.3)
Moderate preterm (28-33 weeks)	-4.7 (-6.2, -3.1)	-2.9 (-4.2, -1.6)
Late preterm (34-36 weeks)	-3.3 (-5.1, -1.4)	-1.6 (-3.2, -0.1)
Early term (37-38 weeks)	-0.9 (-2.1, 0.3)	-0.7 (-1.7, 0.3)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	0.2 (-1.7, 2.1)	0.4 (-1.1, 1.9)
Post term (42 weeks)	0.5 (-4.3, 5.4)	1.9 (-2.3, 6.1)
Continuous: Linear model		
1 week increase in GA	0.5 (0.3, 0.6)	0.3 (0.2, 0.4)
Continuous: Quadratic model		
1 week increase in GA	-0.3 (-2.3, 1.7)	-0.1 (-1.8, 1.6)
Squared term	0.01 (-0.02, 0.04)	0.01 (-0.02, 0.03)

N = 4,450. Weighted mean (SD) scale score on kindergarten reading assessment was 45.0 (15.8). β estimates change in kindergarten reading scale score.
* Adjusted for child's chronological age at assessment, child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Supplemental Table 4.7. Association between gestational age and kindergarten mathematics scale score, applying inverse probability of censoring weights to account for potential selection bias between wave 2 and kindergarten data waves.

Gestational age	Adjusted for chronological age	Fully adjusted*
	β (95% CI)	β (95% CI)
Categorical (1-week categories)		
24	-11.2 (-16.3, -6.1)	-9.5 (-14.9, -4.1)
25	-9.5 (-13.3, -5.7)	-9.5 (-13.5, -5.5)
26	-9.9 (-13.2, -6.7)	-8.3 (-11.1, -5.5)
27	-4.8 (-7.3, -2.4)	-3.8 (-6.2, -1.3)
28	-6.5 (-8.6, -4.4)	-4.7 (-6.8, -2.6)
29	-7.9 (-10.0, -5.9)	-6.6 (-8.6, -4.6)
30	-5.0 (-7.6, -2.4)	-3.5 (-5.9, -1.1)
31	-3.4 (-6.4, -0.4)	-2.6 (-5.3, 0.2)
32	-5.5 (-8.6, -2.3)	-4.1 (-6.8, -1.4)
33	-2.4 (-4.7, 0.0)	-1.1 (-3.2, 1.0)
34	-3.0 (-5.4, -0.7)	-1.8 (-4.0, 0.5)
35	-3.6 (-5.8, -1.5)	-2.7 (-4.7, -0.7)
36	-2.9 (-4.5, -1.3)	-1.6 (-2.9, -0.3)
37	-1.1 (-2.3, 0.1)	-1.0 (-2.1, 0.1)
38	-0.5 (-1.4, 0.4)	-0.3 (-1.1, 0.5)
39	-0.3 (-1.0, 0.5)	-0.2 (-0.9, 0.4)
40		0.0 (Reference)
41	0.6 (-0.8, 2.0)	1.0 (-0.2, 2.1)
42	0.9 (-1.8, 3.7)	1.7 (-0.8, 4.3)
ACOG categories		
Early preterm (22-27 weeks)	-7.7 (-9.4, -5.9)	-6.5 (-8.3, -4.8)
Moderate preterm (28-33 weeks)	-5.1 (-6.1, -4.0)	-3.7 (-4.7, -2.7)
Late preterm (34-36 weeks)	-3.0 (-4.2, -1.8)	-1.8 (-2.9, -0.8)
Early term (37-38 weeks)	-0.6 (-1.3, 0.2)	-0.4 (-1.1, 0.2)
Term (39-40 weeks)	0.0 (Reference)	0.0 (Reference)
Late term (41 weeks)	0.7 (-0.6, 2.1)	1.1 (0.0, 2.1)
Post term (42 weeks)	1.1 (-1.7, 3.8)	1.9 (-0.7, 4.4)
Continuous: Linear model		
1 week increase in GA	0.6 (0.5, 0.7)	0.5 (0.4, 0.5)
Continuous: Quadratic model		
1 week increase in GA	1.4 (0.0, 2.8)	1.3 (0.1, 2.6)
Squared term	-0.01 (-0.03, 0.01)	-0.01 (-0.03, 0.01)

N = 4,450. Weighted mean (SD) scale score on kindergarten reading assessment was 44.2 (10.9). β estimates change in kindergarten mathematics scale score.

* Adjusted for child's chronological age at assessment, child's race/ethnicity, child's sex, maternal age at birth, parity, maternal educational attainment, and household poverty.

Chapter 5: Does socioeconomic status modify the association between preterm birth and children's early cognitive ability and kindergarten academic achievement in the United States?

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Abstract

Preterm birth (PTB) and childhood poverty are each known to influence children's cognitive development and academic outcomes. Using data from 5,250 singleton children enrolled in the Early Childhood Longitudinal Study-Birth Cohort, we examined whether household socioeconomic status (SES) modified the association between PTB and children's scores on cognitive assessments at 2 years and reading and mathematics assessments at kindergarten age. Gestational age was categorized as early preterm, moderate preterm, late preterm, early term, and term. Household SES was measured at 9 months of age using a composite of parental education, occupation, and income. PTB was associated with 0.1-0.6 standard deviation (SD) deficits in both 2-year cognitive ability and kindergarten mathematics scores, and with 0.1-0.4 SD deficits in kindergarten reading scores. Children living in the lowest SES quintile compared with the highest SES quintile scored 0.6 SD lower on 2-year cognitive ability, 1.1 SD lower on kindergarten reading, and 0.9 SD lower on kindergarten mathematics. There was no evidence of additive interaction between PTB and household SES. The estimated joint effects of PTB and household SES did not depart from additivity in their influences on children's outcome scores; doubly exposed children performed at the lowest levels in the study population.

Introduction

Being born premature and growing up in poverty are each known to be associated with worse cognitive and academic outcomes in childhood.[18,61] Children's early cognitive ability and being ready to enter school are important predictors of their later social and academic achievement as well as life course socioeconomic and health trajectories into adulthood.[64,65] Both preterm birth and childhood poverty are prevalent in the United States, where about 10% of children are born preterm and half of children reside in low-income households.[3,17] These risk factors are likely to overlap since women of lower socioeconomic status (SES) are at higher risk of preterm birth.[5] There may be a higher than expected number of US children who experience the "double jeopardy" of both preterm birth and childhood poverty than would be predicted if the two exposures were independently distributed through the population, and it is important to understand the impacts of being doubly exposed.[139–141]

Studies of the cognitive and academic outcomes of preterm birth have often treated SES as a confounding factor due to its association with both preterm birth and these outcomes. There has been recent interest in whether SES acts instead as a modifier of the association between preterm birth and neurodevelopmental outcomes. Children's development is a transactional process wherein children grow and respond to stimuli in their environments, which in turn fosters further learning,[19] and therefore developmental trajectories may be influenced jointly by biological factors such as shortened gestation as well as early childhood socioenvironmental context.[79–81] Among preterm children, those raised in more advantaged environments have been found to have better developmental outcomes compared with those in more disadvantaged environments suggesting that SES may have a buffering effect against the adverse effects of preterm birth.[77,78] Several recent studies have assessed additive interaction between preterm birth and SES, most showing that experiencing lower SES in childhood exacerbates the effects of prematurity on academic outcomes at school entry[99] and in adolescence,[85,101] although another study found no evidence that parenting factors—as more proximal markers of SES—modified the effect of late preterm or early term birth on developmental outcomes in early childhood.[100] More research is required in light of these mixed findings as well as variation across these studies in terms of study populations, SES measures, and ages of and tests used for developmental or academic assessment.

In this study, we assessed whether household SES modifies the association between preterm birth and children's cognitive development at two years of age and reading and mathematics scores at kindergarten age in a population-based cohort of US children born in 2001. We hypothesized that there would be supra-additive interaction between earlier gestational age and lower SES such that deficits between preterm and term children would be larger in families with lower SES compared with families with higher SES.

Methods

The Early Childhood Longitudinal Study-Birth Cohort (ECLS-B) is a population-based longitudinal study that sampled children from the 2001 US birth cohort and followed them through kindergarten. Its design and data collection procedures have been described extensively.[108] More than 14,000 children were selected in a stratified, clustered sample of 2001 birth certificates with oversampling of twins, low birth weight, very low birth weight, and certain racial/ethnic groups. Data collection occurred at 9 months (Wave 1), 2 years (Wave 2), preschool age (Wave 3), and kindergarten age (Waves 4 and 5). Kindergarten data collection occurred in two waves in fall 2006 (Wave 4) and fall 2007 (Wave 5) in order to assess children at the time they entered kindergarten, which differed based on birth date. Some children were assessed in both waves if they repeated kindergarten; for our analyses, we used data from their first entry into kindergarten. Singletons born at 24-40 completed weeks and whose biological mother was the primary respondent at Wave 1 were eligible for our analyses. Children were excluded if they had congenital anomalies or chromosomal abnormalities reported on the birth certificate or by parental report at Wave 1 (list in eTable 1), had missing data on gestational age or birth weight, or if their reported birth weight was implausible for gestational age.[125]

Gestational age at delivery was measured using the clinical estimate of gestation reported on the birth certificate. Gestational age was categorized using categories defined by the American College of Obstetricians and Gynecologists (ACOG) for early preterm (24-27 weeks), moderate preterm (28-33 weeks), late preterm (34-36 weeks), early term (37-38 weeks), and full term (39-40 weeks).[11] Since California did not report clinical estimate of gestation on birth certificates in 2001, these births were excluded from the primary analyses.

Household SES was measured at Wave 1 using a composite index reflecting parental education, parental occupation, and household income that was created, standardized, and categorized into quintiles by ECLS-B study staff.[108] Since the impacts of childhood poverty may differ based on timing and duration of poverty,[76] we considered using multiple measurements of SES to define each child's exposure to poverty. However, SES measurements at 9 months, 2 years, and kindergarten were strongly consistent (Cronbach's alpha = 0.96) and therefore we used Wave 1 measurements as our primary measure.

Cognitive ability at 2 years was measured at Wave 2 with the Bayley Short Form-Research Edition (BSF-R) Mental Scale, an abbreviated version of the Bayley Scales of Infant Development-Second Edition (BSID-II) developed for the ECLS-B.[110] We analyzed children's scale scores reflecting the item response theory (IRT)-based estimate of raw score on the full BSID-II based on performance on the BSF-R Mental Scale; these scores had high reliability (reliability coefficient = 0.88).[127] BSID-II scores are typically normed to a distribution with mean of 100 and standard deviation of 15; however, the ECLS-B reported estimated raw scores on the BSF-R Mental Scale. To enable interpretation of results in terms of standard deviation differences between groups, we analyzed scores after standardizing to a normal distribution with mean of 0 and standard deviation of 1. We adjusted all 2-year outcome analyses for child's age at assessment. Since scale scores were not adjusted for prematurity, we corrected children's testing ages for the estimated number of weeks born before 40 weeks based on clinical estimate of gestational age (e.g., a child born at 36 weeks and tested at 24 months chronological age was assigned a corrected testing age of 23 months).

Reading and mathematics achievement at kindergarten age was measured at Waves 4 and 5 using ECLS-B-designed assessments of knowledge and skills in reading and mathematics.[108] The assessments were created using existing items from standardized instruments and assessment batteries for preschool- and kindergarten-aged children (e.g., Peabody Picture Vocabulary Test, PreLAS® 2000), as well as ECLS-B-developed items.[111] We analyzed scale scores reflecting the IRT-based estimate of the number of items that a child would have answered correctly if they had been asked all of the scored questions; these scores had high reliability coefficients (0.92 for Wave 4, 0.93 for Wave 5).[112] Again, to enable interpretation of results in terms of standard deviation differences between groups, we also analyzed scores after standardizing to a normal distribution with mean of 0 and standard deviation of 1. All kindergarten outcome analyses were adjusted for age at assessment. Age was not corrected for prematurity per clinical recommendations to correct for prematurity only through 2 years.[128]

Univariate frequencies and percentages of gestational age, household SES, and covariates were computed for the 2-year and kindergarten analytic cohorts. To describe the observed joint distribution of gestational and household SES, we computed mean scores and standard deviations for the 25 sub-groups of 5 gestational age categories and 5 household SES quintiles.

Multivariable analyses with generalized estimating equations (GEE) based on the normal distribution were used to estimate risk differences in scores for each outcome accounting for clustering of subjects by ECLS-B-designed sample clusters. Sampling weights were not applied in our main analyses because our primary interest was in obtaining internally valid estimates of the relationships between gestational age, household SES, and outcome scores among study participants rather than in ensuring that our findings were representative of 2001 U.S. births. First, main effects models estimated the mutually adjusted independent associations of gestational age and household SES with each outcome. The presence of additive interaction between gestational age and household SES was tested by adding interaction terms (e.g., early preterm x SES quintile 1) to these models, and testing the statistical significance of the set of interaction terms using the generalized score test statistic. Also, the presence of interaction was assessed by plotting model-predicted scores by gestational age and socioeconomic quintile at mean covariate values and by examining the estimated effects of preterm birth on each of the outcomes after stratifying by socioeconomic quintile. Crude models controlled only for children's age at assessment. Adjusted models also controlled for child's race/ethnicity, child's sex, parity, maternal marital status, and maternal age at delivery, all of which were measured from the birth certificate or Wave 1 parent reports. Finally, we assessed whether relationships between gestational age, household SES, and cognitive/academic outcomes differed by race/ethnicity by adding three-way interaction terms as well as stratifying by race/ethnicity.

We conducted several sensitivity analyses to assess the robustness of our findings. First, we repeated all analyses using gestational age based on reported date of last menstrual period (LMP); these analyses included California births. Second, Wave 2 measurements of SES were used for the kindergarten analyses. Third, we assessed the robustness of our results to our choice of SES measurement variables[142] by repeating 2-year and kindergarten analyses defining SES using maternal education (less than high school, completed high school, some college, bachelor's degree or higher), household income at Wave 1 (<$25,000, $25,000-$75,000, >$75,000), household poverty at Wave 1

(<130% of federal poverty level [FPL], 130-185% of FPL, >185% FPL), and using the SES composite index as a continuous variable. Fourth, we repeated the 2-year analyses without a prematurity correction. Fifth, we repeated the kindergarten analyses with a prematurity correction. Finally, we repeated all analyses using complex sample weights.

Analyses were conducted using SAS v9.3 (Cary, NC). The study was approved by the Emory Institutional Review Board. Unweighted frequencies are rounded to the nearest 50 per National Center for Education Statistics guidelines.

Results

The study sample included 5,250 children in 2-year outcome analyses and 3,800 in kindergarten outcome analyses (Supplemental Figure 5.1). Due to over-sampling of low birth weight children, 17-18% of the 2-year and kindergarten analytic samples were born preterm and another 26-27% were born at early term (Table 5.1). The mean score on the 2-year BSF-R Mental Score assessment was 126.2 (SD = 11.0); scores ranged from 92.4 to 174.1. The mean scores on kindergarten reading and mathematics achievement tests were 44.6 (SD = 14.9, range = 12.4 to 82.5) and 44.0 (SD = 10.5, range = 11.2 to 69.7), respectively (Table 5.2). Table 5.2 reports observed mean scores for all three outcomes stratified by gestational age and household SES. Earlier gestational age and lower household SES both resulted in lower mean scores on all assessments.

When mutually adjusted, there were significant deficits in BSF-R Mental Scale score for each of preterm birth and lower household SES (Table 5.3). In fully adjusted models, 0.1-0.6 standard deviation deficits were observed for children born at early preterm (-7.0, 95% CI: -8.6, -5.4), moderate preterm (-2.9, 95% CI: -4.1, -1.7), and late preterm (-1.3, 95% CI: -2.3, -0.3). Children in lower SES quintiles performed 0.2-0.6 standard deviations lower than those in the highest quintile. Estimated deficits for lower household SES compared with the highest SES quintile ranged from -2.5 points (95% CI: -3.5, -1.5) for the second highest quintile to -6.7 points (95% CI: -7.8, -5.6) for the lowest quintile. There was no statistical evidence of additive interaction between gestational age and household SES (p=0.47; Figure 5.1A). Stratifying by socioeconomic quintile, estimated risk differences for the preterm and early term groups compared with term children were similar across socioeconomic quintiles (Supplemental Table 5.2). When age at assessment was not corrected for prematurity, estimated deficits for the preterm groups were larger and the early term group also experienced a significant deficit in scores compared with the term group. Results were similar when using LMP to measure gestational age, using alternative SES measures, or applying complex sample weights. Three-way interaction with race/ethnicity was not statistically significant nor was the interaction between gestational age and household SES significant in any group in analyses stratified by race/ethnicity.

Preterm birth and lower household SES were each independently associated with lower kindergarten reading scale scores (Table 5.4). In fully adjusted models, 0.1-0.4 standard deviation deficits were observed for the early preterm (-5.3 points, 95%: -7.7, -3.0), moderate preterm (-2.6 points, 95% CI: -3.9, -1.3), and late preterm (-1.5, 95% CI: -3.0, 0.0) groups. Children in lower SES quintiles performed 0.3-0.9 standard deviations lower than those in the highest quintile. Estimated deficits for lower household SES compared with the highest SES quintile ranged from -5.1 points (95% CI: -6.5, -3.7) for the second highest quintile to -12.6 (95% CI: -14.4, -10.9) for the lowest quintile. The addition of interaction terms between gestational age groups and household SES was not statistically significant (p=0.82; Figure 5.1B). Qualitative examination of stratified results suggested that deficits for early preterm children worsened with lower SES quintile, and deficits for moderate preterm and late preterm were attenuated with lower SES quintile, although there was variation across the quintiles (Supplemental Table 5.2). The estimated effects of preterm birth were attenuated when age at assessment was corrected for prematurity; however, results were similar when using LMP to measure gestational age, using alternative SES measures, using the Wave 2 measurement of SES quintile instead of the Wave 1 measurement, and applying complex sample weights. Again, three-way interaction between gestational age, household SES, and race/ethnicity was not significant, and the main interaction between gestational age and household SES was not significant within any racial/ethnic stratum.

Preterm birth and lower household SES were also each independently associated with lower mathematics scale scores (Table 5.5). After adjusting for household SES and other covariates, 0.1-0.6 standard deviation deficits were observed for children born at early preterm (-6.6 points, 95% CI: -8.5, -4.7), moderate preterm (-3.2 points, 95% CI: -4.3, -2.1), and late preterm (-1.4 points, 95% CI: -2.5, -0.4). Children in the highest SES quintile performed 0.3-0.9 standard deviations lower than those in the highest quintile. The estimated deficits for lower household SES compared with the highest SES quintile ranged from -3.6 points (95% CI: -4.4, -2.7) for the second highest quintile to -9.1 points (95% CI: -10.2, -7.9) for the lowest quintile. There was no statistical evidence of additive interaction between gestational age and household SES (p=0.68; Figure 5.1C). Socioeconomic stratum-specific analyses indicated that deficits for early preterm worsened slightly with lower SES quintile and deficits for moderate preterm and late preterm were attenuated (Supplemental Table 5.2). Again, results were similar in sensitivity analyses using LMP to measure gestational age, using alternative SES measures including using the Wave 2 measurement of SES quintile, and applying complex sample weights, with the exception of correcting for prematurity which resulted in attenuated estimated deficits for the preterm groups. Three-way interaction with race/ethnicity was not significant and there was no significant interaction between gestational age and household SES in any racial/ethnic group in analyses stratified by race/ethnicity.

Discussion

Preterm birth and lower household SES were associated with substantial deficits in children's cognitive scores at 2 years of age, and in reading and mathematics achievement at kindergarten age. We found that household SES did not modify the estimated effects of preterm birth on cognitive outcomes. In the absence of statistical interaction, score deficits associated with being doubly exposed to both preterm birth and lower household SES were approximately equal to the sum of the estimated effects of their two separate exposures, and these children performed at the lowest levels on all three outcomes in this study.

This study adds to current mixed evidence on joint effects of preterm birth and childhood poverty on children's cognitive development and academic outcomes. While there has long been an interest in the joint or transactional effects of these factors on children's development, advanced epidemiologic methods for assessing additive interaction have only recently been applied in this area of research. Although one recent study in Canada found no additive interaction between parenting factors—used as a measure of proximal social processes related to SES—and developmental outcomes,[100] our findings contrast with those of studies in the United States[99] and Taiwan[85] that found that lower SES exacerbated the association between preterm birth and children's likelihood of failing their first grade standardized tests (United States) and performing worse on academic tests in adolescence (Taiwan). Our results may differ from previous studies due to the timing and nature of the outcome assessments used in ECLS-B; in-home assessments were used to measure early cognitive ability at 2 years and academic achievement in reading and mathematics skills around the time of entry into kindergarten. Measurement of SES exposure also differed; it is possible, in the case of the US study, that neighborhood-level deprivation was a marker not only of families' socioeconomic status but also community resources and school quality, which may also contribute to exacerbating the impacts of preterm birth on children's school-related outcomes. Our study sample may also differ in terms of access to early intervention and other support services and family- and home environment-related factors such as quality of infant attachment and maternal-child interactions and access to cognitively stimulating experiences.

Poverty profoundly impacts children's cognitive development, academic performance, and chances for adult socioeconomic success.[61,75] While it may be reassuring to find that being raised in a lower SES household did not exacerbate the association between the biological insult of preterm birth and worse cognitive and academic outcomes, the magnitude of the independent associations between poverty, preterm birth, and these outcomes should continue to focus concern on addressing these exposures. It may be possible that the impacts of poverty on children's cognitive and academic outcomes are so substantial that the additional influence of preterm birth may reach a bottom "threshold" in terms of affecting scores. In this study, the estimated disparities comparing the highest and lowest socioeconomic groups were larger than those comparing early preterm with term children. It is also important to note that from the Figures that term-born children in the lowest SES quintile have predicted scores lower than most preterm groups in the highest SES quintile for all three outcomes we studied. The observed impact of the dual insult of preterm birth and childhood poverty should be considered a call for targeting of educational resources and early interventions to these doubly exposed children.

Our study has several important strengths, including that it was conducted using a large, population-based sample of children born across the US and involved rigorous prospective measurements of children's cognitive development and potential for academic achievement at multiple time points. The use of data from a population-based cohort for examination of outcomes of preterm birth, however, comes with the caveat that it may underrepresent children who are more ill and unable or unwilling to participate in such a study. Our study is also strengthened by the fact that we were able to analyze the outcomes of the same group of children as they grew and developed through early childhood to kindergarten, although we were not able to analyze trajectories of cognitive growth due to non-congruity of the 2-year and kindergarten outcomes.

There are also some limitations. It is possible that our analyses suffer from structural confounding due to the intertwined distributions of lower SES and higher risk of preterm birth.[143] Violation of the positivity assumption that our study population contained exposed and unexposed participants at all combinations of exposures and confounders under study is plausible; even though there were participants in each "exposure" group after stratifying by gestational age category and household SES quintile, this assumption may not hold after further stratification by factors such as race/ethnicity and household composition. Further, although the overall sample size was large, there were sparse data in the early range of gestational age, especially for the purposes of detecting interaction with household SES or when stratifying by household SES. Insufficient power was even more likely to be a concern in analyses stratifying by race/ethnicity. Future studies using US data should continue to examine whether potential interaction between preterm birth and household SES varies by racial/ethnic group due to the known socioeconomic disparities across racial/ethnic groups. There was some drop-out from the eligible study population; out of 6,150 eligible children, 85% were included in 2-year analyses and 61% were included in kindergarten analyses. About half of those lost between the 2-year and kindergarten waves, however, were part of a planned reduction in sample size after the preschool wave that was carried out by reducing sampling rates within primary sampling units. Finally, California births were excluded from our primary analyses because gestational age was measured using the clinical estimate on birth certificates; however, sensitivity analyses using LMP-based gestational age and therefore inclusive of California births yielded similar findings.

In conclusion, preterm birth and lower SES were associated with substantial deficits in cognitive scores at 2 years and academic achievement scores at kindergarten age although there was no evidence of additive interaction between the two exposures. Given that these risk factors are prevalent among US children, and that early cognitive development and readiness to enter school are known predictors of later academic and socioeconomic status, continued research in this area is needed to better understand the independent and joint effects of preterm birth and childhood poverty on children's development.

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Table 5.1. Cohort characteristics.

	2-year cohort		Kindergarten cohort	
	n	**(%)**	**n**	**(%)**
Total	5,250	(100.0)	3,800	(100.0)
Gestational age				
Early preterm	150	(3.1)	100	(2.9)
Moderate preterm	350	(7.0)	250	(7.1)
Late preterm	450	(8.6)	300	(7.7)
Early term	1,400	(26.3)	1,000	(26.8)
Term	2,900	(55.0)	2,100	(55.5)
Socioeconomic index				
Quintile 1 (Lowest)	1,000	(18.6)	700	(17.9)
Quintile 2	1,050	(19.9)	750	(20.0)
Quintile 3	1,100	(20.7)	750	(20.1)
Quintile 4	1,050	(19.6)	750	(19.3)
Quintile 5 (highest)	1,100	(21.1)	850	(22.6)
Child's race/ethnicity				
Black or African American, non-Hispanic	950	(18.1)	700	(18.8)
Hispanic	900	(17.5)	650	(17.7)
Asian	500	(9.3)	400	(10.9)
Native Hawaiian or other Pacific Islander	*	(0.4)	*	(0.3)
American Indian or Alaska Native	150	(2.7)	100	(3.2)
More than 1 race, non-Hispanic	450	(8.7)	350	(9.0)
White, non-Hispanic	2,250	(43.2)	1,500	(39.8)
Missing	*	(0.2)	*	(0.3)
Child's age at assessment (months), mean (SD)				
Uncorrected	24.4	(1.2)	68.3	(4.2)
Corrected for prematurity	23.9	(1.4)	Not applicable	
Child's sex				
Female	2,550	(48.7)	1,850	(49.2)
Male	2,700	(51.3)	1,900	(50.8)
Maternal age at birth				
15-17 years	200	(4.1)	150	(3.8)
18-19 years	450	(8.3)	300	(7.8)
20-24 years	1,350	(26.1)	950	(25.5)
25-29 years	1,300	(24.5)	950	(24.7)
30-34 years	1,200	(23.2)	900	(24.2)
35-39 years	600	(11.2)	450	(11.4)
40 years and older	150	(2.6)	100	(2.7)
Parity				
Nulliparous	2,100	(40.3)	1,550	(40.9)
1-2 previous live births	2,600	(49.5)	1,850	(49.4)
3+ previous live births	500	(9.7)	350	(9.3)
Missing	*	(0.5)	*	(0.4)
Marital status				

Married	3,400	(65.0)	2,500	(65.7)
Never married	1,500	(28.6)	1,050	(28.0)
Divorced, widowed, or separated	350	(6.4)	250	(6.3)

Note: Unweighted sample sizes are rounded to the nearest 50 per National Center for Education Statistics guidelines. Frequencies denoted * round to zero. SD = standard deviation.

Table 5.2. Mean cognitive and academic achievement scores, stratified by gestational age and household socioeconomic status.

	Total		Socioeconomic index: Quintile 1 (lowest)		Quintile 2		Quintile 3		Quintile 4		Quintile 5 (highest)	
	n	**mean (SD)**	**n**	**mean (SD)**	**n**	**mean (SD)**	**n**	**mean (SD)**	**n**	**mean (SD)**	**n**	**mean (SD)**
2-year outcome												
BSF-R Mental Scale score												
Total	5,250	126.2 (11.0)	1,000	122.2 (9.8)	1,050	123.5 (9.9)	1,100	126.2 (10.8)	1,050	128.1 (11.4)	1,100	130.3 (10.7)
Term	2,900	127.9 (10.5)	500	123.9 (9.4)	550	124.8 (9.4)	600	128.0 (10.3)	600	130.2 (10.5)	700	131.2 (10.6)
Early term	1,400	126.4 (10.8)	250	122.8 (9.5)	250	124.8 (9.7)	300	125.4 (11.2)	300	127.6 (11.2)	300	130.7 (10.5)
Late preterm	450	124.0 (10.5)	100	120.6 (9.0)	100	122.1 (9.4)	100	124.7 (10.4)	100	126.7 (12.3)	50	128.4 (9.6)
Moderate preterm	350	120.0 (10.2)	100	117.7 (9.8)	100	118.8 (9.1)	50	122.7 (9.4)	50	119.1 (11.4)	50	123.6 (11.1)
Early preterm	150	113.9 (9.7)	50	111.0 (9.3)	50	110.3 (9.1)	50	115.7 (8.8)	50	115.1 (11.4)	*	118.2 (8.0)
Kindergarten outcomes												
Reading scale score												
Total	3,800	44.6 (14.9)	700	36.4 (13.7)	750	39.7 (13.1)	750	44.1 (13.5)	750	47.1 (13.3)	850	53.8 (14.1)
Term	2,100	45.6 (14.8)	350	36.8 (13.6)	400	40.0 (13.0)	400	44.9 (13.7)	400	47.9 (12.7)	550	54.5 (14.0)
Early term	1,000	44.4 (14.9)	200	36.9 (13.0)	200	39.7 (13.2)	200	42.7 (13.1)	200	47.2 (14.2)	250	53.4 (14.7)
Late preterm	300	42.4 (14.7)	100	36.7 (15.0)	50	38.7 (13.7)	50	44.3 (12.7)	50	44.6 (14.5)	50	52.6 (12.5)
Moderate preterm	250	42.1 (13.9)	50	34.4 (14.6)	50	40.5 (12.4)	50	45.1 (12.6)	50	45.0 (12.1)	50	49.4 (13.1)
Early preterm	100	39.9 (15.3)	*	30.5 (13.7)	*	32.7 (11.7)	50	41.7 (15.1)	50	42.7 (13.7)	*	52.3 (13.7)
Mathematics scale score												
Total	3,800	44.0 (10.5)	700	37.7 (9.9)	750	40.4 (9.8)	750	43.8 (9.2)	750	46.0 (9.2)	850	50.8 (9.0)
Term	2,100	45.0 (10.2)	350	38.2 (9.5)	400	41.0 (9.5)	400	44.3 (9.3)	400	47.0 (8.5)	550	51.4 (8.6)
Early term	1,000	44.1 (10.6)	200	38.6 (10.2)	200	40.6 (9.7)	200	43.1 (9.2)	200	46.1 (9.6)	250	51.0 (9.6)
Late preterm	300	42.2 (10.5)	100	37.6 (9.7)	50	38.9 (12.0)	50	44.1 (8.1)	50	45.1 (9.8)	50	48.9 (8.1)
Moderate preterm	250	40.9 (10.1)	50	35.1 (10.4)	50	39.7 (9.5)	50	43.5 (8.4)	50	42.3 (8.7)	50	46.7 (10.0)
Early preterm	100	38.1 (11.1)	*	31.3 (9.7)	*	33.3 (10.1)	50	41.1 (11.0)	50	38.2 (10.6)	*	45.8 (7.9)

Note: Unweighted sample sizes are rounded to the nearest 50 per National Center for Education Statistics guidelines. Frequencies denoted * round to zero. SD = standard deviation.

Table 5.3. Associations between gestational age at delivery, socioeconomic status, and Bayley Short Form-Research Edition Mental Scale score at two years old.

	BSF-R Mental Scale score (age 2 years)			
	Model 1[a]		Model 2[b]	
	β[c]	95% CI	β	95% CI
Gestational age				
Early preterm	-7.3	-8.8, -5.7	-7.0	-8.6, -5.4
Moderate preterm	-2.7	-3.8, -1.5	-2.9	-4.1, -1.7
Late preterm	-1.2	-2.2, -0.2	-1.3	-2.3, -0.3
Early term	-0.4	-1.0, 0.2	-0.2	-0.8, 0.4
Term	0.0	Reference	0.0	Reference
Socioeconomic status				
Quintile 1 (Lowest)	-8.3	-9.2, -7.3	-6.7	-7.8, -5.6
Quintile 2	-6.9	-7.8, -6.1	-6.0	-7.0, -5.1
Quintile 3	-4.3	-5.2, -3.4	-3.8	-4.8, -2.9
Quintile 4	-2.4	-3.4, -1.4	-2.5	-3.5, -1.5
Quintile 5 (Highest)	0.0	Reference	0.0	Reference

[a]Adjusted only for child's age at assessment. [b]Adjusted for child's age at assessment, child's race/ethnicity, child's sex, maternal age at delivery, parity, and maternal marital status. [c]Estimated beta reflects estimated difference in mean outcome score.

Table 5.4. Associations between gestational age at delivery, socioeconomic status, and kindergarten reading scale score.

	Reading scale score (kindergarten age)			
	Model 1[a]		Model 2[b]	
	β[c]	95% CI	β	95% CI
Gestational age				
Early preterm	-5.6	-7.9, -3.2	-5.3	-7.7, -3.0
Moderate preterm	-2.4	-3.8, -1.0	-2.6	-3.9, -1.3
Late preterm	-1.7	-3.3, -0.1	-1.5	-3.0, 0.0
Early term	-0.5	-1.5, 0.5	-0.5	-1.4, 0.5
Term	0.0	Reference	0.0	Reference
Socioeconomic status				
Quintile 1 (Lowest)	-16.8	-18.3, -15.2	-12.6	-14.4, -10.9
Quintile 2	-13.9	-15.3, -12.4	-10.5	-12.0, -8.9
Quintile 3	-9.2	-10.7, -7.8	-6.6	-8.0, -5.2
Quintile 4	-6.8	-8.2, -5.4	-5.1	-6.5, -3.7
Quintile 5 (Highest)	0.0	Reference	0.0	Reference

[a]Adjusted only for child's age at assessment. [b]Adjusted for child's age at assessment, child's race/ethnicity, child's sex, maternal age at delivery, parity, and maternal marital status. [c]Estimated beta reflects estimated difference in mean outcome score.

Table 5.5. Associations between gestational age at delivery, socioeconomic status, and kindergarten mathematics scale score.

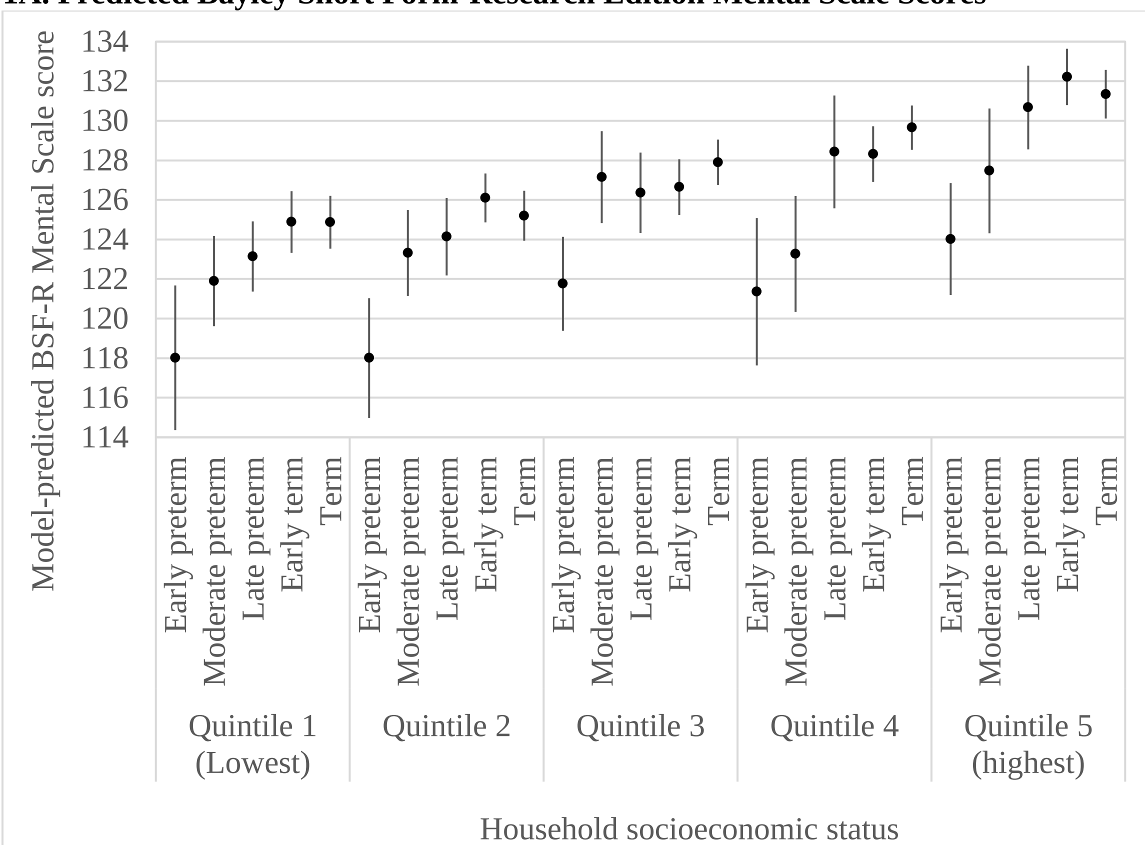
	Mathematics scale score (kindergarten age)			
	Model 1[a]		Model 2[b]	
	β[c]	**95% CI**	**β**	**95% CI**
Gestational age				
Early preterm	-6.8	-8.6, -4.9	-6.6	-8.5, -4.7
Moderate preterm	-3.2	-4.3, -2.1	-3.2	-4.3, -2.1
Late preterm	-1.6	-2.7, -0.5	-1.4	-2.5, -0.4
Early term	-0.2	-0.8, 0.4	-0.2	-0.8, 0.5
Term	0.0	Reference	0.0	Reference
Socioeconomic status				
Quintile 1 (Lowest)	-12.3	-13.3, -11.3	-9.1	-10.2, -7.9
Quintile 2	-10	-10.9, -9.1	-7.5	-8.4, -6.5
Quintile 3	-6.6	-7.6, -5.6	-4.5	-5.5, -3.6
Quintile 4	-4.8	-5.7, -3.9	-3.6	-4.4, -2.7
Quintile 5 (Highest)	0.0	Reference	0.0	Reference

[a]Adjusted only for child's age at assessment. [b]Adjusted for child's age at assessment, child's race/ethnicity, child's sex, maternal age at delivery, parity, and maternal marital status. [c]Estimated beta reflects estimated difference in mean outcome score.

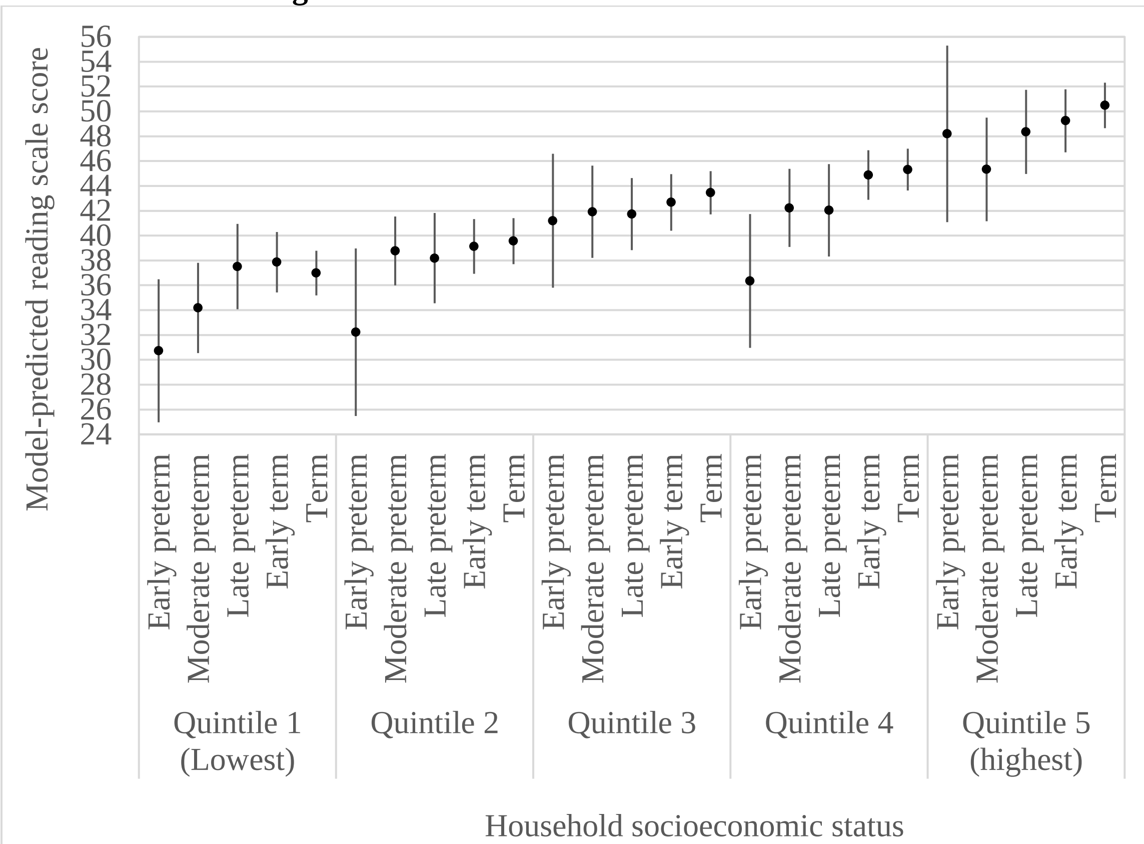
Figure 5.1. Model-predicted cognitive and academic achievement scores and 95% confidence intervals derived from models estimating interaction between gestational age and household socioeconomic status for 2-year Bayley Short Form-Research Edition Mental Scale scores (1A), kindergarten reading scale scores (1B), and kindergarten mathematics scale scores (1C).

Notes: All models adjusted for child’s age at assessment (corrected for prematurity for BSF-R Mental Scale), child’s race/ethnicity, child’s sex, maternal age at delivery, parity, and maternal marital status. Predicted scores are at mean covariate values.

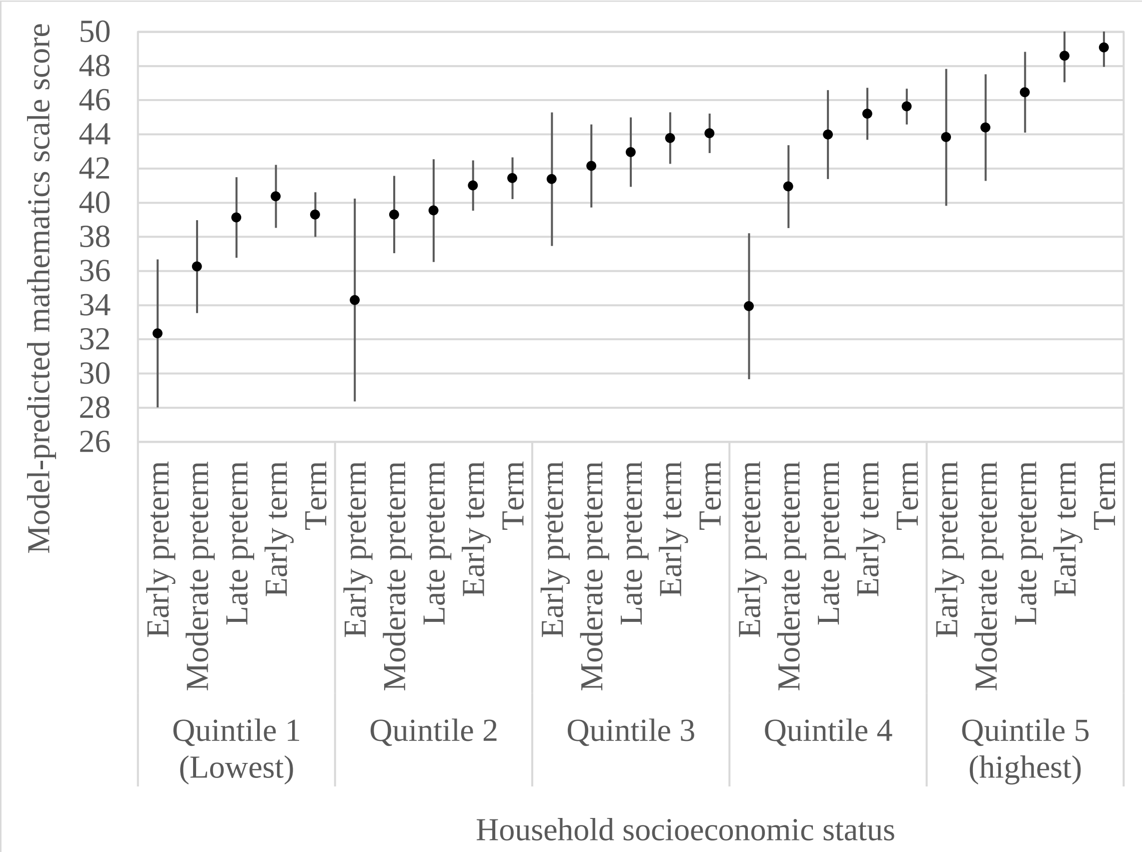
1A. Predicted Bayley Short Form-Research Edition Mental Scale Scores



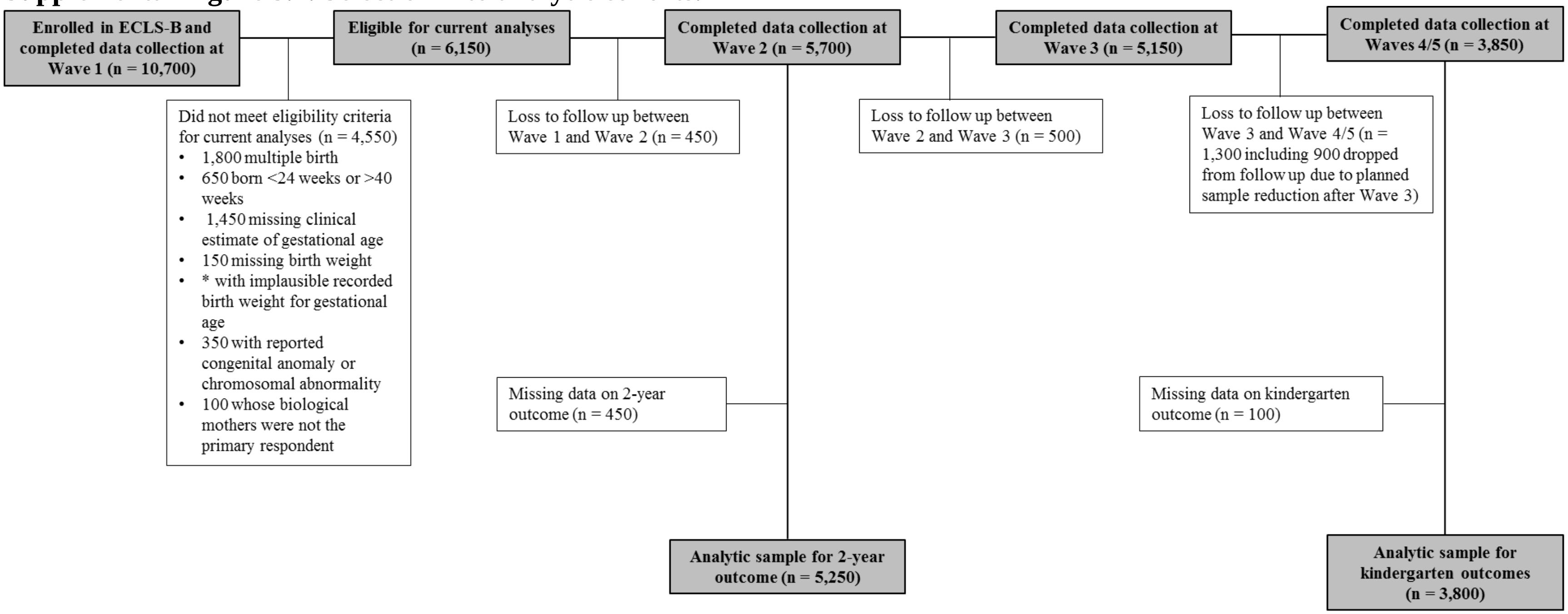
1B. Predicted Reading Scale Scores.



1C. Predicted Mathematics Scale Scores.



Supplemental Figure 5.1. Selection into analytic cohorts.



Supplemental Table 5.1. List of birth conditions excluded from analyses.

Condition	Source
Anencephalus	Birth certificate
Hydrocephalus	Birth certificate
Microcephalus	Birth certificate
Other central nervous system anomaly	Birth certificate
Heart malformations or heart defect	Birth certificate or Wave 1 parent report
Other circulatory/respiratory anomaly	Birth certificate
Rectal atresia/stenosis	Birth certificate
Tracheo-esophageal fistula/esophageal atresia	Birth certificate
Omphalocele/gastroschisis	Birth certificate
Malformed genitalia	Birth certificate
Renal agenesis	Birth certificate
Other urogenital anomalies	Birth certificate
Polydactyly/syndactyly/adactyly	Birth certificate
Club foot	Birth certificate
Diaphragmatic hernia	Birth certificate
Other musculoskeletal/integumental anomalies	Birth certificate
Other chromosomal anomalies	Birth certificate
Other anomalies (no category)	Birth certificate
Cleft lip or palate	Birth certificate or Wave 1 parent report
Spina bifida	Birth certificate or Wave 1 parent report
Down syndrome	Birth certificate or Wave 1 parent report
Turner's syndrome	Wave 1 parent report

Supplemental Table 5.2. Adjusted associations between gestational age at delivery and cognitive and academic achievement scores, stratified by household socioeconomic status quintile.

	Socioeconomic status									
	Quintile 1 (lowest)		**Quintile 2**		**Quintile 3**		**Quintile 4**		**Quintile 5 (highest)**	
	β[a]	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**	**β**	**95% CI**
2-year outcome										
BSF-R Mental Scale score										
Early preterm	-7.8	-11.2, -4.5	-7.3	-10.5, -4.0	-6.4	-9.3, -3.6	-7.1	-11.7, -2.5	-7.0	-10.6, -3.3
Moderate preterm	-3.1	-5.2, -0.9	-1.9	-4.1, 0.3	-1.0	-3.6, 1.5	-5.3	-8.7, -2.0	-4.4	-8.1, -0.7
Late preterm	-2.0	-3.8, -0.3	-1.1	-3.0, 0.9	-1.5	-3.8, 0.9	-0.7	-3.7, 2.3	-0.8	-3.0, 1.5
Early term	-0.2	-1.5, 1.2	0.9	-0.4, 2.2	-1.2	-2.6, 0.2	-1.0	-2.3, 0.3	0.9	-0.4, 2.3
Term	0.0	Reference	0.0	Reference	0.0	Reference	0.0	Reference	0.0	Reference
Kindergarten outcomes										
Reading scale score										
Early preterm	-6.8	-12.7, -0.8	-6.7	-13.3, -0.1	-2.8	-7.8, 2.2	-9.6	-15.0, -4.3	-0.8	-8.3, 6.6
Moderate preterm	-2.8	-6.1, 0.5	-0.6	-3.3, 2.0	-1.7	-5.0, 1.6	-3.6	-6.7, -0.6	-4.2	-8.0, -0.3
Late preterm	0.3	-2.7, 3.3	-1.8	-5.2, 1.7	-1.9	-4.8, 0.9	-3.0	-6.9, 0.9	-2.3	-5.5, 0.8
Early term	1.0	-1.1, 3.1	-0.3	-2.3, 1.6	-0.7	-2.8, 1.4	-0.3	-2.2, 1.6	-1.1	-3.5, 1.2
Term	0.0	Reference	0.0	Reference	0.0	Reference	0.0	Reference	0.0	Reference
Mathematics scale score										
Early preterm	-7.1	-11.6, -2.5	-7.1	-12.4, -1.8	-3.0	-6.6, 0.5	-12.0	-16.0, -8.0	-4.5	-8.6, -0.4
Moderate preterm	-2.9	-5.6, -0.2	-2.2	-4.2, -0.2	-2.0	-4.3, 0.3	-4.6	-7.1, -2.1	-4.1	-7.2, -1.1
Late preterm	0.0	-2.1, 2.0	-2.2	-5.4, 0.9	-1.3	-3.3, 0.8	-1.5	-4.1, 1.1	-2.8	-5.0, -0.6
Early term	1.2	-0.4, 2.8	-0.4	-1.8, 1.1	-0.4	-1.8, 1.0	-0.4	-1.7, 0.9	-0.4	-1.7, 0.9
Term	0.0	Reference	0.0	Reference	0.0	Reference	0.0	Reference	0.0	Reference

All models adjusted for child's age at assessment, child's race/ethnicity, child's sex, maternal age at delivery, maternal marital status, and parity. [a]Estimated beta reflects estimated difference in mean outcome score.

Chapter 6: Preterm birth, childhood poverty, and cognitive development among children in the United Kingdom

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Abstract

Background: Preterm birth and childhood poverty each adversely impact children's cognitive development and academic outcomes. This study investigated whether the relationships between preterm and early term birth and children's cognitive scores at three, five, and seven years old were modified by childhood poverty.

Methods: This study was conducted using data on singletons born at 24-40 weeks gestational age enrolled in the Millennium Cohort Study in the United Kingdom. Linear regression models tested independent and joint associations of gestational age (early or moderate preterm, late preterm, early term compared with full term) and childhood poverty (<60% of median UK income) with children's cognitive scores. Presence of additive interaction between gestational age and poverty was tested using interaction terms.

Results: Cognitive score deficits were observed for preterm and early term children on most of the eight cognitive assessments. Estimated deficits were about 0.2-0.3 standard deviations (SD) for early or moderate preterm, 0.1 SD for late preterm, and 0.05 SD for early term compared with term. Children living in poverty scored 0.3-0.4 SD worse than children not living in poverty on all assessments. For most assessments, there was no evidence of additive interaction between gestational age and poverty.

Conclusions: The estimated adverse effects of earlier gestational age on cognitive scores did not vary by poverty status. Doubly exposed children performed at the lowest levels suggesting the need for targeting of early childhood interventions to reach these highest-risk children.

Introduction

Preterm and early term birth and childhood poverty each adversely impact children's cognitive development and academic outcomes.[18,61] Children's development is a transactional process influenced by both biological and socioenvironmental factors wherein children grow and respond to stimuli in their environments, which in turn fosters further learning.[19] Preterm children may be born with developmentally immature brains due to interruption of fetal brain growth and development, and they are more vulnerable to central nervous system and brain injuries both due to brain immaturity at birth or processes such as infection and inflammation that contribute to preterm deliveries.[25] Postnatal processes of brain growth and development are influenced by children's experiences of sensory enrichment (e.g., high quality and high quantity words and conversations) and deprivation (e.g., lower quality parental engagement and infant attachment).[67] Children raised in poverty are more likely to experience environmental stressors such as material deprivation, fewer cognitively stimulating experiences, and higher levels of family stress that adversely impact their cognitive development and academic outcomes.[63]

Studies of the cognitive and academic outcomes of preterm birth have often treated socioeconomic status (SES) as a confounding factor because it affects both risk of preterm birth and children's postnatal development. Given that both preterm birth and SES independently impact children's brain growth and development as well as their resulting cognitive and academic outcomes, it is important to understand the joint impacts of experiencing both of these exposures. A few recent studies have tested the presence of additive interaction between preterm birth and SES, yielding mixed findings on whether early social factors such as parental education,[85,101] parenting factors,[100] and neighborhood-level deprivation[99] modify the adverse impacts of preterm birth on children's cognitive and academic outcomes. It is plausible that preterm children may be more vulnerable to influences of their early life environments in terms of providing resources necessary for cognitive and academic success—this hypothesis suggests that impacts of preterm birth may be exacerbated in lower SES settings.[88] On the other hand, it is also possible that childhood poverty exerts such profound effects on cognitive outcomes that being born early may not contribute additional substantial risk.[90,92]

In this study, we investigated whether household SES modified the relationship between preterm and early term birth and children's cognitive outcomes in early childhood at three years old, at the time of school entry at five years old, and in middle childhood after several years of schooling at seven years old, by testing additive interaction between the risk factors.

Methods

The Millennium Cohort Study is a longitudinal birth cohort study of children born in the four countries of the United Kingdom (England, Wales, Scotland, and Northern Ireland).[114,144] Children were selected through a stratified clustered sample of births based on national child benefit records in late 2000-early 2002, with oversampling of high racial/ethnic minority areas, disadvantaged areas, and the three smaller UK countries. For these analyses, we used data from MCS Sweeps 1 (9 months), 2 (three years), 3 (five years), and 4 (seven years) on singletons born at 24-40 weeks gestation. Children were excluded if part of a multiple birth (n=522), if the primary family respondent at nine months was not the child's natural mother (n=55), missing gestational age (n=201), if born <24 weeks or >40 weeks (n=4,345), or if they had an implausible reported birth weight for gestational age[125] (n=13), or if their natural mother reported that they had a birth defect at Sweep 1 (n=415) (Supplemental Figure 6.1).

Gestational age at delivery was calculated based on nine-month parent reports of expected due date and birth date. This measure has been shown to have high validity except for post-term births, which were not included in this study.[115] Gestational age was categorized as early or moderate preterm (24-33 weeks), late preterm (34-36 weeks), early term (37-38 weeks), and full term (39-40 weeks).

Studies of socioeconomic inequalities in children's outcomes within the Millennium Cohort Study have used single indicators of SES such as family income,[145] parental occupation,[146] and parental education qualifications,[147,148] and some have compared findings across several of these indicators.[149] In our main analyses, we measured SES at nine months old using a poverty indicator for whether the household earned below 60% median income (equivalized for household size) relative to other UK households. Given that financial income represents only a single dimension of household's SES, we repeated all analyses using a principal components analysis-derived composite measure of parental education, occupation, and income (see detail in Supplement).

Outcomes of interest were children's cognitive abilities and academic achievement as measured with the Bracken School Readiness Assessment-Revised (BSRA-R) and British Ability Scales II (BAS II) naming vocabulary scale at three years old; the BAS II naming vocabulary, picture similarity, and pattern construction scales at five years old; and the BAS II word reading and pattern construction scales and the

National Foundation for Education Research (NFER) number skills assessment at seven years old (see Supplement for details on instrument content and administration procedures). Age-standardized t-scores available from MCS were standardized within our study sample to a normal distribution with mean of 0 and standard deviation (SD) of 1 to enable interpretation of group-wise differences in terms of SD's.[114,144]

Descriptive statistics were calculated to describe the distribution of gestational age and covariates in the eligible analytic samples at each of the four sweeps. The joint distribution of gestational age and household SES was described using mean scores and standard deviations for the analytic samples stratified into eight sub-groups using household poverty (four gestational age categories x two levels of poverty indicator).

We computed risk differences between groups for each outcome using generalized estimating equations based on the normal distribution, accounting for clustering of subjects by MCS sample clusters. We did not apply sampling weights in our main analyses because our objective was to obtain internally valid estimates of the relationships between gestational age, household poverty, and outcome scores among the eligible study subjects rather than ensuring that our estimates were nationally representative. In sensitivity analyses, we applied sampling weights and results were similar. Main effects models estimated the mutually adjusted independent associations of gestational age and household poverty with each cognitive outcome. Presence of additive interaction between gestational age and household poverty was tested by assessing statistical significance of the set of interaction terms using the generalized score test statistic. Model-predicted scores by gestational age and poverty status were plotted to graphically examine potential modification of the effect of gestational age by household poverty. We estimated both main effects and interaction models as crude models and then adjusted for a priori potential confounders (child's race/ethnicity, child's sex, number of siblings in the household at nine months, household structure at nine months, maternal age at delivery).

Analyses were conducted using SAS v9.4 (Cary, NC). MCS data are freely available to bona fide researchers from the United Kingdom Data Service.[144] The Emory University Institutional Review Board (IRB) determined that secondary analyses of MCS data did not constitute human subjects research and therefore did not require IRB review.

Results

There were 13,267 singleton children eligible for our analyses. Of these, 10,649 (80%) were assessed at three years old, 10,494 (79%) were assessed at five years old, and 9,521 (72%) were assessed at seven years old (Supplemental Figure 6.1). About 9% were preterm and 25% were early term (Table 6.1). The sample was mostly white (81%) and lived in two-parent households (83%); 38% lived in poverty at nine months old. Supplemental Table 6.1 reports unadjusted scores stratified by gestational age and household poverty.

At three years old, unadjusted scores on the BSRA-R and naming vocabulary scale were lower for preterm and early term compared with term and for children living under versus above the poverty line (Table 6.2). On the BSRA-R, score deficits were observed for early or moderate preterm children (0.30 standard deviations [SD], 95% CI: 0.19-0.41) and late preterm children (0.14 SD, 95% CI: 0.06-0.22) after covariate adjustment. Children living in poverty scored 0.40 SD (95% CI: 0.35-0.46) lower than children not living in poverty. Similar deficits were observed for the naming vocabulary scale, on which early or moderate preterm children scored 0.29 SD (95% CI: 0.17-0.40) lower and late preterm children scored 0.07 SD (95% CI: 0.15-0.00) lower compared with term children, and children in poverty scored 0.34 SD (95% CI: 0.29-0.39) lower than children not living in poverty. There was no evidence of additive interaction between gestational age and household poverty on either assessment (Figure 6.1(a)-(b); Supplemental Table 6.2). When defining SES using the composite index, estimated deficits for preterm children were similar and there was no evidence of additive interaction between gestational age and household SES (Supplemental Tables 6.5-6.6; Supplemental Figure 6.2(a)-(b)). Children living in the lowest SES quintile scored 0.93 SD (95% CI: 0.84-1.02) and 0.73 SD (95% CI: 0.64-0.81) worse than those in the highest SES quintile on the BSRA-R and naming vocabulary scale, respectively (Supplemental Table 6.5).

At five years old, preterm and early term children scored significantly lower on the pattern construction scale but there was no significant association between gestational age and the naming vocabulary or picture similarity scores (Table 6.3). Children living in poverty scored 0.2-0.3 SD worse on all three assessments compared with children who were not living in poverty. On the pattern construction scale, adjusted deficits ranged from 0.09 SD (95% CI: 0.05-0.13) for early term to 0.38 SD (95% CI: 0.24-0.52) for early or moderate preterm compared with term. There was no evidence of additive interaction between gestational age and household poverty on any of the five-year assessments (Figure 6.1(c)-(e); Supplemental Table 6.3). Again, estimated score deficits associated with preterm and early term birth were similar when we used the composite SES index and there was no evidence of additive interaction between gestational age and household SES (Supplemental Table 6.7-6.8; Supplemental Figure 6.2(c)-(e)). Deficits between children in the lowest and highest SES quintiles ranged from 0.43 SD (95% CI: 0.34-0.51) for the picture similarity scale to 0.77 SD (95% CI: 0.69-0.85) for the naming vocabulary scale (Supplemental Table 6.7).

At seven years old, preterm and early term children scored lower on the word reading and pattern construction scales as well as the NFER number skills assessment (Table 6.4). On the word reading scale, adjusted deficits ranged from 0.05 SD (95% CI: 0.01-0.10) for early term to 0.19 SD (95% CI: 0.04-0.34) for early or moderate preterm compared with term. On the pattern construction scale, adjusted deficits ranged from 0.10 SD (95% CI: 0.05-0.14) for early term to 0.29 SD (95% CI: 0.14-0.43) for early or moderate preterm compared with term. Finally, on the NFER number skills assessment, score deficits ranged from 0.06 (95% CI: 0.01-0.11) for early term to 0.31 SD (95% CI: 0.17-0.44) for early or moderate preterm compared with term. Children living in poverty scored roughly 0.3-0.4 SD worse on all assessments compared with children who were not living in poverty.

Interaction between gestational age and poverty was statistically significant for the pattern construction scale (p=0.04) but not for the word reading scale or the NFER number skills assessment (Figure 6.1(f)-(h); Supplemental Table 6.4). The significant result for the pattern construction scale reflected the fact that early term children scored 14 SD (95% CI: 0.08-0.20) worse than term among children above the poverty line, but there was no association for children below the poverty line (Figure 6.1(g); Supplemental Table 6.4). While the interaction chunk test was not significant for the word reading scale, interaction between early or moderate preterm birth and household poverty was statistically significant (p=0.02) (Figure 1(f); Supplemental Table 6.4). Early or moderate preterm children scored 0.43 SD (95% CI: 0.14-0.72) worse than term among children living under the poverty line, but there was no association for children living above the poverty line. When defining SES using the composite SES index, estimated deficits for preterm and early term children were similar but there was no evidence of overall additive interaction between gestational age and household SES (Supplemental Tables 6.9-6.10; Supplemental Figure 2(f)-(h)). Children in the lowest SES quintile scored 0.86 SD (95% CI: 0.77-0.95) worse on the word reading scale, 0.63 SD (95% CI: 0.55-0.72) worse on the pattern construction scale, and 0.73 SD (95% CI: 0.65-0.82) worse on the NFER number skills assessment than those in the highest SES quintile (Supplemental Table 6.9).

Discussion

Preterm and early term birth were associated with deficits on most of the MCS cognitive assessments at three, five, and seven years old, and children living in poverty consistently scored worse on all assessments. For most outcomes, there was no evidence of additive interaction between the two risk factors. Estimated score deficits associated with preterm or early term birth were relatively constant across poverty level; this still resulted in doubly exposed children having the lowest cognitive scores. Also, the profound impact of poverty on children's cognitive scores resulted in term children living in poverty having lower predicted cognitive scores than preterm children not living in poverty for some outcomes.

There were some exceptions to our finding of no statistical interaction between gestational age and childhood poverty in their estimated effects on children's cognitive scores. The exceptions were at seven years old, when there were significantly different estimated risk differences for the effect of early or moderate preterm birth on BAS II word reading scale score and for the effect of early term birth and BAS II pattern construction scale score. On the word reading scale, the observed deficit for early or moderate preterm children compared with their term-born peers was larger among children living in poverty, suggesting that early childhood poverty exacerbated the impact of early or moderate preterm birth in line with earlier findings of worsened impacts of prematurity among children of lower SES.[84,85,99,101] For example, Wang et al. (2008) found that the adverse effects of preterm birth, low birth weight, or both on Taiwanese adolescents' Mandarin scores were worsened among those whose fathers completed fewer years of education, although no meaningful differences were seen across parental education levels for scores in mathematics and science.[85] In our earlier study in the state of Georgia, we found that the estimated effect of preterm birth on children's likelihood of failing their first grade statewide standardized tests were larger among those living in more deprived neighborhoods.[99]

The opposite pattern, however, was observed for the estimated effect of early term birth on BAS II pattern construction scale scores, where a deficit was observed for children who were not living in poverty but there was no deficit among children living in poverty. A potential explanation for these findings—which are similar to some previous studies[90,92]—is that prematurity may not contribute substantial additional risk of long-term adverse outcomes on top of the adverse impacts of being raised in a lower SES environment.[90] Supporting this competing hypothesis are findings from a study by Turkheimer et al. (2003) of twins enrolled in the National Collaborative Perinatal Project showing that IQ scores among lower SES children were influenced relatively more by environment and less by genetics, with the opposite pattern observed among higher SES children.[93] For the majority of outcomes in our study, however, the effects of preterm birth on cognitive scores were constant across poverty level suggesting that living in poverty neither exacerbated nor attenuated the estimated effects of preterm birth.

Longitudinal studies of cognitive outcomes associated with preterm and early term birth are mostly limited to follow-up of very preterm children, which have yielded mixed findings suggesting that cognitive outcomes of very preterm children may improve,[27] remain stable,[150] or deteriorate[151] with age. In this study, we were able to examine cognitive outcomes for the same population-based sample of children at three ages in early childhood, when they entered school, and in middle childhood after several years of schooling, although we were not able to examine cognitive trajectories due to the fact that no common assessment was repeated at all three time points. We found that early or moderate preterm, late preterm, and early term children consistently scored significantly lower than term-born children on the three-year and seven-year cognitive assessments, but gestational age was a significant predictor of cognitive score for only one of the five-year assessments. Our findings suggest that the adverse impacts of preterm or early term birth persist through middle childhood. The lack of gestational age-related deficits on some assessments at five years old may reflect characteristics of the testing instruments; the impacts of gestational age on cognitive test performance have been found to vary with cognitive workload demands of specific assessments.[152] The estimated effect of poverty on the five-year BAS II picture similarity and naming vocabulary scales was also smaller compared with its effect on scores on the three- and seven-year assessments.

Some studies have found that relative impacts of perinatal factors and social factors on developmental outcomes change with time, with the influence of social factors becoming more pronounced as children enter and progress through school.[153–155] Tong et al. (2006) found that the relationship between birth weight and cognitive outcomes weakened with increasing age while socioenvironmental factors became relatively more important in children assessed at four time points between two and eleven years old.[153] Similarly, Hillemeier et al. (2011) found that while both SES and low birth weight were associated with cognitive delay at two years old, only SES remained significantly associated with cognitive delay at four years old.[154] In contrast with these earlier findings, we found that with the exception of the five-year BAS II picture similarity and naming vocabulary scales, the magnitude of deficits observed for the gestational age groups and for living in poverty remained consistent over the three assessment ages. In the main effects models, the observed deficits were about 0.2-0.3 SD for early or moderate preterm children, 0.1 SD for late preterm children, 0.05 SD for early term children, and 0.3-0.4 SD for children living in poverty. We continued to observe significant deficits in cognitive scores for preterm and early term children even at seven years old.

A major strength of this study was our use of a large, population-based, prospective study of children born in the United Kingdom with rigorous follow-up at multiple ages spanning early to middle childhood. Using data from a population-based cohort, however, comes with the caveat that preterm children who were more sick or impaired may be underrepresented. Since cognitive assessments were not administered if

MCS children had a major disability or behavioral problems, our results should be interpreted as representing those children considered well-functioning enough to participate. While for ease of interpretation and presentation, our main analyses tested interaction between a single indicator of poverty status and gestational age, we also used a comprehensive index measure covering educational, occupational, and income domains. Findings using this index were similar, showing additive adverse impacts of gestational age and lower SES on children's cognitive scores; they showed more granularity in the SES distribution compared with the binary poverty indicator.

Although our analyses were based on a sample that was large overall, stratifying by gestational age and poverty or socioeconomic index quintiles resulted in small sample sizes for examining interaction. There were consistently high follow-up rates of 72-80%. The gestational age distribution remained relatively constant over the four time points, but children remaining in the study at seven years old were slightly less likely to have lived in poverty at nine months (34% versus 38%). The five- and seven-year assessments had only 3% or less missingness per outcome, but larger proportions were missing scores on the three-year BSRA-R (11%) and naming vocabulary scale (6%). These children were more likely to be preterm or early term, non-white, male, and living under the poverty level; our findings may underrepresent these higher-risk children. Also, it is possible that our analyses suffer from uncontrolled structural confounding due to the correlation between poverty status and women's risk of preterm births.[6] We measured children's early socioeconomic environment at nine months old, but children's cognitive outcomes may be influenced not just by their own exposure to disadvantaged environments, but also by their parents' and grandparents' socioeconomic contexts.[156]

Future studies should explore potential pathways through which intergenerational processes of poverty and deprivation influence risks of having preterm births as well as potentially modify children's cognitive trajectories.

Preterm birth and childhood poverty each have important adverse impacts on cognitive outcomes in early childhood, at the age of school entry, and in middle childhood. In the United Kingdom, nearly 30% of births are preterm or early term[2] and another 30% of children live in low-income households.[4] From a population-level perspective, our findings contribute to the existing literature by showing that the adverse effects of early birth and being raised in poverty act additively with doubly exposed children exhibiting the worst cognitive outcomes. Continued research is warranted to better understand the independent and joint effects of prematurity and childhood poverty on children's cognitive and academic outcomes, and to inform the development and targeting of interventions to the highest-risk groups of doubly exposed children.

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Table 6.1. Cohort characteristics.

	All eligible (9 months) n (%)	Completed Sweep 2 (3 years) n (%)	Completed Sweep 3 (5 years) n (%)	Completed Sweep 4 (7 years) n (%)
Total	13,267 (100.0)	10,649 (100.0)	10,494 (100.0)	9,521 (100.0)
Gestational age				
Early or moderate preterm	319 (2.4)	243 (2.3)	241 (2.3)	211 (2.2)
Late preterm	873 (6.6)	686 (6.4)	694 (6.6)	624 (6.6)
Early term	3,368 (25.4)	2,694 (25.3)	2,619 (25.0)	2,389 (25.1)
Term	8,707 (65.6)	7,026 (66.0)	6,940 (66.1)	6,297 (66.1)
Household poverty				
Below poverty level	4,964 (37.5)	3,686 (34.7)	3,656 (34.9)	3,202 (33.7)
Above poverty level	8,261 (62.5)	6,939 (65.3)	6,813 (65.1)	6,298 (66.3)
Missing	42	24	25	21
Child's race/ethnicity				
White	10,795 (81.5)	8,823 (83.0)	8,677 (82.8)	7,912 (83.3)
Mixed	419 (3.2)	318 (3.0)	316 (3.0)	277 (2.9)
Indian	368 (2.8)	292 (2.7)	280 (2.7)	250 (2.6)
Pakistani and Bangladeshi	978 (7.4)	734 (6.9)	719 (6.9)	644 (6.8)
Black or Black British	480 (3.6)	323 (3.0)	338 (3.2)	299 (3.1)
Other	206 (1.6)	143 (1.3)	146 (1.4)	121 (1.3)
Missing	21	16	18	18
Number of siblings in household				
None	5,343 (40.3)	4,205 (39.5)	4,201 (40.0)	3,804 (40.0)
1-2	6,805 (51.3)	5,587 (52.5)	5,441 (51.8)	4,971 (52.2)
3+	1,119 (8.4)	857 (8.0)	852 (8.1)	746 (7.8)
Household structure				
Two parent household	10,980 (82.8)	9,021 (84.7)	8,861 (84.4)	8,100 (85.1)
Single mother	2,287 (17.2)	1,628 (15.3)	1,633 (15.6)	1,421 (14.9)
Mother's age at delivery, years				
14-17	349 (2.6)	250 (2.3)	258 (2.5)	213 (2.2)

18-19	799 (6.0)	561 (5.3)	561 (5.3)	503 (5.3)
20-24	2,549 (19.2)	1,891 (17.8)	1,879 (17.9)	1,669 (17.5)
25-29	3,663 (27.6)	2,926 (27.5)	2,931 (27.9)	2,643 (27.8)
30-34	3,790 (28.6)	3,205 (30.1)	3,115 (29.7)	2,847 (29.9)
35-39	1,829 (13.8)	1,573 (14.8)	1,516 (14.4)	1,428 (15.0)
40+	286 (2.2)	242 (2.3)	233 (2.2)	217 (2.3)
Missing	2	1	1	1
Child's sex				
Male	6,806 (51.3)	5,419 (50.9)	5,355 (51.0)	4,817 (50.6)
Female	6,461 (48.7)	5,230 (49.1)	5,139 (49.0)	4,704 (49.4)

Table 6.2. Associations between gestational age, household poverty, and 3-year outcomes (main effects models).

	Bracken School Readiness Assessment-Revised	BAS II Naming Vocabulary Scale
Regression coefficients	**Beta (95% CI)**	**Beta (95% CI)**
Gestational age		
Early or moderate preterm	-0.30 (-0.41, -0.19)	-0.29 (-0.40, -0.17)
Late preterm	-0.14 (-0.22, -0.06)	-0.07 (-0.15, 0.00)
Early term	-0.04 (-0.09, 0.00)	-0.03 (-0.07, 0.01)
Term	0.00 (Reference)	0.00 (Reference)
Household poverty		
Below poverty level	-0.40 (-0.46, -0.35)	-0.34 (-0.39, -0.29)
Above poverty level	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales.

Table 6.3. Associations between gestational age, household poverty, and 5-year outcomes (main effects models.)

	BAS II Picture Similarity Scale	BAS II Naming Vocabulary Scale	BAS II Pattern Construction Scale
Regression coefficients	**Beta (95% CI)**	**Beta (95% CI)**	**Beta (95% CI)**
Gestational age			
Early or moderate preterm	-0.02 (-0.16, 0.11)	-0.09 (-0.20, 0.03)	-0.38 (-0.52, -0.24)
Late preterm	-0.06 (-0.14, 0.02)	-0.01 (-0.08, 0.06)	-0.15 (-0.23, -0.08)
Early term	-0.02 (-0.07, 0.03)	-0.01 (-0.05, 0.04)	-0.09 (-0.13, -0.05)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Household poverty			
Below poverty level	-0.19 (-0.24, -0.13)	-0.33 (-0.38, -0.28)	-0.22 (-0.28, -0.17)
Above poverty level	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales.

Table 6.4. Associations between gestational age, household poverty, and 7-year outcomes (main effects models).

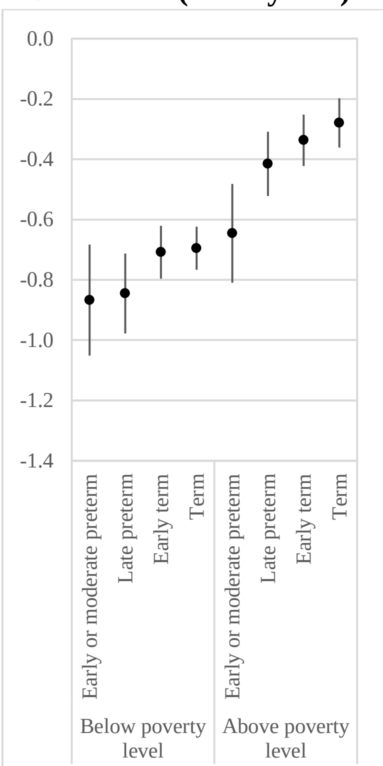
	BAS II Word Reading Scale	BAS II Pattern Construction Scale	NFER Number Skills Assessment
Regression coefficients	**Beta (95% CI)**	**Beta (95% CI)**	**Beta (95% CI)**
Gestational age			
Early or moderate preterm	-0.19 (-0.34, -0.04)	-0.29 (-0.43, -0.14)	-0.31 (-0.44, -0.17)
Late preterm	-0.14 (-0.22, -0.05)	-0.11 (-0.19, -0.03)	-0.09 (-0.16, -0.01)
Early term	-0.05 (-0.10, -0.01)	-0.10 (-0.14, -0.05)	-0.06 (-0.11, -0.01)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Household poverty			
Below poverty level	-0.37 (-0.43, -0.31)	-0.29 (-0.34, -0.23)	-0.30 (-0.36, -0.24)
Above poverty level	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales. NFER = National Foundation for Education Research.

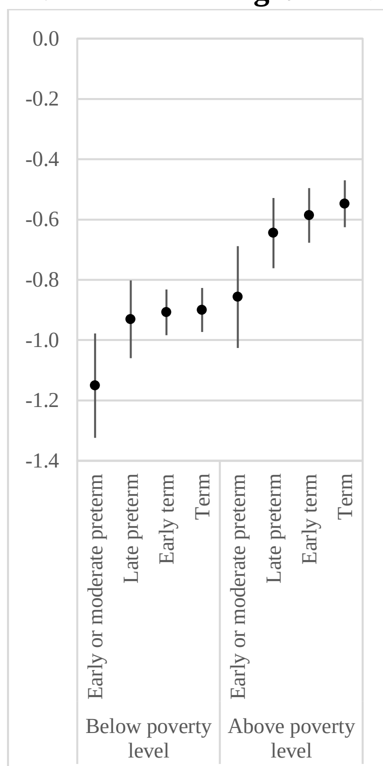
Figure 6.1(a)-(h). Model-predicted scores on cognitive and academic achievement assessments at three, five, and seven years old.

NOTE: All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). Predicted scores are based on sample mean covariate values. BSRA-R = Bracken School Readiness Assessment-Revised. BAS = British Ability Scales. NFER = National Foundation for Education Research.

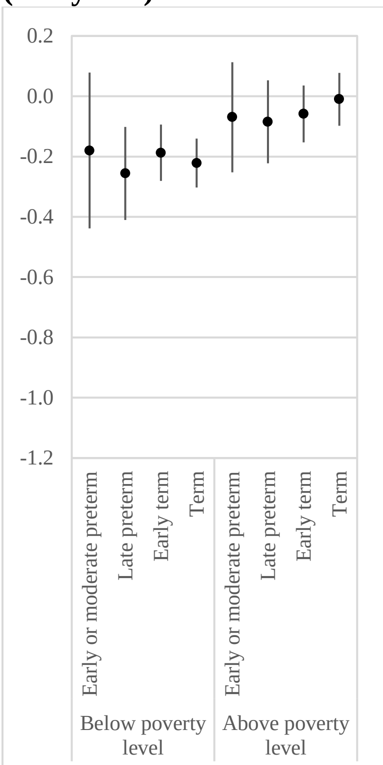
1a. BSRA-R (three years)



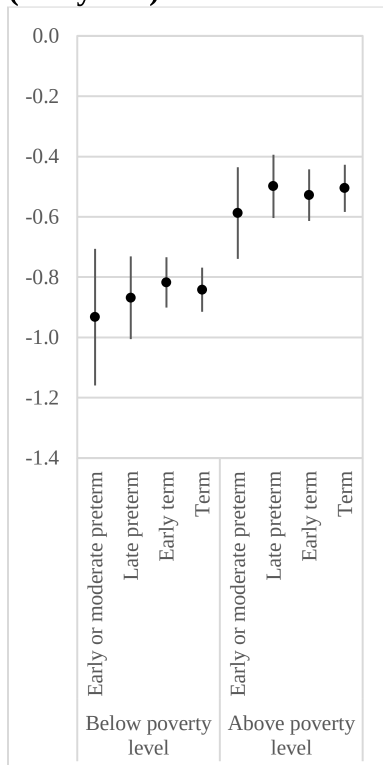
1b. BAS II Naming Vocabulary Scale (three years)



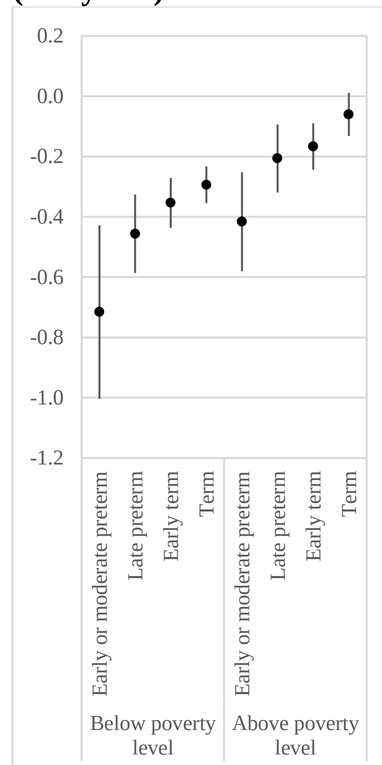
1c. BAS II Picture Similarity Scale (five years)



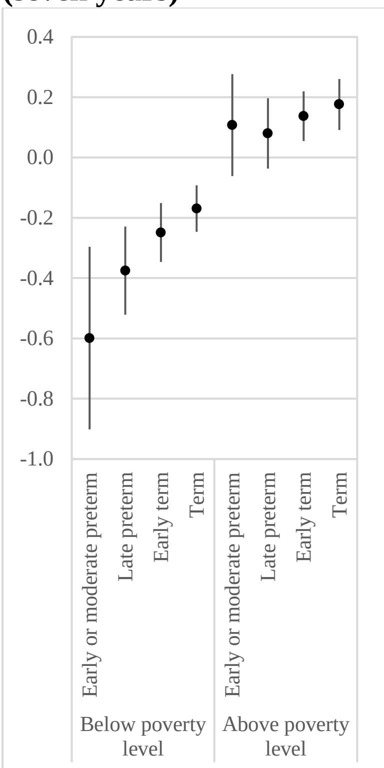
1d. BAS II Naming Vocabulary Scale (five years)



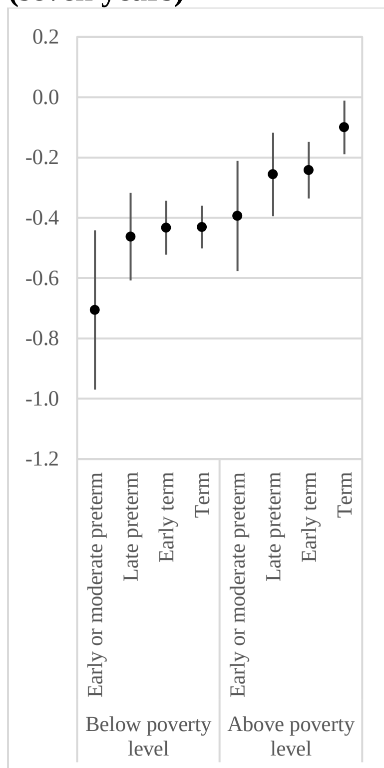
1e. BAS II Pattern Construction Scale (five years)



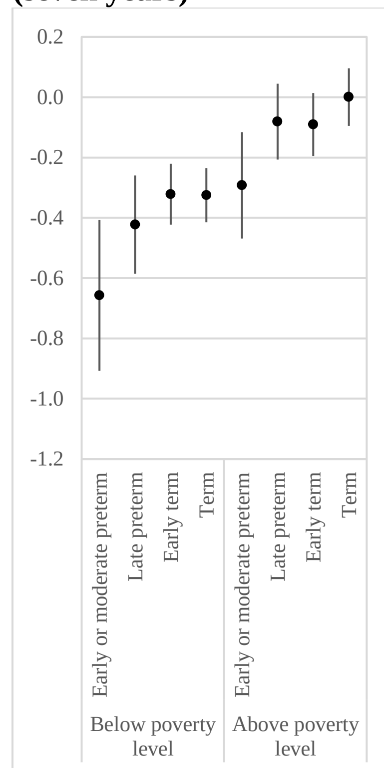
1f. BAS II Word Reading Scale (seven years)



1g. BAS II Pattern Construction Scale (seven years)



1h. NFER Number Skills Assessment (seven years)



Supplement

Creation of socioeconomic composite index

The composite socioeconomic index variable was created using principal components analysis to reflect the domains of parental education, parental occupation, and household income. Educational attainment was ascertained for both parents or guardians using levels of NVQ levels 1 through 5 and none or foreign only. Occupational status was measured for both parents or guardians using the 8-category National Statistics Socio-economic Classification (NS-SEC) designation of never worked, routine occupations, semi-routine occupations, low supervisory and technical occupations, small employers and self-employed, intermediate occupations, lower managerial and professional occupations, and higher managerial and professional occupations. We determined the highest educational attainment level and occupational status level across both parents or guardians. Household income was operationalized as the natural log of equivalized household income. The three variables were standardized (with lower scores reflective of lower socioeconomic status) and entered into PCA. Weights for each component measure were taken from the first component, which explained 74% of the variance. Values of the composite index for each child were calculated by summing the products of component weights x standardized values of the components. These values were separated into 5 quintiles with higher quintiles representing higher socioeconomic status.

Measurement of cognitive ability and academic achievement outcomes

Children's cognitive development was tested at 3 years old using the Bracken School Readiness Assessment-Revised (BSRA-R) and the naming vocabulary scale of the British Ability Scales II (BAS II). The BSRA-R consisted of 6 subtests focused on colors, letters, numbers/counting, sizes, comparisons, and shapes; all children completed the same set of items on each subtest.[114] Age-adjusted standardized scores with a mean of 100 and standard deviation of 15 were used in our analyses; scores were age adjusted within 3-month age bands.[116] The naming vocabulary scale measured expressive language ability by asking children to name objects pictured in a testing booklet. It consisted of an initial routing test administered to all children, followed by progression to more difficult or more simple items based on the child's performance. Since not all children completed the same set of items, item response theory (IRT) methods were used to compute ability scores. Our analyses use age-adjusted t-scores derived from these ability scores; these scores have a mean of 50 and standard deviation of 10, and are age adjusted within 3-month age bands. Conceptually, these scores represent children's performance relative to other children of their same age.[116]

Children's cognitive development at 5 years old was measured using the BAS II naming vocabulary, picture similarity, and pattern construction scales. The naming vocabulary scale was repeated from Sweep 2. The pattern construction scale tested spatial problem solving by asking children to repeat a design using flat squares or solid cubes, and the picture similarities scale tested non-verbal reasoning or problem solving by showing children a row of four pictures and asking them to identify a fifth picture that is most similar to the others.[114] Scoring procedures for all three tests repeated those used for the naming vocabulary test at Sweep 2.[116]

Children's cognitive development and academic achievement at 7 years old was measured using the BAS II pattern construction and word reading scales and the National Foundation for Education Research (NFER) Number Skills assessment. The pattern construction scale was repeated from Sweep 3.[114] The word reading scale tested English reading ability by asking children to read aloud a series of words (potentially 90 words total, broken into blocks of 10). Scoring procedures were similar to the other BAS II scales administered at the previous sweeps, except that standardized scores were normed to a mean of 100 and standard deviation of 10.[114] The NFER Number Skills assessment was adapted from the NFER Progress in Maths (PiM) test that was developed and standardized to the UK population in 2004. The assessment had a two-stage design of an initial routing test and second portion of easier, medium, or harder difficulty; item response theory was used to compute estimated raw scores. Our analyses used age-adjusted standardized scores computed from these estimated raw scores, re-standardized to a normal distribution with mean of 0 and standard deviation of 1.

Supplemental Table 6.1. Mean cognitive and academic achievement scores, stratified by gestational age and household poverty.

	All			Below Poverty Line			Above Poverty Line		
	n	**Mean**	**(SD)**	**n**	**Mean**	**(SD)**	**n**	**Mean**	**(SD)**
Three years old									
BRSA-R									
All	9,463	0.00	(1.00)	3,152	-0.48	(0.95)	6,311	0.24	(0.93)
Term	6,298	0.03	(1.00)	2,077	-0.46	(0.96)	4,221	0.27	(0.93)
Early term	2,351	-0.02	(0.99)	779	-0.47	(0.95)	1,572	0.20	(0.93)
Late preterm	609	-0.12	(1.03)	223	-0.61	(0.98)	386	0.15	(0.95)
Early/moderate preterm	205	-0.26	(0.92)	73	-0.59	(0.83)	132	-0.07	(0.92)
BAS II Naming Vocabulary Scale									
All	9,968	0.00	(1.00)	3,325	-0.43	(0.98)	6,643	0.22	(0.94)
Term	6,602	0.03	(1.00)	2,172	-0.42	(0.98)	4,430	0.24	(0.94)
Early term	2,500	-0.02	(0.98)	839	-0.43	(0.97)	1,661	0.18	(0.92)
Late preterm	636	-0.05	(1.01)	229	-0.42	(0.99)	407	0.16	(0.96)
Early/moderate preterm	230	-0.31	(0.97)	85	-0.70	(0.91)	145	-0.08	(0.93)
Five years old									
BAS II Picture Similarity Scale									
All	10,279	0.00	(1.00)	3,550	-0.19	(1.01)	6,729	0.10	(0.98)
Term	6,801	0.01	(1.00)	2,318	-0.20	(1.01)	4,483	0.12	(0.97)
Early term	2,562	-0.01	(1.00)	893	-0.17	(1.00)	1,669	0.07	(0.98)
Late preterm	680	-0.06	(1.04)	250	-0.23	(1.07)	430	0.04	(1.01)
Early/moderate preterm	236	-0.03	(1.05)	89	-0.17	(1.13)	147	0.06	(0.99)
BAS II Naming Vocabulary Scale									
All	10,285	0.00	(1.00)	3,552	-0.44	(0.99)	6,733	0.23	(0.92)
Term	6,813	0.01	(1.00)	2,322	-0.44	(1.00)	4,491	0.24	(0.92)
Early term	2,556	-0.01	(1.00)	892	-0.43	(0.99)	1,664	0.21	(0.93)
Late preterm	679	0.01	(1.01)	249	-0.42	(1.00)	430	0.26	(0.93)
Early/moderate preterm	237	-0.11	(0.98)	89	-0.52	(0.93)	148	0.13	(0.93)
BAS II Pattern Construction Scale									
All	10,249	0.00	(1.00)	3,532	-0.25	(1.02)	6,717	0.13	(0.97)
Term	6,791	0.05	(1.00)	2,312	-0.21	(0.99)	4,479	0.18	(0.97)
Early term	2,547	-0.05	(0.99)	886	-0.28	(1.05)	1,661	0.07	(0.94)
Late preterm	676	-0.12	(0.99)	247	-0.37	(0.99)	429	0.02	(0.97)
Early/moderate preterm	235	-0.35	(1.11)	87	-0.63	(1.23)	148	-0.19	(0.99)
Seven years old									
BASI II Word Reading Scale									
All	9,205	0.00	(1.00)	3,075	-0.33	(1.03)	6,130	0.17	(0.94)
Term	6,105	0.03	(0.99)	2,016	-0.29	(1.01)	4,089	0.18	(0.94)
Early term	2,297	-0.03	(1.01)	769	-0.37	(1.07)	1,528	0.14	(0.93)
Late preterm	602	-0.12	(1.02)	224	-0.50	(1.02)	378	0.11	(0.96)
Early/ moderate preterm	201	-0.14	(1.12)	66	-0.73	(1.19)	135	0.15	(0.97)

BAS II Pattern Construction Scale									
All	9,274	0.00	(1.00)	3,080	-0.30	(1.00)	6,194	0.15	(0.96)
Term	6,156	0.04	(1.00)	2,017	-0.29	(1.00)	4,139	0.20	(0.96)
Early term	2,311	-0.06	(0.99)	771	-0.30	(1.00)	1,540	0.05	(0.96)
Late preterm	602	-0.09	(0.99)	222	-0.31	(0.97)	380	0.04	(0.97)
Early/moderate preterm	205	-0.27	(1.03)	70	-0.58	(1.06)	135	-0.11	(0.97)
NFER Number Skills Assessment									
All	9,307	0.00	(1.00)	3,099	-0.31	(1.00)	6,208	0.16	(0.96)
Term	6,172	0.03	(1.00)	2,028	-0.30	(0.99)	4,144	0.19	(0.96)
Early term	2,317	-0.03	(1.01)	772	-0.30	(1.02)	1,545	0.10	(0.97)
Late preterm	612	-0.07	(0.99)	229	-0.38	(0.97)	383	0.12	(0.96)
Early/moderate preterm	206	-0.28	(1.00)	70	-0.62	(0.95)	136	-0.10	(0.99)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. BRSA-R = Bracken School Readiness Assessment-Revised. BAS = British Ability Scales. NFER = National Foundation for Education Research.

Supplemental Table 6.2. Associations between gestational age, household poverty, and 3-year outcomes (interaction models).

	Bracken School Readiness Assessment-Revised	BAS II Naming Vocabulary Scale
Regression coefficients	**Beta (95% CI)**	**Beta (95% CI)**
Gestational age		
Early or moderate preterm	-0.37 (-0.51, -0.22)	-0.31 (-0.46, -0.16)
Late preterm	-0.14 (-0.23, -0.04)	-0.10 (-0.19, 0.00)
Early term	-0.06 (-0.11, 0.00)	-0.04 (-0.09, 0.01)
Term	0.00 (Reference)	0.00 (Reference)
Household poverty		
Below poverty level	-0.42 (-0.48, -0.35)	-0.35 (-0.41, -0.29)
Above poverty level	0.00 (Reference)	0.00 (Reference)
Interaction terms		
Early or moderate preterm x Poverty	0.19 (-0.04, 0.43)	0.06 (-0.17, 0.29)
Late preterm x Poverty	-0.01 (-0.17, 0.14)	0.07 (-0.09, 0.22)
Early term x Poverty	0.04 (-0.04, 0.13)	0.03 (-0.05, 0.12)
Interaction p-values		
Overall	0.38	0.74
Early or moderate preterm x Poverty	0.10	0.61
Late preterm x Poverty	0.86	0.39
Early term x Poverty	0.33	0.48
Estimated poverty strata-specific contrasts		
Below poverty level		
Early or moderate preterm	-0.17 (-0.35, 0.01)	-0.25 (-0.43, -0.07)
Late preterm	-0.15 (-0.28, -0.02)	-0.03 (-0.15, 0.08)
Early term	-0.01 (-0.09, 0.06)	-0.01 (-0.07, 0.06)
Term	0.00 (Reference)	0.00 (Reference)
Above poverty level		
Early or moderate preterm	-0.37 (-0.51, -0.22)	-0.31 (-0.46, -0.16)
Late preterm	-0.14 (-0.23, -0.04)	-0.10 (-0.19, 0.00)

Early term	-0.06 (-0.11, 0.00)	-0.04 (-0.09, 0.01)
Term	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales.

Supplemental Table 6.3. Associations between gestational age, household poverty, and 5-year outcomes (interaction models).

	BAS II Picture Similarity Scale	BAS II Naming Vocabulary Scale	BAS II Pattern Construction Scale
Regression coefficients	**Beta (95% CI)**	**Beta (95% CI)**	**Beta (95% CI)**
Gestational age			
Early or moderate preterm	-0.06 (-0.22, 0.10)	-0.08 (-0.22, 0.06)	-0.36 (-0.51, -0.20)
Late preterm	-0.07 (-0.18, 0.03)	0.01 (-0.08, 0.09)	-0.15 (-0.24, -0.05)
Early term	-0.05 (-0.10, 0.01)	-0.02 (-0.07, 0.03)	-0.11 (-0.16, -0.06)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Household poverty			
Below poverty level	-0.21 (-0.27, -0.15)	-0.34 (-0.39, -0.28)	-0.23 (-0.29, -0.18)
Above poverty level	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Interaction terms			
Early or moderate preterm x Poverty	0.10 (-0.18, 0.39)	-0.01 (-0.27, 0.25)	-0.07 (-0.40, 0.27)
Late preterm x Poverty	0.04 (-0.13, 0.21)	-0.03 (-0.18, 0.12)	-0.02 (-0.19, 0.15)
Early term x Poverty	0.08 (-0.02, 0.18)	0.05 (-0.03, 0.13)	0.05 (-0.04, 0.14)
Interaction p-values			
Overall	0.42	0.61	0.69
Early or moderate preterm x Poverty	0.49	0.95	0.70
Late preterm x Poverty	0.65	0.66	0.85
Early term x Poverty	0.11	0.26	0.31
Estimated poverty strata-specific contrasts			
Below poverty level			
Early or moderate preterm	0.04 (-0.20, 0.28)	-0.09 (-0.30, 0.12)	-0.42 (-0.71, -0.13)
Late preterm	-0.03 (-0.17, 0.10)	-0.03 (-0.15, 0.10)	-0.16 (-0.30, -0.03)
Early term	0.03 (-0.05, 0.12)	0.02 (-0.05, 0.09)	-0.06 (-0.14, 0.02)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Above poverty level			
Early or moderate preterm	-0.06 (-0.22, 0.10)	-0.08 (-0.22, 0.06)	-0.36 (-0.51, -0.20)
Late preterm	-0.07 (-0.18, 0.03)	0.01 (-0.08, 0.09)	-0.15 (-0.24, -0.05)
Early term	-0.05 (-0.10, 0.01)	-0.02 (-0.07, 0.03)	-0.11 (-0.16, -0.06)

Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales.

Supplemental Table 6.4. Associations between gestational age, household poverty, and 7-year outcomes (interaction models).

Regression coefficients	BAS II Word Reading Scale Beta (95% CI)	BAS II Pattern Construction Scale Beta (95% CI)	NFER Number Skills Assessment Beta (95% CI)
Gestational age			
Early or moderate preterm	-0.07 (-0.22, 0.09)	-0.29 (-0.46, -0.13)	-0.29 (-0.45, -0.13)
Late preterm	-0.10 (-0.19, 0.00)	-0.16 (-0.26, -0.05)	-0.08 (-0.18, 0.02)
Early term	-0.04 (-0.09, 0.02)	-0.14 (-0.20, -0.08)	-0.09 (-0.14, -0.04)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Household poverty			
Below poverty level	-0.35 (-0.41, -0.28)	-0.33 (-0.39, -0.27)	-0.33 (-0.39, -0.26)
Above poverty level	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Interaction terms			
Early or moderate preterm x Poverty	-0.36 (-0.67, -0.05)	0.02 (-0.26, 0.30)	-0.04 (-0.33, 0.25)
Late preterm x Poverty	-0.11 (-0.29, 0.07)	0.12 (-0.06, 0.31)	-0.02 (-0.19, 0.16)
Early term x Poverty	-0.04 (-0.14, 0.06)	0.14 (0.04, 0.24)	0.09 (0.00, 0.19)
Interaction p-values			
Overall	0.11	0.04	0.27
Early or moderate preterm x Poverty	0.02	0.90	0.79
Late preterm x Poverty	0.22	0.19	0.86
Early term x Poverty	0.43	0.005	0.06
Estimated poverty strata-specific contrasts			
Below poverty level			
Early or moderate preterm	-0.43 (-0.72, -0.14)	-0.27 (-0.53, -0.02)	-0.33 (-0.57, -0.09)
Late preterm	-0.21 (-0.35, -0.06)	-0.03 (-0.17, 0.11)	-0.10 (-0.24, 0.04)
Early term	-0.08 (-0.16, 0.01)	0.00 (-0.08, 0.07)	0.00 (-0.08, 0.08)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Above poverty level			
Early or moderate preterm	-0.07 (-0.22, 0.09)	-0.29 (-0.46, -0.13)	-0.29 (-0.45, -0.13)
Late preterm	-0.10 (-0.19, 0.00)	-0.16 (-0.26, -0.05)	-0.08 (-0.18, 0.02)
Early term	-0.04 (-0.09, 0.02)	-0.14 (-0.20, -0.08)	-0.09 (-0.14, -0.04)

Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales. NFER = National Foundation for Education Research.

Supplemental Table 6.5. Associations between gestational age, household socioeconomic index, and 3-year outcomes (main effects models).

	Bracken School Readiness Assessment-Revised	BAS II Naming Vocabulary Scale
Regression coefficients	**Beta (95% CI)**	**Beta (95% CI)**
Gestational age		
Early or moderate preterm	-0.27 (-0.38, -0.16)	-0.28 (-0.39, -0.17)
Late preterm	-0.13 (-0.21, -0.06)	-0.08 (-0.15, -0.01)
Early term	-0.04 (-0.08, 0.01)	-0.02 (-0.06, 0.02)
Term	0.00 (Reference)	0.00 (Reference)
Household socioeconomic index		
Lowest quintile	-0.93 (-1.02, -0.84)	-0.73 (-0.81, -0.64)
Second quintile	-0.72 (-0.79, -0.66)	-0.51 (-0.57, -0.44)
Third quintile	-0.49 (-0.55, -0.43)	-0.34 (-0.40, -0.28)
Fourth quintile	-0.22 (-0.27, -0.17)	-0.10 (-0.16, -0.04)
Highest quintile	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales.

Supplemental Table 6.6. Associations between gestational age, household socioeconomic index, and 3-year outcomes (interaction models).

Regression coefficients	Bracken School Readiness Assessment-Revised Beta (95% CI)	BAS II Naming Vocabulary Scale Beta (95% CI)
Gestational age		
Early or moderate preterm	-0.16 (-0.40, 0.08)	-0.19 (-0.48, 0.10)
Late preterm	-0.17 (-0.33, -0.01)	-0.08 (-0.24, 0.08)
Early term	-0.05 (-0.14, 0.03)	-0.02 (-0.11, 0.07)
Term	0.00 (Reference)	0.00 (Reference)
Household socioeconomic index		
Lowest quintile	-0.91 (-1.01, -0.81)	-0.72 (-0.81, -0.62)
Second quintile	-0.77 (-0.85, -0.69)	-0.52 (-0.59, -0.44)
Third quintile	-0.49 (-0.57, -0.42)	-0.37 (-0.44, -0.29)
Fourth quintile	-0.22 (-0.28, -0.15)	-0.06 (-0.13, 0.01)
Highest quintile	0.00 (Reference)	0.00 (Reference)
Interaction terms		
Early or moderate preterm x Lowest quintile	-0.04 (-0.49, 0.42)	-0.25 (-0.64, 0.15)
Late preterm x Lowest quintile	-0.13 (-0.39, 0.13)	0.03 (-0.19, 0.25)
Early term x Lowest quintile	-0.05 (-0.19, 0.10)	-0.03 (-0.16, 0.10)
Early or moderate preterm x Second quintile	-0.02 (-0.32, 0.28)	0.00 (-0.34, 0.35)
Late preterm x Second quintile	0.23 (0.00, 0.45)	0.08 (-0.13, 0.28)
Early term x Second quintile	0.12 (-0.01, 0.26)	0.01 (-0.11, 0.13)
Early or moderate preterm x Third quintile	-0.18 (-0.53, 0.17)	-0.04 (-0.43, 0.36)
Late preterm x Third quintile	0.15 (-0.09, 0.39)	0.10 (-0.13, 0.33)
Early term x Third quintile	-0.01 (-0.14, 0.13)	0.10 (-0.04, 0.23)
Early or moderate preterm x Fourth quintile	-0.30 (-0.67, 0.08)	-0.20 (-0.58, 0.19)
Late preterm x Fourth quintile	-0.05 ('-0.28, 0.19)	-0.17 (-0.41, 0.06)
Early term x Fourth quintile	0.01 (-0.12, 0.14)	-0.09 (-0.21, 0.03)
Interaction p-values		
Overall	0.22	0.18

Early or moderate preterm x Lowest quintile	0.88	0.22
Late preterm x Lowest quintile	0.33	0.80
Early term x Lowest quintile	0.54	0.64
Early or moderate preterm x Second quintile	0.91	0.99
Late preterm x Second quintile	0.05	0.48
Early term x Second quintile	0.07	0.87
Early or moderate preterm x Third quintile	0.32	0.86
Late preterm x Third quintile	0.23	0.39
Early term x Third quintile	0.92	0.16
Early or moderate preterm x Fourth quintile	0.12	0.31
Late preterm x Fourth quintile	0.70	0.15
Early term x Fourth quintile	0.88	0.15
Estimated socioeconomic strata-specific contrasts		
Lowest quintile		
Early or moderate preterm	-0.20 (-0.58, 0.19)	-0.44 (-0.70, -0.17)
Late preterm	-0.30 (-0.50, -0.10)	-0.05 (-0.20, 0.10)
Early term	-0.10 (-0.22, 0.02)	-0.05 (-0.14, 0.04)
Term	0.00 (Reference)	0.00 (Reference)
Second quintile		
Early or moderate preterm	-0.18 (-0.37, 0.02)	-0.19 (-0.37, -0.01)
Late preterm	0.05 (-0.10, 0.21)	-0.01 (-0.14, 0.13)
Early term	0.07 (-0.04, 0.18)	-0.01 (-0.09, 0.08)
Term	0.00 (Reference)	0.00 (Reference)
Third quintile		
Early or moderate preterm	-0.34 (-0.59, -0.09)	-0.23 (-0.49, 0.04)
Late preterm	-0.03 (-0.20, 0.15)	0.02 (-0.14, 0.18)
Early term	-0.06 (-0.16, 0.04)	0.08 (-0.01, 0.17)
Term	0.00 (Reference)	0.00 (Reference)
Fourth quintile		
Early or moderate preterm	-0.46 (-0.73, -0.18)	-0.39 (-0.66, -0.12)
Late preterm	-0.22 (-0.37, -0.07)	-0.26 (-0.42, -0.09)

Early term	-0.04 (-0.13, 0.05)	-0.11 (-0.19, -0.02)
Term	0.00 (Reference)	0.00 (Reference)
Highest quintile		
Early or moderate preterm	-0.16 (-0.40, 0.08)	-0.19 (-0.48, 0.10)
Late preterm	-0.17 (-0.33, -0.01)	-0.08 (-0.24, 0.08)
Early term	-0.05 (-0.14, 0.03)	-0.02 (-0.11, 0.07)
Term	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales.

Supplemental Table 6.7. Associations between gestational age, household socioeconomic index, and 5-year outcomes (main effects models).

	BAS II Picture Similarity Scale	BAS II Naming Vocabulary Scale	BAS II Pattern Construction Scale
Regression coefficients	**Beta (95% CI)**	**Beta (95% CI)**	**Beta (95% CI)**
Gestational age			
Early or moderate preterm	-0.01 (-0.15, 0.12)	-0.07 (-0.18, 0.04)	-0.38 (-0.52, -0.25)
Late preterm	-0.06 (-0.14, 0.02)	-0.01 (-0.08, 0.06)	-0.15 (-0.23, -0.07)
Early term	-0.02 (-0.07, 0.02)	0.00 (-0.05, 0.04)	-0.09 (-0.13, -0.04)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Household socioeconomic index			
Lowest quintile	-0.43 (-0.51, -0.34)	-0.77 (-0.85, -0.69)	-0.53 (-0.62, -0.44)
Second quintile	-0.32 (-0.40, -0.25)	-0.57 (-0.63, -0.51)	-0.40 (-0.47, -0.32)
Third quintile	-0.25 (-0.32, -0.18)	-0.38 (-0.44, -0.32)	-0.27 (-0.34, -0.21)
Fourth quintile	-0.17 (-0.23, -0.11)	-0.19 (-0.25, -0.14)	-0.15 (-0.21, -0.10)
Highest quintile	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales.

Supplemental Table 6.8. Associations between gestational age, household socioeconomic index, and 5-year outcomes (interaction models).

Regression coefficients	BAS II Picture Similarity Scale Beta (95% CI)	BAS II Naming Vocabulary Scale Beta (95% CI)	BAS II Pattern Construction Scale Beta (95% CI)
Gestational age			
Early or moderate preterm	-0.06 (-0.35, 0.22)	-0.03 (-0.25, 0.18)	-0.41 (-0.71, -0.12)
Late preterm	-0.10 (-0.29, 0.10)	-0.05 (-0.21, 0.11)	-0.22 (-0.39, -0.05)
Early term	-0.06 (-0.16, 0.03)	-0.03 (-0.12, 0.05)	-0.12 (-0.20, -0.04)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Household socioeconomic index			
Lowest quintile	-0.45 (-0.55, -0.36)	-0.77 (-0.85, -0.69)	-0.52 (-0.62, -0.43)
Second quintile	-0.37 (-0.45, -0.28)	-0.60 (-0.67, -0.53)	-0.46 (-0.55, -0.37)
Third quintile	-0.26 (-0.33, -0.18)	-0.40 (-0.47, -0.34)	-0.29 (-0.36, -0.21)
Fourth quintile	-0.16 (-0.24, -0.09)	-0.19 (-0.25, -0.13)	-0.15 (-0.22, -0.09)
Highest quintile	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Interaction terms			
Early or moderate preterm x Lowest quintile	-0.08 (-0.57, 0.41)	-0.23 (-0.59, 0.13)	-0.34 (-0.88, 0.20)
Late preterm x Lowest quintile	-0.01 (-0.29, 0.27)	-0.07 (-0.29, 0.15)	-0.03 (-0.28, 0.21)
Early term x Lowest quintile	0.13 (-0.03, 0.29)	0.04 (-0.09, 0.17)	0.01 (-0.13, 0.15)
Early or moderate preterm x Second quintile	0.07 (-0.32, 0.47)	0.02 (-0.28, 0.32)	0.24 (-0.18, 0.65)
Late preterm x Second quintile	0.22 (-0.06, 0.49)	0.09 (-0.13, 0.31)	0.24 (0.00, 0.48)
Early term x Second quintile	0.10 (-0.04, 0.25)	0.09 (-0.03, 0.20)	0.16 (0.03, 0.29)
Early or moderate preterm x Third quintile	0.04 (-0.33, 0.42)	0.11 (-0.20, 0.43)	0.12 (-0.26, 0.51)
Late preterm x Third quintile	0.00 (-0.24, 0.25)	0.16 (-0.05, 0.38)	0.07 (-0.16, 0.30)
Early term x Third quintile	0.03 (-0.11, 0.16)	0.05 (-0.08, 0.17)	0.03 (-0.09, 0.15)
Early or moderate preterm x Fourth quintile	0.22 (-0.22, 0.65)	-0.12 (-0.46, 0.23)	0.02 (-0.40, 0.43)
Late preterm x Fourth quintile	-0.03 (-0.29, 0.23)	0.01 (-0.22, 0.24)	0.08 (-0.16, 0.32)
Early term x Fourth quintile	-0.03 (-0.16, 0.10)	-0.01 (-0.12, 0.10)	-0.02 (-0.16, 0.11)
Interaction p-values			
Overall	0.54	0.47	0.21

Early or moderate preterm x Lowest quintile	0.76	0.21	0.21
Late preterm x Lowest quintile	0.95	0.54	0.79
Early term x Lowest quintile	0.12	0.56	0.91
Early or moderate preterm x Second quintile	0.72	0.90	0.26
Late preterm x Second quintile	0.12	0.42	0.05
Early term x Second quintile	0.17	0.15	0.01
Early or moderate preterm x Third quintile	0.82	0.48	0.53
Late preterm x Third quintile	0.99	0.13	0.54
Early term x Third quintile	0.70	0.45	0.63
Early or moderate preterm x Fourth quintile	0.33	0.50	0.93
Late preterm x Fourth quintile	0.81	0.96	0.53
Early term x Fourth quintile	0.68	0.88	0.72
Estimated socioeconomic strata-specific contrasts			
Lowest quintile			
Early or moderate preterm	-0.14 (-0.54, 0.25)	-0.26 (-0.54, 0.01)	-0.75 (-1.20, -0.30)
Late preterm	0.01 (-0.26, 0.28)	-0.12 (-0.27, 0.04)	-0.25 (-0.44, -0.07)
Early term	0.07 (-0.06, 0.19)	0.01 (-0.10, 0.11)	-0.11 (-0.23, 0.00)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Second quintile			
Early or moderate preterm	0.01 (-0.26, 0.28)	-0.02 (-0.23, 0.20)	-0.17 (-0.47, 0.13)
Late preterm	0.12 (-0.07, 0.31)	0.04 (-0.11, 0.20)	0.02 (-0.16, 0.19)
Early term	0.04 (-0.06, 0.15)	0.05 (-0.04, 0.14)	0.04 (-0.06, 0.15)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Third quintile			
Early or moderate preterm	-0.02 (-0.29, 0.25)	0.08 (-0.16, 0.32)	-0.29 (-0.53, -0.05)
Late preterm	-0.09 (-0.25, 0.07)	0.12 (-0.10, 0.25)	-0.15 (-0.29, -0.01)
Early term	-0.04 (-0.13, 0.06)	0.01 (-0.08, 0.11)	-0.09 (-0.18, 0.00)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Fourth quintile			
Early or moderate preterm	0.15 (-0.18, 0.48)	-0.15 (-0.43, 0.13)	-0.39 (-0.70, -0.09)
Late preterm	-0.13 (-0.31, 0.06)	-0.04 (-0.20, 0.12)	-0.14 (-0.32, 0.04)

Early term	-0.09 (-0.19, 0.01)	-0.04 (-0.13, 0.04)	-0.15 (-0.24, -0.05)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Highest quintile			
Early or moderate preterm	-0.06 (-0.35, 0.22)	-0.03 (-0.25, 0.18)	-0.41 (-0.71, -0.12)
Late preterm	-0.10 (-0.29, 0.10)	-0.05 (-0.21, 0.11)	-0.22 (-0.39, -0.05)
Early term	-0.06 (-0.16, 0.03)	-0.03 (-0.12, 0.05)	-0.12 (-0.20, -0.04)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales.

Supplemental Table 6.9. Associations between gestational age, household socioeconomic index, and 7-year outcomes (main effects models).

	BAS II Word Reading Scale	BAS II Pattern Construction Scale	NFER Number Skills Assessment
Regression coefficients	**Beta (95% CI)**	**Beta (95% CI)**	**Beta (95% CI)**
Gestational age			
Early or moderate preterm	-0.15 (-0.30, 0.00)	-0.26 (-0.41, -0.11)	-0.28 (-0.42, -0.15)
Late preterm	-0.13 (-0.22, -0.05)	-0.12 (-0.20, -0.04)	-0.09 (-0.16, -0.01)
Early term	-0.05 (-0.10, -0.01)	-0.09 (-0.14, -0.05)	-0.06 (-0.10, -0.01)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Household socioeconomic index			
Lowest quintile	-0.86 (-0.95, -0.77)	-0.63 (-0.72, -0.55)	-0.73 (-0.82, -0.65)
Second quintile	-0.65 (-0.72, -0.59)	-0.52 (-0.59, -0.44)	-0.57 (-0.64, -0.49)
Third quintile	-0.45 (-0.52, -0.39)	-0.37 (-0.43, -0.30)	-0.42 (-0.49, -0.36)
Fourth quintile	-0.24 (-0.30, -0.19)	-0.18 (-0.24, -0.12)	-0.23 (-0.29, -0.17)
Highest quintile	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales. NFER = National Foundation for Education Research.

Supplemental Table 6.10. Associations between gestational age, household socioeconomic index, and 7-year outcomes (interaction models).

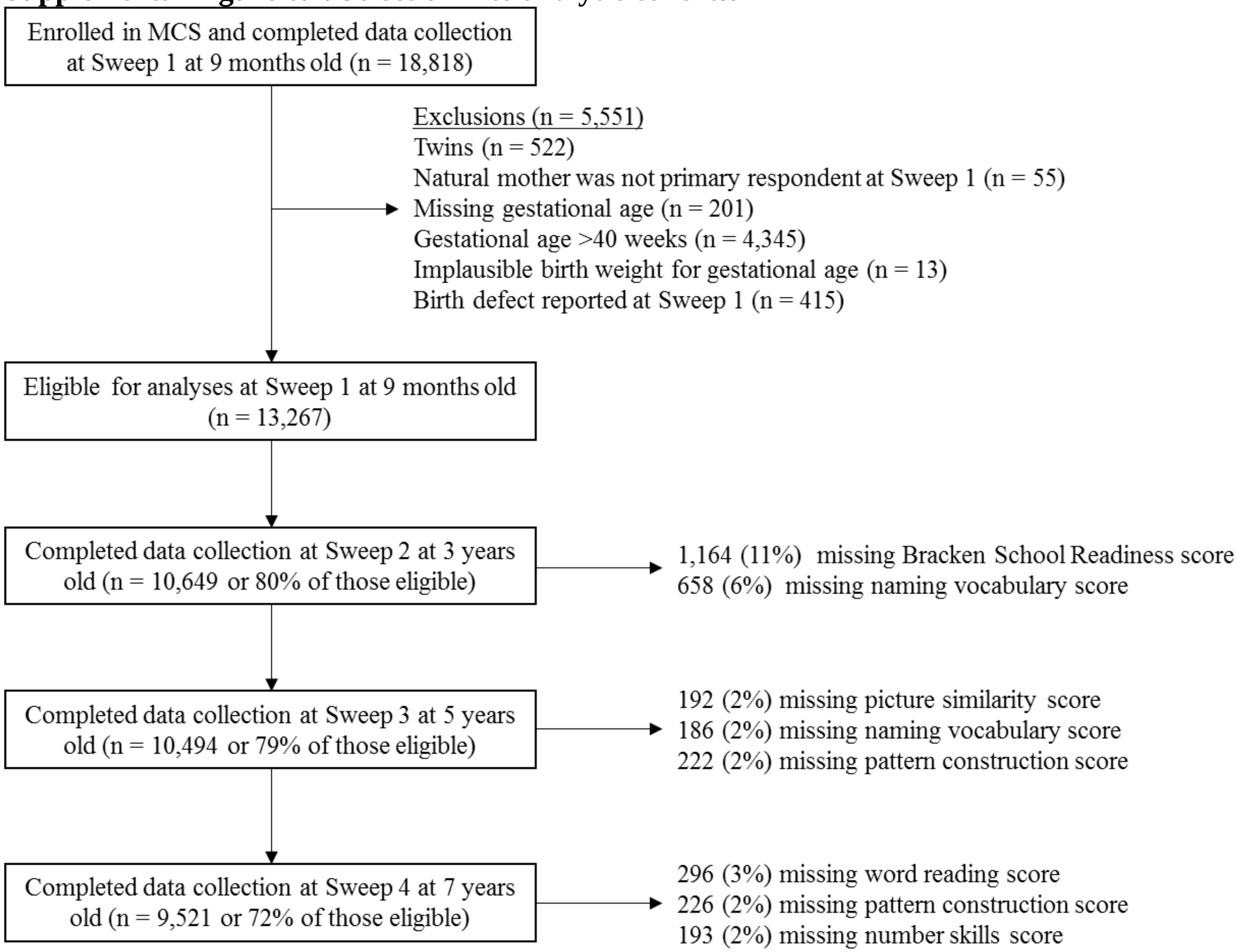
Regression coefficients	BAS II Word Reading Scale Beta (95% CI)	BAS II Pattern Construction Scale Beta (95% CI)	NFER Number Skills Assessment Beta (95% CI)
Gestational age			
Early or moderate preterm	0.01 (-0.26, 0.27)	-0.24 (-0.54, 0.07)	-0.13 (-0.41, 0.15)
Late preterm	-0.10 (-0.26, 0.07)	-0.15 (-0.31, 0.02)	0.01 (-0.16, 0.18)
Early term	-0.02 (-0.10, 0.06)	-0.13 (-0.23, -0.03)	-0.08 (-0.16, 0.01)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Household socioeconomic index			
Lowest quintile	-0.81 (-0.91, -0.71)	-0.66 (-0.76, -0.57)	-0.73 (-0.83, -0.63)
Second quintile	-0.66 (-0.74, -0.58)	-0.57 (-0.65, -0.48)	-0.60 (-0.68, -0.51)
Third quintile	-0.42 (-0.50, -0.35)	-0.35 (-0.43, -0.27)	-0.40 (-0.48, -0.32)
Fourth quintile	-0.24 (-0.31, -0.18)	-0.18 (-0.25, -0.11)	-0.21 (-0.28, -0.14)
Highest quintile	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Interaction terms			
Early or moderate preterm x Lowest quintile	-0.42 (-0.86, 0.03)	-0.08 (-0.59, 0.42)	-0.10 (-0.55, 0.34)
Late preterm x Lowest quintile	-0.16 (-0.44, 0.12)	0.10 (-0.15, 0.36)	-0.16 (-0.39, 0.07)
Early term x Lowest quintile	-0.10 (-0.24, 0.04)	0.10 (-0.06, 0.26)	0.04 (-0.11, 0.19)
Early or moderate preterm x Second quintile	-0.15 (-0.55, 0.25)	0.18 (-0.21, 0.57)	-0.25 (-0.63, 0.14)
Late preterm x Second quintile	-0.03 (-0.28, 0.22)	0.08 (-0.18, 0.34)	-0.10 (-0.35, 0.15)
Early term x Second quintile	0.04 (-0.09, 0.17)	0.17 (0.02, 0.31)	0.16 (0.02, 0.30)
Early or moderate preterm x Third quintile	-0.15 (-0.55, 0.25)	-0.04 (-0.47, 0.40)	-0.17 (-0.55, 0.22)
Late preterm x Third quintile	-0.07 (-0.31, 0.16)	0.04 (-0.19, 0.28)	-0.08 (-0.33, 0.17)
Early term x Third quintile	-0.09 (-0.23, 0.04)	-0.08 (-0.23, 0.07)	-0.05 (-0.19, 0.08)
Early or moderate preterm x Fourth quintile	-0.12 (-0.50, 0.26)	-0.22 (-0.60, 0.16)	-0.21 (-0.60, 0.19)
Late preterm x Fourth quintile	0.05 (-0.19, 0.29)	-0.05 (-0.28, 0.18)	-0.14 (-0.38, 0.10)
Early term x Fourth quintile	-0.02 (-0.14, 0.10)	0.01 (-0.12, 0.15)	-0.04 (-0.17, 0.09)
Interaction p-values			

Overall	0.61	0.15	0.31
Early or moderate preterm x Lowest quintile	0.07	0.74	0.65
Late preterm x Lowest quintile	0.26	0.43	0.17
Early term x Lowest quintile	0.15	0.22	0.58
Early or moderate preterm x Second quintile	0.46	0.37	0.21
Late preterm x Second quintile	0.81	0.55	0.41
Early term x Second quintile	0.57	0.02	0.02
Early or moderate preterm x Third quintile	0.46	0.86	0.39
Late preterm x Third quintile	0.55	0.71	0.55
Early term x Third quintile	0.19	0.31	0.46
Early or moderate preterm x Fourth quintile	0.55	0.26	0.31
Late preterm x Fourth quintile	0.66	0.67	0.25
Early term x Fourth quintile	0.78	0.85	0.58
Estimated socioeconomic strata-specific contrasts			
Lowest quintile			
Early or moderate preterm	-0.41 (-0.79, -0.03)	-0.32 (-0.73, 0.09)	-0.24 (-0.59, 0.12)
Late preterm	-0.26 (-0.48, -0.04)	-0.04 (-0.24, 0.15)	-0.15 (-0.31, 0.00)
Early term	-0.12 (-0.24, -0.01)	-0.03 (-0.15, 0.09)	-0.04 (-0.15, 0.08)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Second quintile			
Early or moderate preterm	-0.15 (-0.46, 0.17)	-0.06 (-0.33, 0.21)	-0.38 (-0.65, -0.11)
Late preterm	-0.12 (-0.30, 0.05)	-0.07 (-0.26, 0.13)	-0.10 (-0.28, 0.09)
Early term	0.02 (-0.09, 0.12)	0.04 (-0.06, 0.14)	0.08 (-0.03, 0.19)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Third quintile			
Early or moderate preterm	-0.15 (-0.45, 0.16)	-0.27 (-0.58, 0.03)	-0.30 (-0.56, -0.04)
Late preterm	-0.17 (-0.35, 0.01)	-0.10 (-0.26, 0.05)	-0.07 (-0.26, 0.12)
Early term	-0.11 (-0.22, 0.00)	-0.21 (-0.31, -0.10)	-0.13 (-0.23, -0.02)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Fourth quintile			

Early or moderate preterm	-0.11 (-0.39, 0.17)	-0.45 (-0.73, -0.18)	-0.34 (-0.64, -0.04)
Late preterm	-0.04 (-0.21, 0.13)	-0.20 (-0.37, -0.02)	-0.13 (-0.29, 0.03)
Early term	-0.04 (-0.13, 0.06)	-0.12 (-0.21, -0.02)	-0.11 (-0.21, -0.02)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)
Highest quintile			
Early or moderate preterm	0.01 (-0.26, 0.27)	-0.24 (-0.54, 0.07)	-0.13 (-0.41, 0.15)
Late preterm	-0.10 (-0.26, 0.07)	-0.15 (-0.31, 0.02)	0.01 (-0.16, 0.18)
Early term	-0.02 (-0.10, 0.06)	-0.13 (-0.23, -0.03)	-0.08 (-0.16, 0.01)
Term	0.00 (Reference)	0.00 (Reference)	0.00 (Reference)

Cognitive scores are standardized to the normal distribution with mean of 0 and standard deviation of 1. Beta coefficients represent standard deviation changes. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). BAS = British Ability Scales. NFER = National Foundation for Education Research.

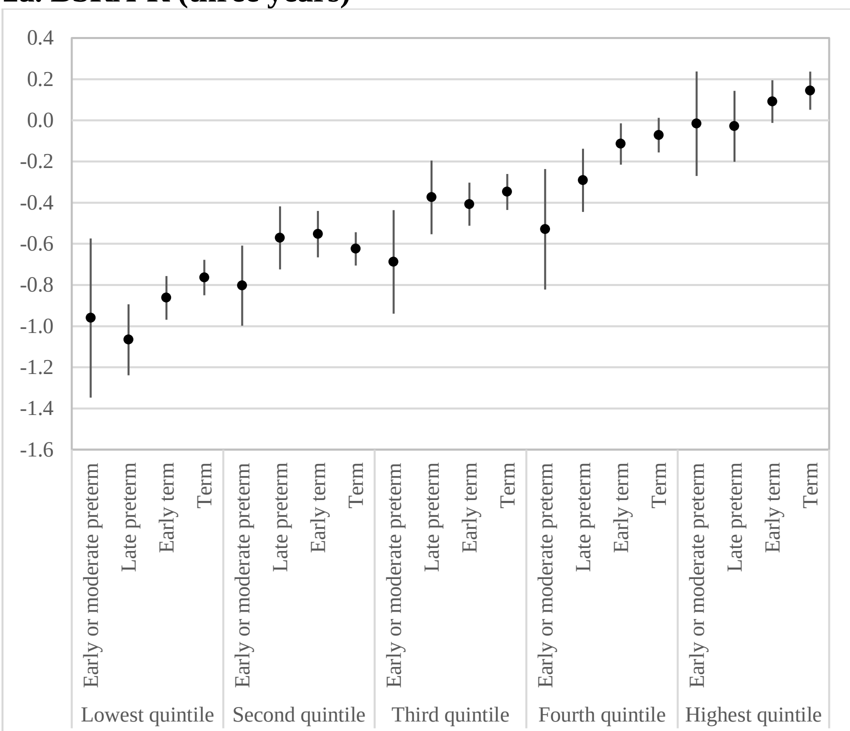
Supplemental Figure 6.1. Selection into analytic cohorts.



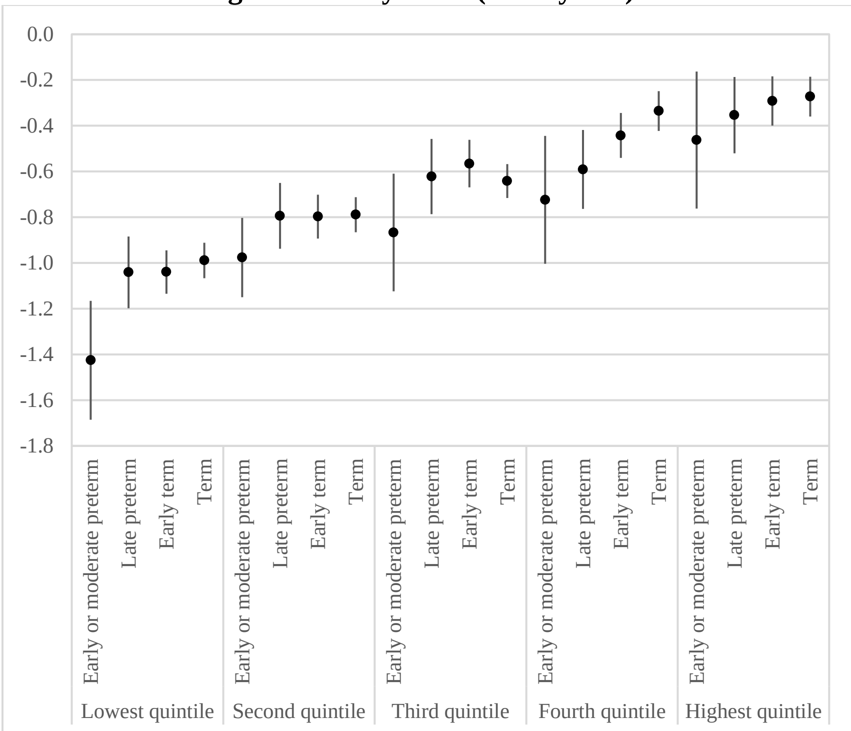
Supplemental Figure 6.2(a)-(h). Model-predicted scores on cognitive and academic achievement assessments at three, five, and seven years old.

NOTE: Error bars reflect 95% confidence intervals. All models adjusted for child's race/ethnicity (Black, Indian, Mixed, Pakistani/Bangladeshi, White, Other), number of siblings in the household (none, 1-2, 3 or more), household structure (two-parent household, single mother), mother's age at delivery (14-17 years, 18-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40 or more years), and child's sex (male, female). Predicted scores are based on sample mean covariate values. BSRA-R = Bracken School Readiness Assessment-Revised. BAS = British Ability Scales. NFER = National Foundation for Education Research.

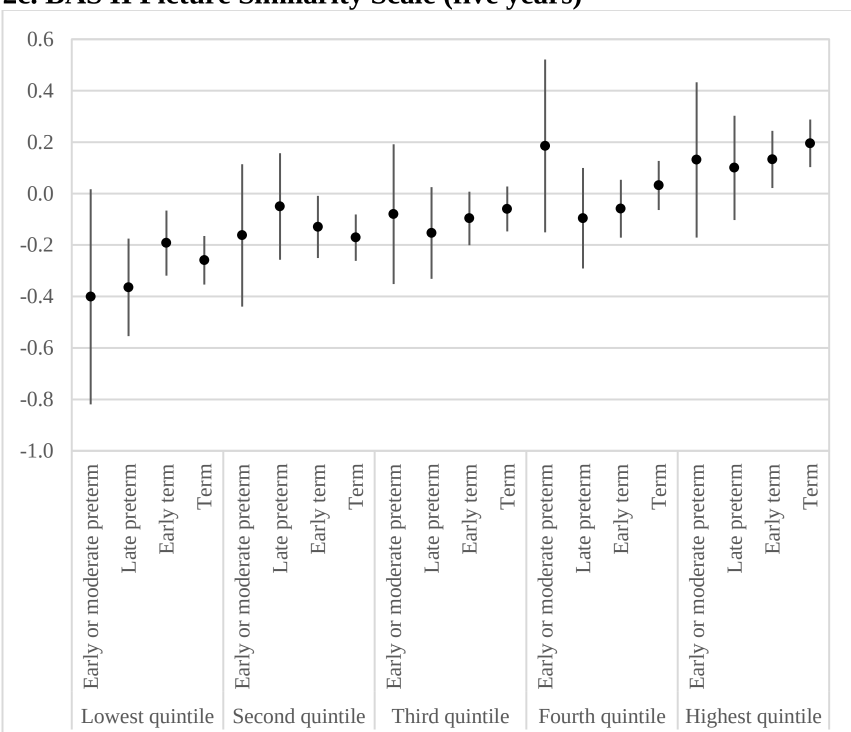
2a. BSRA-R (three years)



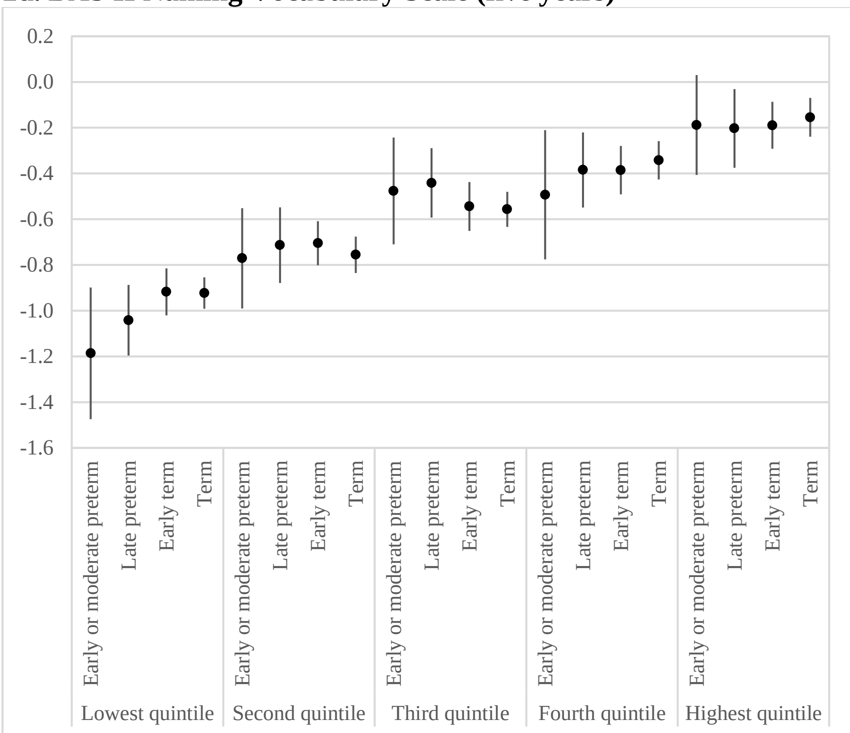
2b. BAS II Naming Vocabulary Scale (three years)



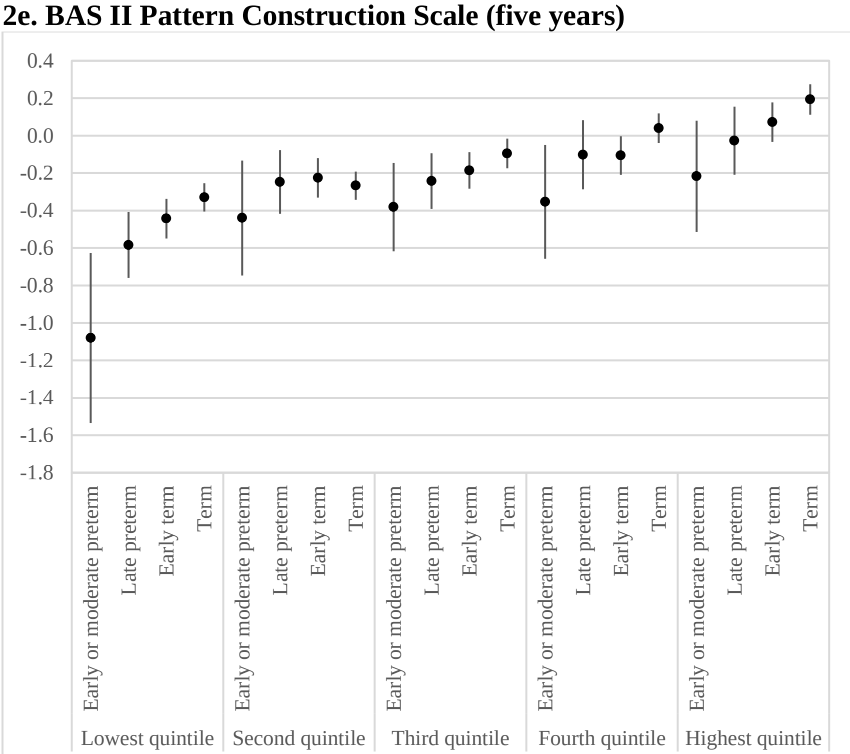
2c. BAS II Picture Similarity Scale (five years)



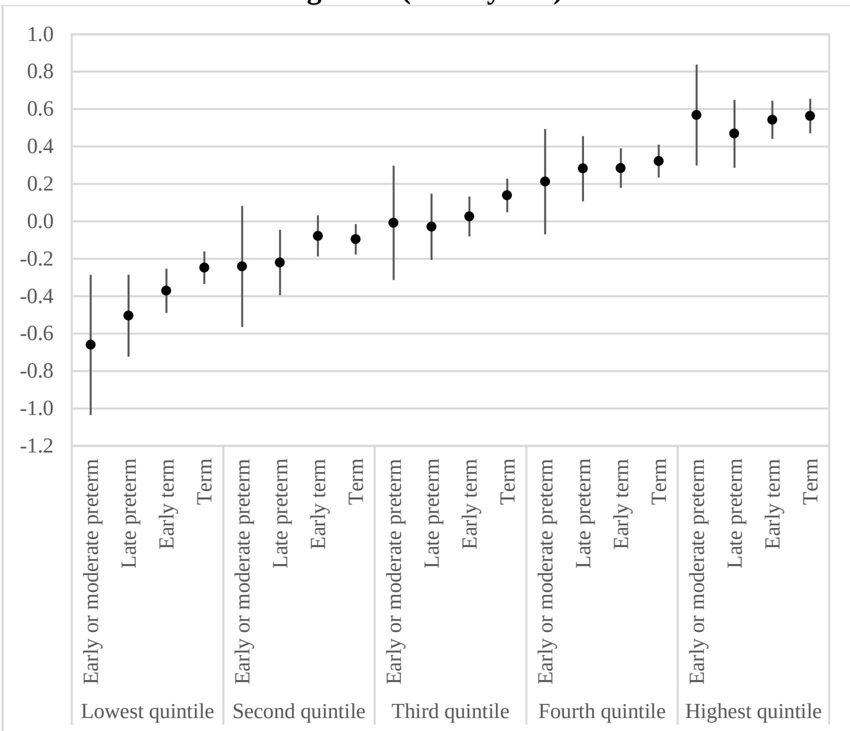
2d. BAS II Naming Vocabulary Scale (five years)



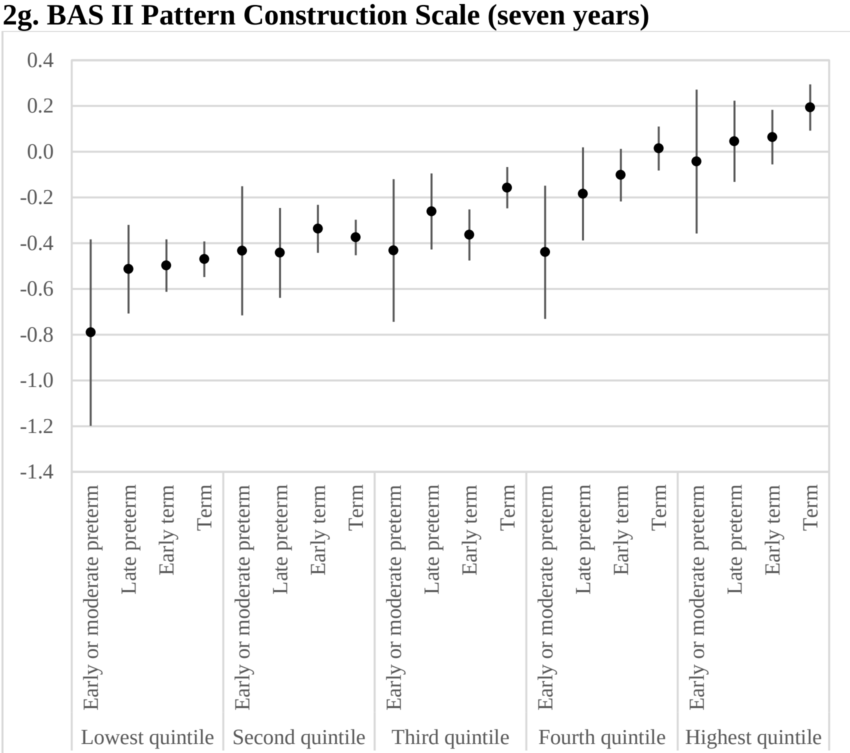
2e. BAS II Pattern Construction Scale (five years)



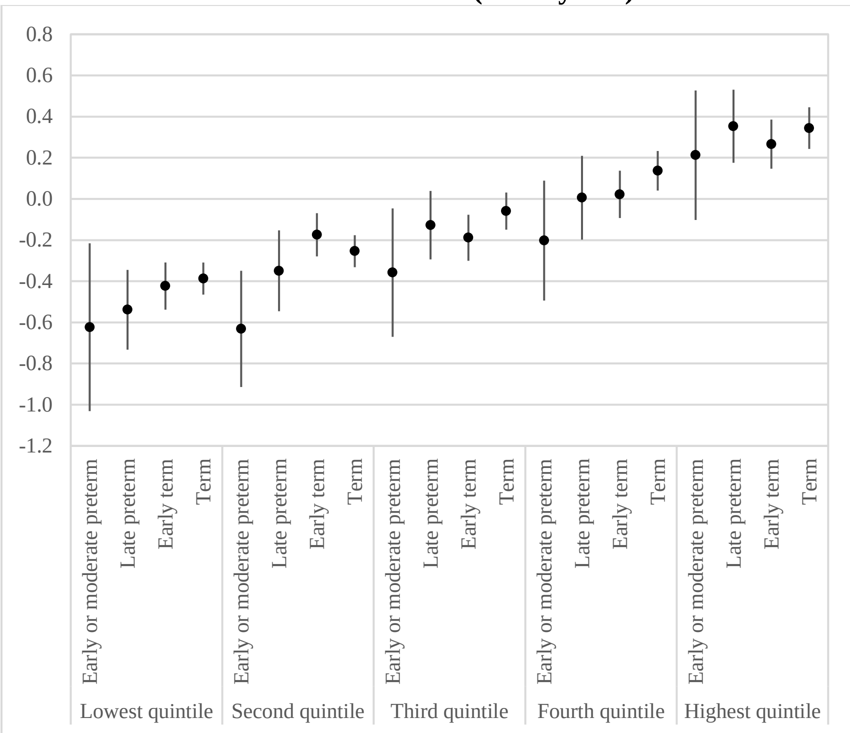
2f. BAS II Word Reading Scale (seven years)



2g. BAS II Pattern Construction Scale (seven years)



2h. NFER Number Skills Assessment (seven years)



Chapter 7: Conclusions and Future Directions

7.1 Summary of Findings

This dissertation investigated the joint impacts of preterm and early term birth and socioeconomic status in early childhood on children's cognitive and academic outcomes using data from large, longitudinal birth cohort studies in the United State and the United Kingdom. Our findings suggest that both preterm and early term birth and lower socioeconomic status adversely affected children's cognitive and academic outcomes, with those children who are "doubly exposed" performing at the lowest levels. In general, there was no evidence that socioeconomic status acted as an effect modifier of the relationship between preterm and early term birth and children's outcomes. Rather, the impacts of the risk factors on children's outcomes appeared to be strictly additive. Given that both preterm and early term birth and childhood poverty are prevalent in both countries studied in this dissertation, our findings continue the call for understanding and addressing the impact of these risk factors on children's early cognitive development, performance in school, and chances for educational and socioeconomic success continuing into adulthood. From a population perspective, this dissertation provides compelling evidence that children who are both born preterm or early term and living in poverty should be a high priority for early childhood interventions.

In the first study of this dissertation (**Aim 1; Chapter 4**), we described the shapes of the relationships between gestational age and children's early cognitive outcomes at two years old and academic achievement outcomes at kindergarten entry. This study used data on singleton children born at 24-42 weeks gestation in the Early Childhood Longitudinal Study-Birth Cohort (n = 6,150 at two years old; n = 4,450 at kindergarten age). The purpose of this formative aim was to more fully understand the patterns of cognitive and academic scores with each additional week of gestation, since most previous studies have categorized gestational age in some way. We also compared multiple approaches for modeling the full range of gestational age in order to inform our choice of how to measure gestational age for the remainder of this dissertation.

We found that children born at early preterm, moderate preterm, and late preterm exhibited deficits in cognitive ability at two years old and reading and mathematics achievements scores at kindergarten age compared with children born at full term. The magnitude of estimated deficits increased with decreasing gestational age. On the two-year Bayley Short Form-Research Edition (BSF-R) Mental Scale, the mean score was 126.1 (standard deviation [SD] = 11.0, range 92.4-174.1). Significant deficits were observed for early preterm (-6.6 points, 95% CI: -8.1, -5.0), moderate preterm (-2.9 points, 95% CI: -4.0, -1.8), and late preterm (-1.3 points, 95% CI: -2.3, -0.4) compared with term. On the kindergarten reading assessment, the mean score was 44.4 (SD = 14.8, range 12.4-82.5). Significant deficits were observed for early preterm (-5.1 points, 95% CI: -7.2, -3.0), moderate preterm (-3.0 points, 95% CI: -4.3, -1.8), and late preterm (-1.8 points, 95% CI: -3.3, -0.4). On the kindergarten mathematics assessment, the mean score was 43.9 (SD = 10.5, range 11.2-69.7). Again, significant deficits were observed for early preterm (-6.7 points, 95% CI: -8.5, -4.9), moderate preterm (-3.6 points, 95% CI: -4.6, -2.7), and late preterm (-1.6 points, 95% CI: -2.6, -0.6). In our comparison of multiple approaches for modeling gestational age, we found that categories defined by the American Congress of Obstetricians and Gynecologists (ACOG) were a useful, parsimonious approach for capturing the overall patterns in cognitive and achievement scores by gestational age.

The second and third studies of this dissertation explicitly tested the presence of additive interaction between gestational age and socioeconomic status in their effects on children's cognitive and academic outcomes, to evaluate the hypothesis that socioeconomic status acts as a modifier of the effect of preterm and early term birth on these outcomes. Examining potential causal relationships in multiple cohorts with different confounding structures can be informative; if similar results are found in such cohorts, this evidence may strengthen arguments for or against a potentially causal relationship between exposure and outcome. The MCS and the ECLS-B were similar in terms of timing of enrollment, with both enrolling children born in 2001; timing of data collection over longitudinal follow-up, with both studies collecting data at 9 months, 2-3 years, and 5 years (plus additional later time points in the case of MCS); and collection of a large breadth of data on birth conditions, socioeconomic status, as well as direct assessments of children's cognitive abilities and academic achievement.

In the second study of this dissertation (**Aim 2; Chapter 5**), we found that preterm birth and lower household socioeconomic status exerted independent adverse effects on children's early cognitive outcomes at two years old and academic achievement at kindergarten entry, although there was no evidence of additive interaction between the two risk factors. This study used data on singleton children born at 24-40 weeks in the Early Childhood Longitudinal Study-Birth Cohort (n = 5,250 children at two years old; n = 3,800 at kindergarten). On the two-year BSF-R Mental Scale, the mean score was 126.2 (SD = 11.0, range 92.4-174.1). Main effects models showed that there were significant deficits for children born at early preterm (-7.0 points, 95% CI: -8.6, -5.4), moderate preterm (-2.9 points, 95% CI: -4.1, -1.7), and late preterm (-1.3 points, 95% CI: -2.3, -0.3) compared with term. Children in the lowest socioeconomic quintile (defined using a composite of parental education, occupation, and income) scored 6.7 points (95% CI: 5.6, 7.6) lower than those in the highest quintile. On the kindergarten reading scale, the mean score was 44.6 (SD = 14.9, range 12.4-82.5). Main effects models showed that there were significant deficits for children born at early preterm (-5.3 points, 95% CI: -7.7, -3.0), moderate preterm (-2.6 points, 95% CI: -3.9, -1.3), and late preterm (-1.5 points, 95% CI: -3.0, 0.0) compared with term. Children in the lowest SES quintile scored 12.6 points (95% CI: 10.9, 14.4) lower than those in the highest quintile. On the kindergarten mathematics scale, the mean score was 44.0 (SD = 10.5, range 11.2-69.7). Main effects models showed that there were significant deficits for children born at early preterm (-6.6 points, 95% CI: -8.5, -4.7), moderate preterm (-3.2 points, 95% CI: -4.3, -2.1), and late preterm (-1.4 points, 95% CI: -2.5, -0.4). Again, children in the lowest SES quintile scored substantially lower than those in the highest quintile, with a deficit of 9.1 points (95% CI: 7.9, 10.2).

For all three outcomes, there was no evidence of additive interaction through testing the statistical significance of interaction terms, suggesting that living in more deprived socioeconomic circumstances neither exacerbated nor attenuated the estimated effects of preterm birth on cognitive and achievement scores. Plots of model-predicted scores by strata of gestational age and SES quintile demonstrated that the estimated joint effects of the two risk factors were additive. Predicted scores were generally highest for term children in the highest SES quintile and lowest for early preterm children in the lowest SES quintile. Patterns of deficits associated with earlier gestational age group were relatively consistent across SES quintiles; however, as a group, each lower SES quintile scored worse. Children who were doubly exposed to both preterm birth and lower household SES performed at the lowest levels on all outcomes.

The findings of the third study of this dissertation (**Aim 3; Chapter 6**) were similar to those of the second study in that we did not find statistical evidence of additive interaction between gestational age and poverty in their effects on children's cognitive outcomes. In this study, we were able to analyze children's outcomes not only in early childhood and at the age of school entry, but also in middle childhood at seven years old after they had had several years of exposure to school—which may potentially play an equalizing role or exacerbate differences between children living in better-off or worse-off areas and families. The data source for this study was singleton children born at 24-40 weeks in the MCS (n = 10,649 at three years old; n = 10,494 at five years old; n = 9,521 at seven years old).

We found that preterm birth was associated with deficits on most MCS cognitive assessments with the exception of picture similarity and naming vocabulary assessments at five years old. Living in poverty in early childhood was associated with deficits on all MCS cognitive assessments. At three years old, there were approximately 0.3-0.4 SD deficits for early or moderate preterm and 0.1 SD deficits for late preterm children on the Bracken School Readiness assessment and the British Ability Scales II (BAS II) naming vocabulary assessment. Children living in poverty scored 0.3-0.4 SD worse than those not living in poverty. At five years old, there was a significant effect of preterm birth for the BAS II pattern construction score but not for the BAS II picture similarity or naming vocabulary scales. On the pattern construction assessment, significant deficits were observed for early or moderate preterm (-0.38 SD, 95% CI: -0.52, -0.24), late preterm (-0.15 SD, 95% CI: -0.23, -0.08), and early term (-0.09 SD, 95% CI: -0.13, -0.05) compared with term. Living in poverty was associated with a 0.2-0.3 SD deficit in score on all five-year assessments. At seven years old, significant deficits were observed for early or moderate preterm (about 0.2-0.4 SD), late preterm (about 0.1 SD), and early term (about 0.05-0.1 SD) compared with term, and children living in poverty scored 0.3-0.4 SD lower than children who were not living in poverty. The pattern of results across assessment ages suggests that deficits associated with preterm birth persist at least through seven years old; notably, if our analyses stopped at the five-year assessments, we might have concluded that the estimated effects of preterm birth appear to wane by five years. The persistence of deficits up through seven years old suggests that other factors may be responsible for the lack of gestational age effect on some five year assessments, such as the level of cognitive workload required by those specific tests. Further, we observed a persistent effect of living in poverty that roughly equaled the impact of being born early or moderate preterm.

While there was no evidence of additive interaction between gestational age and poverty for most cognitive outcomes studied in Aim 3, some significant findings must be noted. On the seven-year word reading scale, we found that the estimated deficit for early or moderate preterm children compared with term was larger among children living in poverty, compared with children not living in poverty. This finding is in line with the hypothesis that growing up in lower socioeconomic settings exacerbates the adverse impacts of preterm birth.[84,85,99,101] However, on the seven-year pattern construction scale, we found a significant deficit associated with early term birth among children who were not living in poverty, but no effect of early term birth among children living in poverty. This contrasting finding is in line with the hypothesis that the estimated effect of preterm birth may be attenuated among children living in lower socioeconomic settings, due to the profound impact of poverty on cognitive development—in other words, that the dual impacts of these two risk factors reach a threshold "floor".[90–92]

Collectively, findings from Aims 2 and 3 suggest that preterm birth and childhood poverty—or lower socioeconomic status—each adversely impact children's cognitive and academic achievement scores. We found that early term children performed slightly worse than full term children on most cognitive and achievement tests studied in this dissertation; however, the deficits were only statistically significant on the seven-year assessments in the MCS. While a number of recent studies have found a detrimental effect of early term birth on children's cognitive and school outcomes,[132,157] this has not been found in all studies.[158]

This dissertation sought specifically to assess the presence of additive interaction between gestational age and childhood socioeconomic status in their effects on cognitive and academic outcomes. Additive interaction is informative from a public health perspective because it directly estimates the excess risk associated with interaction between the two factors. Assessing additive interaction can provide information on the absolute reduction in risk or continuous outcome that a certain sub-group would experience if the exposure were removed. Estimation of strata-specific absolute measures can also enable us to identify high-risk sub-groups for targeting of interventions to those groups. In Aims 2 and 3, we found that the joint impacts of preterm birth and lower socioeconomic status were additive; socioeconomic status was not found to be an effect modifier of the relationship between preterm birth and these outcomes. Even in the absence of statistical evidence for interaction, we examined the impacts of being doubly exposed by plotting model-predicted cognitive and achievement scores by strata of gestational age and socioeconomic status. This revealed the profound impact of living in a family in poverty or with lower socioeconomic status; “baseline” scores—or predicted scores for the term reference group—were substantially lower among children of lower versus higher socioeconomic status. When comparing across socioeconomic strata, the within-strata estimated effects of earlier gestational age compared with term were relatively consistent. The summation of the effects of these two risk factors revealed a compelling message in the gradient in predicted scores with term, high socioeconomic status children performing the best all the way down to early preterm, low socioeconomic status children performing the worst. Children who were doubly exposed to both early delivery and lower socioeconomic status were predicted to fare the worst. From a public health perspective, this strongly suggests that both factors should be taken into account when targeting high-risk groups for early childhood interventions to support cognitive development.

7.2 Strengths and Limitations

A major strength of this dissertation is our use of data from two large, nationally representative longitudinal studies of children enrolled close to birth and followed through childhood. These datasets provided high quality data on gestational age and early socioeconomic status, as well as prospective, direct assessments of children's cognitive development and academic achievement.

The use of data from population-based cohort studies, however, comes with some limitations in terms of studying the cognitive and academic outcomes of early life exposures like preterm birth and childhood poverty. First, while sample sizes from both the ECLS-B and MCS were large overall, stratification by both gestational age and socioeconomic status resulted in comparatively sparse data for some groups. Second, there is a possibility that sicker preterm children and families living in poverty were less likely to enroll in these complex, multi-year studies. Guarding against the possibility of resulting bias is the fact that both studies accounted for non-response in generating sample weights. We did not employ sampling weights in our main analyses because we were primarily interested in estimating internally valid relationships between exposure, modifier, and outcome rather than ensuring that our findings were nationally representative for the United States and United Kingdom. However, we did account for sampling weights in sensitivity analyses for all three dissertation studies, and found that this did not meaningfully change our findings in any of the studies. We also examined factors associated with dropping out of the two studies in order to better understand the potential for resulting selection bias. In the ECLS-B, children who dropped out of the study between the two-year and kindergarten waves were more likely to be non-Hispanic white, be preterm, live in poverty, and have younger and less educated mothers. Reassuringly, however, they did not differ in terms of their two-year cognitive scores, and application of inverse probability of censorship weights in a sensitivity analyses to account for drop-out did not meaningfully change our results. In the MCS, retention was high across the three-, five-, and seven-year follow-ups. Comparison of cohort characteristics for eligible children across the nine-month and three later follow-up time points showed that the gestational age distribution remained relatively constant, but children who remained in the study at seven years were slightly less likely to have lived in poverty at nine months.

Using data from both the ECSL-B and MCS, we were able to analyze outcomes of the same population of children as they grew and developed from early childhood to kindergarten age (ECLS-B) and from early childhood to middle childhood after children had been through several years of schooling (MCS). There are numerous factors that may impact variation in findings from studies of cognitive outcomes of preterm children, including study populations (e.g., hospital- versus population-based, range of gestational age studied), specific outcomes studied, how investigators measured those outcomes, ages at which children were assessed, and our studies benefitted from having measurements at multiple ages within the same populations. Unfortunately, due to the fact that no common cognitive assessment was administered at multiple ages in either the ECLS-B or MCS, we were not able to analyze trajectories of cognitive growth by gestational age and socioeconomic status. Future studies could, for example, examine whether socioeconomic status plays a modifying role in whether cognitive outcomes of preterm children compared with term improve, deteriorate, or remain stable over time.

In our studies of modification of the effect of preterm birth on cognitive and academic outcomes by socioeconomic status, we treated preterm and early term birth and socioeconomic status as independent risk factors influencing children’s outcomes. However, it is known that socioeconomic status affects women’s risk of preterm birth and therefore it is conceivable that socioeconomic status influences both our exposure of preterm or early term birth and children's later outcomes. Further, children's cognitive outcomes may be influenced not only by their own experiences of socioenvironmental conditions, but also by the socioeconomic contexts of their parents and grandparents. In this dissertation, we measured children's socioeconomic status once in early childhood, and treated it as a static condition that may potentially modify risks of adverse cognitive outcomes. Future studies should investigate how intergenerational processes of socioeconomic deprivation and inequality impact risks of preterm births, as well as potentially modify children's cognitive trajectories.

7.3 Public Health Implications and Future Directions

Both preterm birth and childhood poverty are important public health problems in the United States and the United Kingdom. In both countries, 8-10% of children are born preterm[2,17] and 25-30% of children live in poverty with another large proportion living in lower-income families.[3,4] In this dissertation, we found that preterm birth and lower socioeconomic status each adversely impact children's cognitive and academic scores in early childhood, at the age of entering school, and in middle childhood. Cognitive ability in early childhood and being prepared to enter school are important predictors of children's later social and academic success as well as their socioeconomic and health trajectories over the life course into adulthood.[64–66]

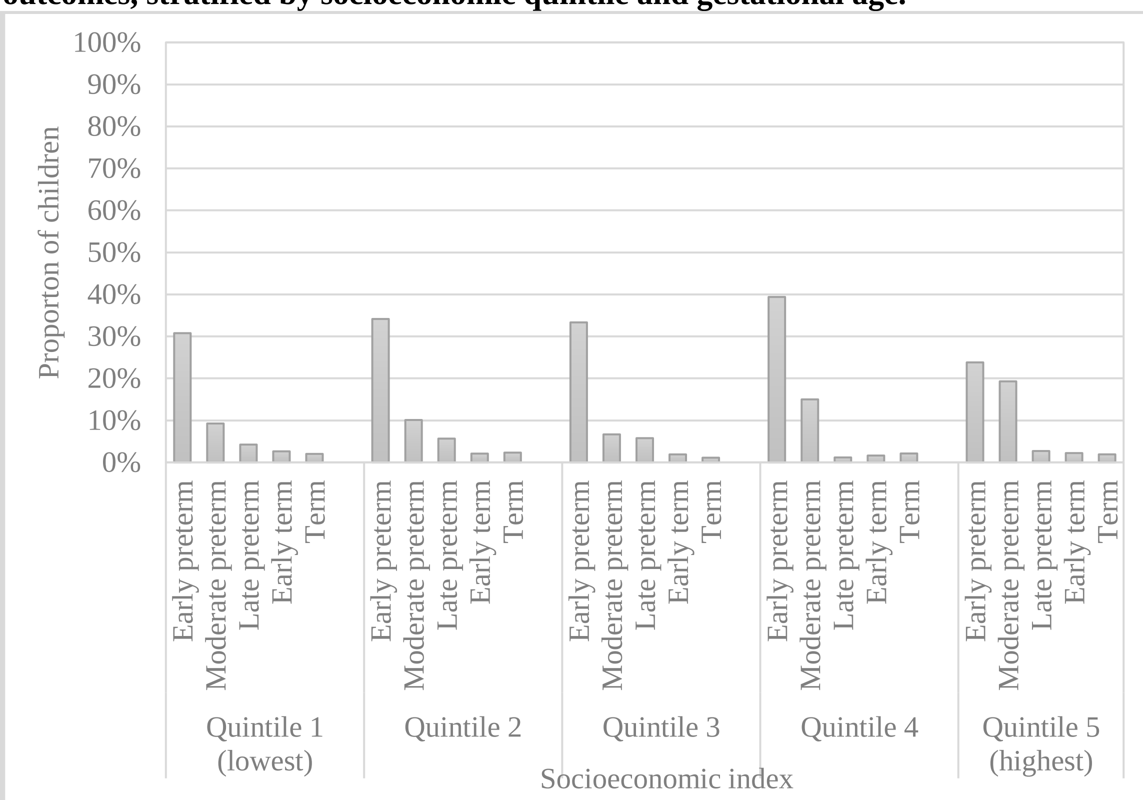
From a public health perspective, the major finding of this dissertation is that children exposed to both preterm birth and childhood poverty are suffering from the additive impacts of these two adverse exposures. Our unadjusted findings showed overwhelmingly that when stratified by both gestational age and poverty, doubly exposed children performed at the lowest levels, and these findings persisted in multivariable analyses. Our findings echo the call for early intervention for children who are born preterm and/or are being raised in poverty, and perhaps most importantly, for children affected by both.

Early interventions targeted at developmental outcomes focus on areas such as enhancing the parent-infant relationship; parent support or education about skills development; and improvements to enhance the home environment to be more supportive of learning.[159] Early intervention services may also include services for the child such as provision of assistive technology, hearing services, speech and language services, medical services, nutrition services, occupational therapy, physical therapy, and psychological services.[160] All of these services may be implemented through home- or center-based programs, or combinations thereof. According to a 2015 Cochrane review of 25 trials spanning infancy to adulthood, early intervention programs for preterm infants positively impact cognitive outcomes in infancy and into preschool age although long-term benefits were unclear due to the small number of studies that have been conducted.[159]

An important issue related to early interventions is access to these services. In the United States, federally mandated and state coordinated Part C Early Intervention (EI) programs provide early intervention services to children under three years old with disabilities or suspected developmental delays regardless of financial status. While states vary in terms of specific eligibility criteria, generally children are eligible for Part C early intervention programs if they have a developmental delay (in the five domains of cognitive development, motor development, communication development, social or emotional development, and adaptive behavior), diagnosed condition that is highly likely to result in developmental delay (e.g., cerebral palsy, Down syndrome), or are considered "at risk" (e.g., children affected by child abuse or neglect).[161,162] Rates of referral to EI programs are reportedly high in some states,[163] but several studies have noted that rates of enrollment and use by eligible children are low and vary across states.[163–165] Among ECLS-B children included in Chapter 5 analyses of this dissertation, we found that parent-reported receipt of EI services by 2 years old was low (Figure 7.1). Parents of early preterm children reported that 24% received early intervention services by 9 months old and 33% received such services by 2 years old, although most of these children should fall into the extremely preterm or low birth weight eligibility criterion for Part C EI programs. Interestingly, these rates did not vary substantially by SES, although we found in this dissertation that children who are born both preterm and in lower SES families perform at the lowest levels on cognitive assessments. Reasons for low rates of early intervention use for these extremely preterm children may include lack of referrals or access to early intervention services for children who should be receiving services.[162] More research is needed to elucidate potential barriers to accessing early intervention services.

Additionally, while our findings in this dissertation confirm that moderate and late preterm children—and in the case of some MCS outcomes, early term—also experience cognitive deficits, but these children may not be eligible for services through Part C EI programs unless they show early signs of developmental delays because they do not fall under state-specific birth weight cut-offs. Among ECLS-B children, rates of early intervention services were much lower in these groups, with 11% of moderate preterm and 4% of late preterm children receiving early intervention services by 2 years old (Figure 7.1). For these children who are born more mildly premature, questions remain regarding availability and access to early intervention services, including whether these children should be considered eligible for federally funded EI programs and how else to ensure that these children—who, while not extremely premature, are still at risk of worsened cognitive and academic outcomes—receive services that could benefit them.

Figure 7.1. Receipt of early intervention services by 2 years old among singleton children enrolled in ECLS-B and included in Chapter 5 analyses for 2-year outcomes, stratified by socioeconomic quintile and gestational age.



Finally, putting the findings of this dissertation in context, it is important to note that our studies focused on assessment of children’s cognitive development and academic achievement using specific suites of ability and achievement tests. There may be different results when studying the actual physical growth and development of children's brains. Studies utilizing neuroimaging show that both preterm birth and childhood poverty adversely affect the physical growth and development of children's brains. Children born at very early gestational ages are at higher risk for brain injuries such as intraventricular hemorrhage and white matter injuries such as periventricular leukomalacia,[166,167] and such injuries have been linked with cognitive deficits.[168] Besides direct injury to the brain, preterm birth also affects brain volume overall and in specific areas linked to cognitive functions; these deficits have also been linked with worse developmental outcomes.[22,23] Similarly, worse socioeconomic conditions have been linked to smaller brain volumes.[68,69] Future neuroimaging studies should investigate the joint influences of preterm birth and socioeconomic status on brain growth and development.

Similarly, future studies should also explore the joint impacts of preterm birth and socioeconomic status on children's educational outcomes at school. Performance in school requires not only cognitive abilities but also aptitude in areas such as socioemotional skills, behavior, executive function, and attention. Only one study of interaction between preterm birth and socioeconomic status has analyzed school-related outcomes in mid-childhood; this study found that higher levels of neighborhood deprivation exacerbated the estimated adverse impacts of preterm birth on children's likelihood of failing their first grade statewide standardized tests.[99] Children's experiences of individual-poverty or deprivation may be compounded by the influences of lower school and teacher quality in impoverished neighborhoods once they enter school. The quality of children's preschool and school experiences may play a critical role in attenuating or exacerbating the influences of their early biological and social exposures.

In conclusion, the findings of this dissertation contribute to the state of knowledge about the impacts of preterm birth and socioeconomic status on children's cognitive and academic outcomes in a few important ways. We described cognitive outcomes along the full range of gestational age in a population-based US birth cohort, and found that categories defined by ACOG were a useful, parsimonious approach for capturing the overall patterns in these outcomes by gestational age. In population-based birth cohorts in both the US and the UK, we found that socioeconomic status did not act as an effect modifier of the relationship between preterm or early term birth and children's cognitive outcomes. Rather, the estimated effects of these two risk factors were additive, still resulting in doubly exposed children having the lowest cognitive scores at multiple time points spanning early to middle childhood. Efforts are needed to target these highest risk children for early childhood interventions that may help to improve their cognitive development and academic success.

References

1. Hamilton BE MJ Osterman MJK, Curtin SC. Births: preliminary data for 2013. *Natl Vital Stat Rep*. 2014;63(2). http://www.cdc.gov/nchs/data/nvsr/nvsr63/nvsr63_02.pdf.

2. Birth characteristics - Office for National Statistics. http://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/datasets/birthcharacteristicsinenglandandwales. Accessed October 25, 2016.

3. NCCP | Basic Facts About Low-income Children. http://www.nccp.org/publications/pub_1076.html. Accessed November 18, 2014.

4. Households below average income: 1994/95 to 2014/15 - Publications - GOV.UK. https://www.gov.uk/government/statistics/households-below-average-income-199495-to-201415. Accessed November 7, 2016.

5. Messer LC, Vinikoor LC, Laraia BA, et al. Socioeconomic domains and associations with preterm birth. *Soc Sci Med*. 2008;67(8):1247-1257. doi:10.1016/j.socscimed.2008.06.009.

6. Snelgrove JW, Murphy KE. Preterm birth and social inequality: assessing the effects of material and psychosocial disadvantage in a UK birth cohort. *Acta Obstet Gynecol Scand*. 2015;94(7):766-775. doi:10.1111/aogs.12648.

7. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *The Lancet*. 2008;371(9606):75-84. doi:10.1016/S0140-6736(08)60074-4.

8. Blencowe H, Cousens S, Chou D, et al. Born Too Soon: The global epidemiology of 15 million preterm births. *Reprod Health*. 2013;10(Suppl 1):S2. doi:10.1186/1742-4755-10-S1-S2.

9. Muglia LJ, Katz M. The enigma of spontaneous preterm birth. *N Engl J Med*. 2010;362(6):529-535. doi:10.1056/NEJMra0904308.

10. Loftin RW, Habli M, Snyder CC, Cormier CM, Lewis DF, DeFranco EA. Late preterm birth. *Rev Obstet Gynecol*. 2010;3(1):10-19.

11. ACOG Committee Opinion No. 579: Definition of term pregnancy. *Obstet Gynecol*. 2013;122(5):1139-1140.

12. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. *The Lancet*. 2015;385(9966):430-440. doi:10.1016/S0140-6736(14)61698-6.

13. Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. *The Lancet*. 2012;379(9832):2162-2172. doi:10.1016/S0140-6736(12)60820-4.

14. Chang HH, Larson J, Blencowe H, et al. Preventing preterm births: analysis of trends and potential reductions with interventions in 39 countries with very high human development index. *The Lancet*. 2013;381(9862):223-234. doi:10.1016/S0140-6736(12)61856-X.

15. Zeitlin J, Szamotulska K, Drewniak N, et al. Preterm birth time trends in Europe: a study of 19 countries. *BJOG*. 2013;120(11):1356-1365. doi:10.1111/1471-0528.12281.

16. Zeitlin J, Mortensen L, Cuttini M, et al. Declines in stillbirth and neonatal mortality rates in Europe between 2004 and 2010: results from the Euro-Peristat project. *J Epidemiol Community Health*. December 2015:jech-2015-207013. doi:10.1136/jech-2015-207013.

17. Hamilton BE, Martin JA, Osterman MJ, Curtin SC, Mathews T. Births: Final data for 2014. http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_12.pdf. Published December 23, 2015. Accessed July 22, 2016.

18. Institute of Medicine (US) Committee on Understanding Premature Birth and Assuring Healthy Outcomes. *Preterm Birth: Causes, Consequences, and Prevention*. (Behrman RE, Butler AS, eds.). Washington (DC): National Academies Press (US); 2007. http://www.ncbi.nlm.nih.gov/books/NBK11362/. Accessed August 18, 2014.

19. Thompson RA. Development in the first years of life. *Future Child*. 2001;11(1):21-33. doi:10.2307/1602807.

20. Guihard-Costa A-M, Larroche J-C. Differential growth between the fetal brain and its infratentorial part. *Early Hum Dev*. 1990;23(1):27-40. doi:10.1016/0378-3782(90)90126-4.

21. Kinney HC. The near-term (late preterm) human brain and risk for periventricular leukomalacia: A review. *Semin Perinatol*. 2006;30(2):81-88. doi:10.1053/j.semperi.2006.02.006.

22. Keunen K, Kersbergen KJ, Groenendaal F, Isgum I, de Vries LS, Benders MJNL. Brain tissue volumes in preterm infants: prematurity, perinatal risk factors and neurodevelopmental outcome: A systematic review. *J Matern Fetal Neonatal Med*. 2012;25(S1):89-100.

23. de Kieviet JF, Zoetebier L, van Elburg RM, Vermeulen RJ, Oosterlaan J. Brain development of very preterm and very low-birthweight children in childhood and

adolescence: a meta-analysis. *Dev Med Child Neurol*. 2012;54(4):313-323. doi:10.1111/j.1469-8749.2011.04216.x.

24. Peterson BS, Anderson AW, Ehrenkranz R, et al. Regional brain volumes and their later neurodevelopmental correlates in term and preterm infants. *Pediatrics*. 2003;111(5 Pt 1):939-948.

25. Burd I, Balakrishnan B, Kannan S. Models of fetal brain injury, intrauterine inflammation, and preterm birth. *Am J Reprod Immunol*. 2012;67(4):287-294. doi:10.1111/j.1600-0897.2012.01110.x.

26. Weisglas-Kuperus N, Baerts W, Smrkovsky M, Sauer PJ. Effects of biological and social factors on the cognitive development of very low birth weight children. *Pediatrics*. 1993;92(5):658-665.

27. Ment LR, Vohr B, Allan W, et al. Change in cognitive function over time in very low-birth-weight infants. *JAMA*. 2003;289(6):705-711.

28. Hintz SR, Kendrick DE, Vohr BR, Poole WK, Higgins RD, National Institute of Child Health and Human Development Neonatal Research Network. Changes in neurodevelopmental outcomes at 18 to 22 months' corrected age among infants of less than 25 weeks' gestational age born in 1993-1999. *Pediatrics*. 2005;115(6):1645-1651. doi:10.1542/peds.2004-2215.

29. Whitaker AH, Feldman JF, Lorenz JM, et al. Motor and cognitive outcomes in nondisabled low-birth-weight adolescents: early determinants. *Arch Pediatr Adolesc Med*. 2006;160(10):1040-1046. doi:10.1001/archpedi.160.10.1040.

30. Neubauer A-P, Voss W, Kattner E. Outcome of extremely low birth weight survivors at school age: the influence of perinatal parameters on neurodevelopment. *Eur J Pediatr*. 2008;167(1):87-95.

31. Luu TM, Ment LR, Schneider KC, Katz KH, Allan WC, Vohr BR. Lasting effects of preterm birth and neonatal brain hemorrhage at 12 years of age. *Pediatrics*. 2009;123(3):1037-1044.

32. Allen MC. Neurodevelopmental outcomes of preterm infants. *Curr Opin Neurol*. 2008;21(2):123-128.

33. Aylward GP. Neurodevelopmental outcomes of infants born prematurely. *J Dev Behav Pediatr*. 2005;26(6):427-440.

34. Aarnoudse-Moens CSH, Weisglas-Kuperus N, van Goudoever JB, Oosterlaan J. Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children. *Pediatrics*. 2009;124(2):717-728. doi:10.1542/peds.2008-2816.

35. Anderson PJ. Neuropsychological outcomes of children born very preterm. *Semin Fetal Neonatal Med*. 2014;19(2):90-96. doi:10.1016/j.siny.2013.11.012.

36. Barre N, Morgan A, Doyle LW, Anderson PJ. Language abilities in children who were very preterm and/or very low birth weight: a meta-analysis. *J Pediatr*. 2011;158(5):766-774.e1. doi:10.1016/j.jpeds.2010.10.032.

37. Baron IS, Erickson K, Ahronovich MD, Coulehan K, Baker R, Litman FR. Visuospatial and verbal fluency relative deficits in “complicated” late-preterm preschool children. *Early Hum Dev*. 2009;85(12):751-754. doi:10.1016/j.earlhumdev.2009.10.002.

38. Delobel-Ayoub M, Arnaud C, White-Koning M, et al. Behavioral problems and cognitive performance at 5 years of age after very preterm birth: the EPIPAGE Study. *Pediatrics*. 2009;123(6):1485-1492. doi:10.1542/peds.2008-1216.

39. de Kieviet JF, Piek JP, Aarnoudse-Moens CS, Oosterlaan J. Motor development in very preterm and very low-birth-weight children from birth to adolescence: a meta-analysis. *JAMA*. 2009;302(20):2235-2242. doi:10.1001/jama.2009.1708.

40. Mulder H, Pitchford NJ, Hagger MS, Marlow N. Development of executive function and attention in preterm children: a systematic review. *Dev Neuropsychol*. 2009;34(4):393-421. doi:10.1080/87565640902964524.

41. Ferrari F, Gallo C, Pugliese M, et al. Preterm birth and developmental problems in the preschool age. Part I: minor motor problems. *J Matern Fetal Neonatal Med*. 2012;25(11):2154-2159. doi:10.3109/14767058.2012.696164.

42. Bhutta AT, Cleves MA, Casey PH, Cradock MM, Anand KJS. Cognitive and behavioral outcomes of school-aged children who were born preterm: a meta-analysis. *JAMA*. 2002;288(6):728-737.

43. Kerr-Wilson CO, Mackay DF, Smith GCS, Pell JP. Meta-analysis of the association between preterm delivery and intelligence. *J Public Health*. 2012;34(2):209-216. doi:10.1093/pubmed/fdr024.

44. Johnson S. Cognitive and behavioural outcomes following very preterm birth. *Semin Fetal Neonatal Med*. 2007;12(5):363-373.

45. Caravale B, Tozzi C, Albino G, Vicari S. Cognitive development in low risk preterm infants at 3-4 years of life. *Arch Dis Child Fetal Neonatal Ed*. 2005;90(6):F474-479. doi:10.1136/adc.2004.070284.

46. Mikkola K, Ritari N, Tommiska V, et al. Neurodevelopmental outcome at 5 years of age of a national cohort of extremely low birth weight infants who were born in 1996-1997. *Pediatrics*. 2005;116(6):1391-1400. doi:10.1542/peds.2005-0171.

47. Hack M, Taylor HG, Drotar D, et al. Poor predictive validity of the Bayley Scales of Infant Development for cognitive function of extremely low birth weight children at school age. *Pediatrics*. 2005;116(2):333-341. doi:10.1542/peds.2005-0173.

48. Vohr BR. Neurodevelopmental outcomes of extremely preterm infants. *Clin Perinatol*. 2014;41(1):241-255. doi:10.1016/j.clp.2013.09.003.

49. de Jong M, Verhoeven M, van Baar AL. School outcome, cognitive functioning, and behaviour problems in moderate and late preterm children and adults: a review. *Semin Fetal Neonatal Med*. 2012;17(3):163-169. doi:10.1016/j.siny.2012.02.003.

50. Jarjour IT. Neurodevelopmental outcome after extreme prematurity: A review of the literature. *Pediatr Neurol*. November 2014. doi:10.1016/j.pediatrneurol.2014.10.027.

51. Kelly MM. Comparison of functional status of 8- to 12-year-old children born prematurely: an integrative review of literature. *J Pediatr Nurs*. 2012;27(4):299-309. doi:10.1016/j.pedn.2011.03.010.

52. Dong Y, Chen S, Yu J. A systematic review and meta-analysis of long-term development of early term infants. *Neonatology*. 2012;102(3):212-221.

53. McGowan JE, Alderdice FA, Holmes VA, Johnston L. Early childhood development of late-preterm infants: a systematic review. *Pediatrics*. 2011;127(6):1111-1124. doi:10.1542/peds.2010-2257.

54. Anderson PJ, Doyle LW. Cognitive and educational deficits in children born extremely preterm. *Semin Perinatol*. 2008;32(1):51-58. doi:10.1053/j.semperi.2007.12.009.

55. Doyle LW, Anderson PJ. Adult outcome of extremely preterm infants. *Pediatrics*. 2010;126(2):342-351. doi:10.1542/peds.2010-0710.

56. Hack M. Young adult outcomes of very-low-birth-weight children. *Semin Fetal Neonatal Med*. 2006;11(2):127-137. doi:10.1016/j.siny.2005.11.007.

57. Nepomnyaschy L, Hegyi T, Ostfeld BM, Reichman NE. Developmental outcomes of late-preterm infants at 2 and 4 years. *Matern Child Health J*. 2012;16(8):1612-1624. doi:10.1007/s10995-011-0853-2.

58. MacKay DF, Smith GCS, Dobbie R, Pell JP. Gestational age at delivery and special educational need: retrospective cohort study of 407,503 schoolchildren. *PLoS Med*. 2010;7(6):e1000289. doi:10.1371/journal.pmed.1000289.

59. Yang S, Platt RW, Kramer MS. Variation in child cognitive ability by week of gestation among healthy term births. *Am J Epidemiol*. 2010;171(4):399-406.

60. Noble KG, Fifer WP, Rauh VA, Nomura Y, Andrews HF. Academic achievement varies with gestational age among children born at term. *Pediatrics*. 2012;130(2):e257-e264.

61. Brooks-Gunn J, Duncan GJ. The effects of poverty on children. *Future Child*. 1997;7(2):55-71.

62. Lee VE, Burkam DT. *Inequality at the Starting Gate: Social Background Differences in Achievement as Children Begin School.* Economic Policy Institute, Washington, DC; 2002. http://eric.ed.gov/?id=ED470551. Accessed August 16, 2014.

63. Johnson SB, Riis JL, Noble KG. State of the art review: Poverty and the developing brain. *Pediatrics*. 2016;137(4). doi:10.1542/peds.2015-3075.

64. Conti G, Heckman JJ. Understanding the early origins of the education-health gradient: A framework that can also be applied to analyze gene-environment interactions. *Perspect Psychol Sci*. 2010;5(5):585-605. doi:10.1177/1745691610383502.

65. Heckman JJ. Skill formation and the economics of investing in disadvantaged children. *Science*. 2006;312(5782):1900-1902. doi:10.1126/science.1128898.

66. Ritchie SJ, Bates TC. Enduring links from childhood mathematics and reading achievement to adult socioeconomic status. *Psychol Sci*. 2013;24(7):1301-1308. doi:10.1177/0956797612466268.

67. Stiles J, Jernigan TL. The basics of brain development. *Neuropsychol Rev*. 2010;20(4):327-348. doi:10.1007/s11065-010-9148-4.

68. Noble KG, Houston SM, Brito NH, et al. Family income, parental education and brain structure in children and adolescents. *Nat Neurosci*. 2015;18(5):773-778. doi:10.1038/nn.3983.

69. Hair NL, Hanson JL, Wolfe BL, Pollak SD. Association of child poverty, brain development, and academic achievement. *JAMA Pediatr*. 2015;169(9):822-829. doi:10.1001/jamapediatrics.2015.1475.

70. Huston AC, Bentley AC. Human development in societal context. *Annu Rev Psychol*. 2010;61:411-437, C1. doi:10.1146/annurev.psych.093008.100442.

71. Hillemeier MM, Farkas G, Morgan PL, Martin MA, Maczuga SA. Disparities in the prevalence of cognitive delay: how early do they appear? *Paediatr Perinat Epidemiol*. 2009;23(3):186-198. doi:10.1111/j.1365-3016.2008.01006.x.

72. Conger RD, Donnellan MB. An interactionist perspective on the socioeconomic context of human development. *Annu Rev Psychol*. 2007;58:175-199. doi:10.1146/annurev.psych.58.110405.085551.

73. Duncan GJ, Magnuson K. Socioeconomic status and cognitive functioning: moving from correlation to causation. *Wiley Interdiscip Rev Cogn Sci*. 2012;3(3):377-386. doi:10.1002/wcs.1176.

74. Dickerson A, Popli G. *Persistent Poverty and Children's Cognitive Development: Evidence from the UK Millennium Cohort Study*. The University of Sheffield, Department of Economics; 2011. http://ideas.repec.org/p/shf/wpaper/2011023.html. Accessed August 15, 2014.

75. Duncan GJ, Yeung WJ, Brooks-Gunn J, Smith JR. How much does childhood poverty affect the life chances of children? *Am Sociol Rev*. 1998;63(3):406. doi:10.2307/2657556.

76. Guo G. The timing of the influences of cumulative poverty on children's cognitive ability and achievement. *Soc Forces*. 1998;77(1):257-287. doi:10.1093/sf/77.1.257.

77. Bendersky M, Lewis M. Environmental risk, biological risk, and developmental outcome. *Dev Psychol*. 1994;30(4):484-494. doi:10.1037/0012-1649.30.4.484.

78. Sameroff AJ. Environmental context of child development. *J Pediatr*. 1986;109(1):192-200.

79. Cohen SE, Parmelee AH, Beckwith L, Sigman M. Cognitive development in preterm infants: birth to 8 years. *J Dev Behav Pediatr*. 1986;7(2):102-110.

80. Koeppen-Schomerus G, Eley TC, Wolke D, Gringras P, Plomin R. The interaction of prematurity with genetic and environmental influences on cognitive development in twins. *J Pediatr*. 2000;137(4):527-533. doi:10.1067/mpd.2000.108445.

81. Ben-Shlomo Y, Kuh D. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *Int J Epidemiol*. 2002;31(2):285-293. doi:10.1093/ije/31.2.285.

82. Melnyk BM, Feinstein N, Fairbanks E. Two decades of evidence to support implementation of the COPE program as standard practice with parents of young unexpectedly hospitalized/critically ill children and premature infants. *Pediatr Nurs*. 2006;32(5):475-481.

83. White-Traut R, Norr K. An ecological model for premature infant feeding. *J Obstet Gynecol Neonatal Nurs*. 2009;38(4):478-489; quiz 489-490. doi:10.1111/j.1552-6909.2009.01046.x.

84. Gisselmann M, Koupil I, De Stavola BL. The combined influence of parental education and preterm birth on school performance. *J Epidemiol Community Health*. 2011;65(9):764-769. doi:10.1136/jech.2009.105569.

85. Wang W-L, Sung Y-T, Sung F-C, Lu T-H, Kuo S-C, Li C-Y. Low birth weight, prematurity, and paternal social status: impact on the basic competence test in Taiwanese adolescents. *J Pediatr*. 2008;153(3):333-338. doi:10.1016/j.jpeds.2008.04.017.

86. Christensen DL, Schieve LA, Devine O, Drews-Botsch C. Socioeconomic status, child enrichment factors, and cognitive performance among preschool-age children: results from the Follow-Up of Growth and Development Experiences study. *Res Dev Disabil*. 2014;35(7):1789-1801. doi:10.1016/j.ridd.2014.02.003.

87. Guo G, Harris KM. The mechanisms mediating the effects of poverty on children's intellectual development. *Demography*. 2000;37(4):431-447.

88. Escalona SK. Babies at double hazard: early development of infants at biologic and social risk. *Pediatrics*. 1982;70(5):670-676.

89. Brooks-Gunn J, Liaw F, Klebanov PK. Effects of early intervention on cognitive function of low birth weight preterm infants. *J Pediatr*. 1992;120(3):350-359. doi:10.1016/S0022-3476(05)80896-0.

90. Hack M, Klein NK, Taylor HG. Long-term developmental outcomes of low birth weight infants. *Future Child*. 1995;5(1):176-196.

91. Hack M, Breslau N, Aram D, Weissman B, Klein N, Borawski-Clark E. The effect of very low birth weight and social risk on neurocognitive abilities at school age. *J Dev Behav Pediatr*. 1992;13(6):412-420.

92. Drews-Botsch C, Schieve LA, Kable J, Coles C. Socioeconomic differences and the impact of being small for gestational age on neurodevelopment among preschool-aged children. *Rev Environ Health*. 2011;26(3):221-229.

93. Turkheimer E, Haley A, Waldron M, D'Onofrio B, Gottesman II. Socioeconomic status modifies heritability of IQ in young children. *Psychol Sci*. 2003;14(6):623-628. doi:10.1046/j.0956-7976.2003.psci_1475.x.

94. Ross G, Lipper EG, Auld PA. Educational status and school-related abilities of very low birth weight premature children. *Pediatrics*. 1991;88(6):1125-1134.

95. Teplin SW, Burchinal M, Johnson-Martin N, Humphry RA, Kraybill EN. Neurodevelopmental, health, and growth status at age 6 years of children with birth weights less than 1001 grams. *J Pediatr*. 1991;118(5):768-777.

96. Breslau N, DelDotto JE, Brown GG, et al. A gradient relationship between low birth weight and IQ at age 6 years. *Arch Pediatr Adolesc Med*. 1994;148(4):377-383.

97. Saigal S, Szatmari P, Rosenbaum P, Campbell D, King S. Cognitive abilities and school performance of extremely low birth weight children and matched term control children at age 8 years: a regional study. *J Pediatr*. 1991;118(5):751-760.

98. Levy-Shiff R, Einat G, Mogilner MB, Lerman M, Krikler R. Biological and environmental correlates of developmental outcome of prematurely born infants in early adolescence. *J Pediatr Psychol*. 1994;19(1):63-78.

99. Richards JL, Chapple-McGruder T, Williams BL, Kramer MR. Does neighborhood deprivation modify the effect of preterm birth on children’s first grade academic performance? *Soc Sci Med*. 2015;132:122-131. doi:10.1016/j.socscimed.2015.03.032.

100. Brown HK, Speechley KN, Macnab J, Natale R, Campbell MK. Mild prematurity, proximal social processes, and development. *Pediatrics*. 2014;134(3):e814-e824. doi:10.1542/peds.2013-4092.

101. Ekeus C, Lindström K, Lindblad F, Rasmussen F, Hjern A. Preterm birth, social disadvantage, and cognitive competence in Swedish 18- to 19-year-old men. *Pediatrics*. 2010;125(1):e67-73. doi:10.1542/peds.2008-3329.

102. Potijk MR, Kerstjens JM, Bos AF, Reijneveld SA, de Winter AF. Developmental delay in moderately preterm-born children with low socioeconomic status: risks multiply. *J Pediatr*. 2013;163(5):1289-1295. doi:10.1016/j.jpeds.2013.07.001.

103. VanderWeele, T.J. and Knol, M.J. A tutorial on interaction. *Epidemiol Methods*. May 2014. doi:0.1515/em-2013-0005.

104. VanderWeele TJ, Robins JM. Four types of effect modification: a classification based on directed acyclic graphs. *Epidemiology*. 2007;18(5):561-568. doi:10.1097/EDE.0b013e318127181b.

105. Rothman K, Lash T, Greenland S. *Modern Epidemiology*. 3rd ed. Lippincott Williams & Wilkins; 2012.

106. VanderWeele TJ, Robins JM. The identification of synergism in the sufficient-component-cause framework. *Epidemiology*. 2007;18(3):329-339. doi:10.1097/01.ede.0000260218.66432.88.

107. U.S. Department of Education, National Center for Education Statistics, Early Childhood Longitudinal Study, Birth Cohort (ECLS-B) Nine-Month Data Collection, 2001–02.

108. National Center for Education Statistics. Early Childhood Longitudinal Study, Birth Cohort (ECLS-B), Kindergarten 2006 and 2007: Data File User’s Manual (2010-010). 2010.

109. SOC 2000 - 2000 SOC Major Groups. http://www.bls.gov/soc/2000/soc_majo.htm. Accessed December 5, 2014.

110. National Center for Education Statistics. Early Childhood Longitudinal Study, Birth Cohort (ECLS-B), User’s Manual for the ECLS-B Longitudinal 9-month-2-year Data File and Electronic Codebook. May 2006.

111. National Center for Education Statistics. The ECLS-B Direct Assessment: Choosing the Appropriate Score for Analysis. http://nces.ed.gov/ecls/pdf/birth/ChoosingScores.pdf. Accessed March 11, 2015.

112. Najarian M, Snow K, Lennon J, Kinsey S, Mulligan G. Early Childhood Longitudinal Study, Birth Cohort (ECLS-B), Preschool—Kindergarten 2007 Psychometric Report. April 2010.

113. Welcome to the Millennium Cohort Study - Centre for Longitudinal Studies. http://www.cls.ioe.ac.uk/page.aspx?sitesectionid=851. Accessed October 26, 2016.

114. Hansen K. *Millennium Cohort Study First, Second, Third, and Fourth Surveys: A Guide to the Datasets (Seventh Edition)*. Center for Longitudinal Studies, Institute of Education, University of London; 2012.

115. Poulsen G, Kurinczuk JJ, Wolke D, et al. Accurate reporting of expected delivery date by mothers 9 months after birth. *J Clin Epidemiol*. 2011;64(12):1444-1450. doi:10.1016/j.jclinepi.2011.03.007.

116. Connelly R. *Millennium Cohort Study Data Note: Interpreting Test Scores*. Centre for Longitudinal Studies, Institute of Education, University of London; 2013.

117. Keunen K, Kersbergen KJ, Groenendaal F, Isgum I, de Vries LS, Benders MJNL. Brain tissue volumes in preterm infants: prematurity, perinatal risk factors and neurodevelopmental outcome: A systematic review. *J Matern Fetal Neonatal Med*. 2012;25(S1):89-100.

118. Chyi LJ, Lee HC, Hintz SR, Gould JB, Sutcliffe TL. School outcomes of late preterm infants: special needs and challenges for infants born at 32 to 36 weeks gestation. *J Pediatr*. 2008;153(1):25-31.

119. Morse SB, Zheng H, Tang Y, Roth J. Early school-age outcomes of late preterm infants. *Pediatrics*. 2009;123(4):e622-629.

120. Stephens BE, Vohr BR. Neurodevelopmental outcome of the premature infant. *Pediatr Clin North Am*. 2009;56(3):631-646.

121. Poulsen G, Wolke D, Kurinczuk JJ, et al. Gestational age and cognitive ability in early childhood: a population-based cohort study. *Paediatr Perinat Epidemiol*. 2013;27(4):371-379.

122. Rose O, Blanco E, Martinez SM, et al. Developmental scores at 1 year with increasing gestational age, 37–41 weeks. *Pediatrics*. 2013;131(5):e1475-e1481.

123. MacKay DF, Smith GCS, Dobbie R, Pell JP. Gestational age at delivery and special educational need: retrospective cohort study of 407,503 schoolchildren. *PLoS Med*. 2010;7(6):e1000289.

124. Mathiasen R, Hansen BM, Andersen A-MNN, Forman JL, Greisen G. Gestational age and basic school achievements: a national follow-up study in Denmark. *Pediatrics*. 2010;126(6):e1553-1561. doi:10.1542/peds.2009-0829.

125. Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. *Obstet Gynecol*. 1996;87(2):163-168.

126. Martin JA, Osterman MJ, Kirmeyer SE, Gregory EC. Measuring gestational age in vital statistics data: transitioning to the obstetric estimate. National Vital Statistics Reports, Volume 64, Number 5. http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_05.pdf.

127. Andreassen C, Fletcher P, Park J. *Early Childhood Longitudinal Study, Birth Cohort (ECLS–B) Psychometric Report for the 2-Year Data Collection*. National Center for Education Statistics; 2007. http://nces.ed.gov/pubsearch/pubsinfo.asp?pubid=2007084. Accessed March 11, 2015.

128. Committee on Fetus and Newborn. Age terminology during the perinatal period. *Pediatrics*. 2004;114(5):1362-1364.

129. vaan Buren S, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained Equations in R. *J Stat Softw*. 2011;45(3). https://stat.ethz.ch/education/semesters/ss2012/ams/paper/mice.pdf. Accessed July 18, 2016.

130. Howe CJ, Cole SR, Lau B, Napravnik S, Eron JJ. Selection Bias Due to Loss to Follow Up in Cohort Studies. *Epidemiology*. 2016;27(1):91-97.

131. Cole SR, Hernán MA. Constructing inverse probability weights for marginal structural models. *Am J Epidemiol*. 2008;168(6):656-664.

132. Quigley MA, Poulsen G, Boyle E, et al. Early term and late preterm birth are associated with poorer school performance at age 5 years: a cohort study. *Arch Dis Child Fetal Neonatal Ed*. 2012;97(3):F167-173. doi:10.1136/archdischild-2011-300888.

133. Wilson-Ching M, Pascoe L, Doyle LW, Anderson PJ. Effects of correcting for prematurity on cognitive test scores in childhood. *J Paediatr Child Health*. 2014;50(3):182-188.

134. Parekh SA, Boyle EM, Guy A, et al. Correcting for prematurity affects developmental test scores in infants born late and moderately preterm. *Early Hum Dev*. 2016;94:1-6.

135. van Veen S, Aarnoudse-Moens CSH, van Kaam AH, Oosterlaan J, van Wassenaer-Leemhuis AG. Consequences of correcting intelligence quotient for prematurity at age 5 years. *J Pediatr*. 2016;173:90-95.

136. Wilson SL, Cradock MM. Review: Accounting for prematurity in developmental assessment and the use of age-adjusted scores. *J Pediatr Psychol*. 2004;29(8):641-649.

137. D'Agostino JA, Gerdes M, Hoffman C, Manning ML, Phalen A, Bernbaum J. Provider use of corrected age during health supervision visits for premature infants. *J Pediatr Health Care*. 2013;27(3):172-179.

138. Ananth CV. Menstrual versus clinical estimate of gestational age dating in the United States: temporal trends and variability in indices of perinatal outcomes. *Paediatr Perinat Epidemiol*. 2007;21:22-30.

139. Acevedo-Garcia D, Osypuk TL, McArdle N, Williams DR. Toward a policy-relevant analysis of geographic and racial/ethnic disparities in child health. *Health Aff (Millwood)*. 2008;27(2):321-333. doi:10.1377/hlthaff.27.2.321.

140. Collins JW, Rankin KM, David RJ. African American women's lifetime upward economic mobility and preterm birth: the effect of fetal programming. *Am J Public Health*. 2011;101(4):714-719. doi:10.2105/AJPH.2010.195024.

141. Kramer MR, Cooper HL, Drews-Botsch CD, Waller LA, Hogue CR. Metropolitan isolation segregation and Black-White disparities in very preterm birth: a test of mediating pathways and variance explained. *Soc Sci Med*. 2010;71(12):2108-2116. doi:10.1016/j.socscimed.2010.09.011.

142. Rehkopf DH, Glymour MM, Osypuk TL. The consistency assumption for causal inference in social epidemiology: When a rose is not a rose. *Curr Epidemiol Rep*. 2016;3(1):63-71. doi:10.1007/s40471-016-0069-5.

143. Messer LC, Oakes JM, Mason S. Effects of socioeconomic and racial residential segregation on preterm birth: a cautionary tale of structural confounding. *Am J Epidemiol*. 2010;171(6):664-673. doi:10.1093/aje/kwp435.

144. Connelly R, Platt L. Cohort Profile: UK Millennium Cohort Study (MCS). *Int J Epidemiol*. February 2014. doi:10.1093/ije/dyu001.

145. Kelly Y, Sacker A, Bono ED, Francesconi M, Marmot M. What role for the home learning environment and parenting in reducing the socioeconomic gradient in child development? Findings from the Millennium Cohort Study. *Arch Dis Child*. 2011;96(9):832-837. doi:10.1136/adc.2010.195917.

146. Kelly Y, Watt R. Breast-feeding initiation and exclusive duration at 6 months by social class – results from the Millennium Cohort Study. *Public Health Nutr*. 2005;8(04). doi:10.1079/PHN2004702.

147. Taylor-Robinson DC, Pearce A, Whitehead M, Smyth R, Law C. Social inequalities in wheezing in children: findings from the UK Millennium Cohort Study. *Eur Respir J*. 2016;47(3):818-828. doi:10.1183/13993003.01117-2015.

148. Becker B. Social disparities in children's vocabulary in early childhood. Does pre-school education help to close the gap? *Br J Sociol*. 2011;62(1):69-88. doi:10.1111/j.1468-4446.2010.01345.x.

149. Zilanawala A, Sacker A, Nazroo J, Kelly Y. Ethnic differences in children's socioemotional difficulties: Findings from the Millennium Cohort Study. *Soc Sci Med*. 2015;134:95-106. doi:10.1016/j.socscimed.2015.04.012.

150. Mangin KS, Horwood LJ, Woodward LJ. Cognitive Development Trajectories of Very Preterm and Typically Developing Children. *Child Dev*. July 2016. doi:10.1111/cdev.12585.

151. O'Brien F, Roth S, Stewart A, Rifkin L, Rushe T, Wyatt J. The neurodevelopmental progress of infants less than 33 weeks into adolescence. *Arch Dis Child*. 2004;89(3):207-211.

152. Jaekel J, Baumann N, Wolke D. Effects of gestational age at birth on cognitive performance: A function of cognitive workload demands. *PLoS ONE*. 2013;8(5). doi:10.1371/journal.pone.0065219.

153. Tong S, Baghurst P, McMichael A. Birthweight and cognitive development during childhood. *J Paediatr Child Health*. 2006;42(3):98-103. doi:10.1111/j.1440-1754.2006.00805.x.

154. Hillemeier MM, Morgan PL, Farkas G, Maczuga SA. Perinatal and Socioeconomic Risk Factors for Variable and Persistent Cognitive Delay at 24 and 48 Months of Age in a National Sample. *Matern Child Health J*. 2011;15(7):1001-1010. doi:10.1007/s10995-010-0656-x.

155. Resnick MB, Gueorguieva RV, Carter RL, et al. The impact of low birth weight, perinatal conditions, and sociodemographic factors on educational outcome in kindergarten. *Pediatrics*. 1999;104(6):e74.

156. Najman JM, Aird R, Bor W, O'Callaghan M, Williams GM, Shuttlewood GJ. The generational transmission of socioeconomic inequalities in child cognitive development and emotional health. *Soc Sci Med*. 2004;58(6):1147-1158.

157. Chan E, Quigley MA. School performance at age 7 years in late preterm and early term birth: a cohort study. *Arch Dis Child - Fetal Neonatal Ed*. 2014;99(6):F451-F457. doi:10.1136/archdischild-2014-306124.

158. Chan E, Leong P, Malouf R, Quigley MA. Long-term cognitive and school outcomes of late-preterm and early-term births: a systematic review. *Child Care Health Dev*. 2016;42(3):297-312. doi:10.1111/cch.12320.

159. Spittle A, Orton J, Anderson PJ, Boyd R, Doyle LW. Early developmental intervention programmes provided post hospital discharge to prevent motor and

cognitive impairment in preterm infants. *Cochrane Database Syst Rev*. 2015;(11):CD005495. doi:10.1002/14651858.CD005495.pub4.

160. Overview of Early Intervention | Center for Parent Information and Resources. http://www.parentcenterhub.org/repository/ei-overview/. Accessed December 8, 2016.

161. Government Accountability Office. Education Should Provide Additional Guidance to Help States Smoothly Transition Children to Preschool. http://www.gao.gov/products/GAO-06-26. Published December 2005. Accessed December 8, 2016.

162. Hebbeler K, Spiker D, Bailey D, et al. Early intervention for infants and toddlers with disabilities and their families: Participants, services, and outcomes. Final Report of the National Early Intervention Longitudinal Study (NEILS). https://www.sri.com/sites/default/files/publications/neils_finalreport_200702.pdf. Published January 2007. Accessed December 8, 2016.

163. Rosenberg SA, Zhang D, Robinson CC. Prevalence of developmental delays and participation in early intervention services for young children. *Pediatrics*. 2008;121(6):e1503-1509. doi:10.1542/peds.2007-1680.

164. Rosenberg SA, Robinson CC, Shaw EF, Ellison MC. Part C early intervention for infants and toddlers: Percentage eligible versus served. *Pediatrics*. 2013;131(1):38-46. doi:10.1542/peds.2012-1662.

165. Wang CJ, Elliott MN, Rogowski J, Lim N, Ratner JA, Schuster MA. Factors influencing the enrollment of eligible extremely-low-birth-weight children in the part C early intervention program. *Acad Pediatr*. 2009;9(4):283-287. doi:10.1016/j.acap.2009.04.001.

166. Volpe JJ. Brain injury in the premature infant: overview of clinical aspects, neuropathology, and pathogenesis. *Semin Pediatr Neurol*. 1998;5(3):135-151.

167. Back SA. Perinatal white matter injury: The changing spectrum of pathology and emerging insights into pathogenetic mechanisms. *Ment Retard Dev Disabil Res Rev*. 2006;12(2):129-140. doi:10.1002/mrdd.20107.

168. Marret S, Marchand-Martin L, Picaud J-C, et al. Brain injury in very preterm children and neurosensory and cognitive disabilities during childhood: the EPIPAGE cohort study. *PloS One*. 2013;8(5):e62683. doi:10.1371/journal.pone.0062683.

169. Wong HS, Edwards P. Nature or nurture: a systematic review of the effect of socio-economic status on the developmental and cognitive outcomes of children born preterm. *Matern Child Health J*. 2013;17(9):1689-1700. doi:10.1007/s10995-012-1183-8.

170. Andreias L, Borawski E, Schluchter M, Taylor HG, Klein N, Hack M. Neighborhood influences on the academic achievement of extremely low birth weight children. *J Pediatr Psychol*. 2010;35(3):275-283. doi:10.1093/jpepsy/jsp057.

171. Potharst ES, van Wassenaer AG, Houtzager BA, van Hus JWP, Last BF, Kok JH. High incidence of multi-domain disabilities in very preterm children at five years of age. *J Pediatr*. 2011;159(1):79-85. doi:10.1016/j.jpeds.2010.12.055.

172. Dall'oglio AM, Rossiello B, Coletti MF, et al. Do healthy preterm children need neuropsychological follow-up? Preschool outcomes compared with term peers. *Dev Med Child Neurol*. 2010;52(10):955-961. doi:10.1111/j.1469-8749.2010.03730.x.

173. Fuertes M, Faria A, Soares H, Crittenden P. Developmental and evolutionary assumptions in a study about the impact of premature birth and low income on mother–infant interaction. *Acta Ethologica*. 2009;12(1):1-11. doi:10.1007/s10211-008-0051-4.

174. McGauhey PJ, Starfield B, Alexander C, Ensminger ME. Social environment and vulnerability of low birth weight children: a social-epidemiological perspective. *Pediatrics*. 1991;88(5):943-953.

Appendix

Appendix Table A.1. Studies assessing interaction between prematurity and socioeconomic status in their effects on children's neurodevelopmental outcomes.

Brown et al. (2014)[100]	**Research question:** To assess poor developmental outcomes among late preterm and early term children, after controlling for social and biological factors, and to assess how proximal social process (parenting) modify the effect of gestational age on poor developmental outcomes. **Study type/location:** Prospective cohort (National Longitudinal Survey of Children and Youth, NLSCY) in Canada **Sample:** 15,099 at 2-3 years, 12,302 at 4-5 years **Exposure(s):** Gestational age: 34-41 weeks, categorized as late preterm (34-36 weeks), early term (37-38 weeks), or full term (39-41 weeks). SES: Proximal social processes (parenting): parenting interactions, parenting effectiveness, parenting consistency **Outcome(s):** Developmental delay (Motor and Social Development Scale), Receptive vocabulary delay (Peabody Picture Vocabulary Test-Revised) **Age at assessment:** 2-3 years (developmental delay), 4-5 years (receptive vocabulary) **Findings:** After adjusting for perinatal variables, gestational age, family structure, family resources, family functioning, proximal social processes, and other covariates (e.g., child gender), late preterm and early term birth were not associated with significantly increased risk of developmental delay at 2-3 years or receptive vocabulary delay at 4-5 years. Negative, ineffective, or inconsistent parenting was significantly associated with delay at 2-3 years and 4-5 years. Additive interaction between gestational age and each of parenting interactions, parenting effectiveness, and parenting consistency was tested by including interaction terms and calculating RERI (i.e., 6 RERI calculations for each outcome). Results were null.
Wong et al. (2013)[169]	**Research question:** To review the literature on the association of SES with cognitive outcome in preterm children. **Study type/location:** Systematic review of English-language studies published in January 1990-July 2011 that reported the effect of at least 1 SES indicator on cognitive outcome in preterm children (<37 weeks). **Sample:** Eligibility criteria: cohort or case-control design, children born in or after 1990, children born <37 weeks. Exclusion criteria: included children based on LBW criterion (<2500 g) [however, studies that reported on VLBW or ELBW were included], included only a subgroup of the preterm population (e.g., children with IVH), reported only on language or executive function. **Birth years:** N/A **Exposure(s):** Gestational age: <37 weeks or VLBW (<1500 g) or ELBW (<1000 g). SES: Socioeconomic variables were classified in 4 categories: individual-level, family-structure, contextual, composite. **Outcome(s):** Cognitive outcome tested by psychometric assessment **Age at assessment:** N/A

	Findings: 15 longitudinal cohort studies included in this review. 14 studies reported a significant effect of at least 1 indicator of SES on cognitive outcome (the other study sampled participants from one center) - in all cases, lower SES was associated with worse cognitive performance. Results were heterogeneous due to variation in measurement of SES, study populations, study designs, and inconsistent confounding adjustment (or none at all). Selection bias (e.g., higher drop-out among lower SES children) was a noted concern. 2 studies assessed interaction between maternal and parental education and preterm birth on cognitive outcome. In one study (Dall'Oglio 2010), interaction between maternal education and preterm birth in their effect on cognitive outcome was not significant. In the other study (Potharst 2011), there was borderline significant interaction between parental education and preterm birth (IQ difference between high and low parental education was 17 points in preterm versus 8 points in term).
Potijk et al. (2013)[102]	**Research question:** To assess the separate and joint effects of moderate prematurity and low SES on developmental delay in early childhood. **Study type/location:** Prospective cohort in the Netherlands (Longitudinal Preterm Outcome Project, or Lollipop) **Sample:** Cases: 926 moderate preterm, Controls: 544 term **Birth years:** 2002-2003 **Exposure(s):** Gestational age: 32-35 weeks versus 38-42 weeks [in analytic models, GA was defined using a standardized N(0,1) variable]. SES: Standardized [N(0,1)] composite SES score based on father's education, mother's education, family income, father's occupation, mother's occupation. **Outcome(s):** Ages and Stages Questionnaire (Dutch version), completed by parents; Domain scores: fine motor, gross motor, communication, problem-solving, personal-social skills **Age at assessment:** 4 years **Findings:** In unadjusted models for the association of standardized GA, SES, and GA*SES with abnormal scores in each of the 5 domains, both decreasing SES and decreasing GA were independently associated with abnormal score. Significant interaction observed only for communication skills. After adjustment for sex, number of siblings, and maternal age, results were similar. Significant interaction was only observed for communication skills (OR for decreasing SES = 1.50, 95% CI: 1.18-1.90; OR for decreasing GA = 1.60, 95% CI: 1.22-2.10; OR for GA*SES = 0.73, 95% CI: 0.55-0.98). Cautionary note: Sample selected to have fewer term (n=544) than moderate preterm (n=926); relative positioning within a standardized distribution may not reflect GA risk.
Andreias et al. (2010)[170]	**Research question:** To assess the role of neighborhood, family, and individual characteristics on academic achievement in ELBW children compared to NBW controls, using multilevel modeling. **Study type/location:** Prospective follow-up of NICU graduates, with matching (on race, sex, age, and school) of controls in the United States **Sample:** Cases: 183 ELBW, Controls: 176 NBW **Birth years:** 1992-1995

	Exposure(s): Gestational age: ELBW (<1000 g). SES: Family-level—race, parental education, parental marital status, Perceived Neighborhood Scale, Parent Protection Scale; Neighborhood-level—poverty rate, high school dropout rate. **Outcome(s):** Academic Skills Cluster of Woodcock-Johnson Tests of Achievement III (composite of subtests in Letter-Word Identification, Math Calculation, and Spelling) **Age at assessment:** 8 years **Findings:** After adjustment for individual, family, and neighborhood level factors, ELBW, male sex, ADHD symptoms, less parental education, parental protection, and poverty rate were associated with worse academic performance at age 8. Interactions between ELBW and all factors were tested; they were not significant. Study population was predominantly urban, lower SES; cases and controls were matched on school, so presumably similar in SES.
Potharst et al. (2011)[171]	**Research question:** To describe developmental disabilities at 5 years in very preterm children versus term-born controls, and to investigate the association between developmental delay and parental education (as a proxy for SES). **Study type/location:** Prospective cohort in the Netherlands **Sample:** Cases: 104 very preterm, Controls: 95 term, had to be enrolled in mainstream school **Birth years:** Reached age 5 years in 2007-2009 **Exposure(s):** Gestational age: <30 week or <1000 g, versus ≥37 weeks and >2500 g. SES: Parental education (dichotomized as high versus middle or low). **Outcome(s):** Primary endpoints were 2 composite disability scores: (1) Total number of mild-to-severe disabilities, (2) Sum of all severe disabilities **Age at assessment:** 5 years **Findings:** After adjustment for parental education and parental country of birth, very preterm birth was significantly associated with having at least one disability (mild or severe), and having severe disability. Parental education was also significantly associated with both of these outcomes. Interaction between very preterm birth and parental education was tested for IQ and behavior (which were found to be significantly associated with parental education), using ANOVA (unadjusted). Interactions were not significant, but results suggested a trend toward a larger difference between very preterm and term groups among those with lower parental education. For full-scale IQ, the mean difference between groups was 14 IQ points in the low parental education group, 8 points in the middle group, and 5 points in the high group.
Gisselmann et al. (2010)[84]	**Research question:** To assess how a more advantageous cognitive environment (measured by parental education) modifies the effect of preterm birth on school performance. **Study type/location:** Retrospective cohort in Sweden **Sample:** Cases: 437 preterm, Controls: 10,305 term **Birth years:** 1973-1981

	Exposure(s): Gestational age: <37 weeks. SES: Parental education (higher = at least 3 years of secondary education; lower = <3 years of secondary education). Classified as concordantly high, discordant, or concordantly low. **Outcome(s):** Grades in Swedish language (categorized as low, medium, high) recorded at the end of grade 9 (last year of compulsory school, grades used to apply for admission to secondary school) **Age at assessment:** 15-16 years **Findings:** After adjusting for child's birth year, gender, parity, and fetal growth, higher parental education was associated with higher odds of achieving higher grades in Swedish (OR=1.94, 95% CI: 1.77-2.13 for discordant; OR=4.59, 95% CI: 4.13-5.09 for concordant high), and preterm birth was associated with lower odds of achieving higher grades in Swedish (OR=0.81, 95% CI: 0.66-0.98) (ordinal logistic regression). In interaction models containing terms for interaction between preterm birth and parental education, there was significant interaction. Preterm birth was significantly associated with lower odds of achieving higher grades in Swedish only among those with concordantly low parental education [OR=0.59, 95% CI: 0.33-0.79] (OR's were null for discordant [OR=0.95, 95% CI: 0.66-1.37] and concordantly high categories [OR=1.21, 95% CI: 0.82-1.82]).
Ekeus et al. (2010)[101]	**Research question:** To assess whether socioeconomic variables modify the effect of gestational age on cognitive competence in adolescence. **Study type/location:** Retrospective cohort in Sweden **Sample:** Cases: 63 at 24-28 weeks, 565 at 29-32 weeks, 1088 at 33-34 weeks, 3981 at 35-36 weeks, 19,146 at 37-38 weeks; Controls: 94,281 at 39-41 weeks **Birth years:** 1973-1976 **Exposure(s):** Gestational age: Gestational age categorized as: 24-28 weeks, 29-32 weeks, 33-34 weeks, 35-36 weeks, 37-38 weeks, and 39-41 weeks. SES: Childhood SES defined using 6-category variable created by Statistics Sweden, based on occupation. The occupation variable was categorized into high SES (white collar 2 and 3 households in which the head of household has a qualified non-manual employment) and low SES (all other households). **Outcome(s):** Score on a general intellectual performance test administered at time of conscription into military service, including 4 sub-tests on logical, spatial, verbal, and technical capabilities. Scores were standardized and categorized into 9 score bands (1-9) **Age at assessment:** 18 years **Findings:** Lower gestational age and lower SES were each associated with lower intellectual test scores. There was a suggestion of a gradient effect towards lower scores with decreasing gestational age (categorized as 24-32, 33-34, 35-36, 37-38, and 39-41 weeks), and decreasing SES category (using the 6-category definition). For all gestational age categories, high SES subjects had higher mean scores than low SES subjects. Interaction between gestational age (24-32, 33-36, 37-38, 39-41 week) and SES (low versus high) was tested by including interaction terms in a multiple linear regression model, with intellectual test score as the outcome. Only the interaction term for 33-36 weeks was significant (B=0.16, p<0.01); this beta estimate suggested positive additive interaction.

Dall'oglio et al. (2010)[172]	**Research question:** To assess cognitive and neuro-psychological abilities required for academic learning among healthy preterm children and term-born controls, in order to identify targets of environment support and specific intervention. **Study type/location:** Prospective follow-up of NICU graduates from a large referral pediatric hospital, with controls selected from a nursery school near the hospital in Italy **Sample:** Cases: 35 very preterm, Controls: 50 term **Birth years:** 1998-1999 **Exposure(s):** Gestational age: <33 weeks. SES: Maternal education. **Outcome(s):** Griffiths Mental Developmental Scales , as well as standardized psychometric tests assessing language; short-term memory; visual, motor, and constructive spatial abilities; and visual processing **Age at assessment:** 4 years **Findings:** Most of the very preterm children scored within the normal range on the Griffiths scale (>90), but their mean scores were significantly lower than term controls and the normative reference. Very preterm birth was associated with lower global Griffiths score, after adjusting for sex, birth order, maternal age, and maternal education (mean difference = -5.3 points, 95% CI: -8.3, -2.2 for 30-32 weeks, mean difference = -6.7, 95% CI: -11.1, -2.3 for <30 weeks). More maternal education was associated with higher scores. In these linear models, there was no significant interaction between preterm birth and either of maternal education or birth order. This study had a very small sample size, and very few subjects had mothers with the lowest level of education (reference group).
Fuertes et al. (2009)[173]	**Research question:** To assess the isolated and aggregated effects of premature birth and low income on maternal sensitivity and infant cooperative behavior, and to assess the link between maternal behavior and infant styles of interactive behavior under the influence of low SES and premature birth. **Study type/location:** Cross-sectional study in Portugal **Sample:** Full term, middle class: 99 mother-infant dyads; Premature, middle class:63 mother-infant dyads; Full term, low income: 22 mother-infant dyads; Premature, low income: 21 mother-infant dyads **Birth years:** Not stated **Exposure(s):** Gestational age: Prematurity defined as <36 weeks. SES: Low income defined as household annual income of 2,100-7,000 Euros. **Outcome(s):** Rating of mother-child dyad interaction in 3-minute unstructured play situation. CARE Index used to rate maternal behavior (sensitive, controlling, unresponsive) and infant interactive behavior (cooperative, compliant, difficult, passive). Main outcomes were maternal sensitive behavior and infant cooperative behavior. **Age at assessment:** Mean corrected age ranged from 5.9 months for the full-term, middle class group to 8.4 months for the full-term, low income group **Findings:** Full term, middle class group had the highest scores on maternal sensitivity and infant cooperative behavior. Low income groups had the lowest scores on both outcomes. A formal test of interaction was not performed; the

	paper presents unadjusted scores for each of the four groups. For maternal sensitivity, the crude difference comparing premature to full term is larger among middle class compared with low income. For infant cooperative behavior, the crude difference is larger among middle class; full term low income infants scored worse than premature low income infants. In linear regression models, significant predictors of maternal sensitivity and infant cooperative behavior were SES, infant health status, and maternal education. The authors controlled for both preterm and gestational age.
Wang et al. (2008)[85]	**Research question:** To assess whether lower birth weight and family social class (measured by paternal education) have independent and interactive effects on learning achievement in adolescence. **Study type/location:** Retrospective cohort in Taiwan **Sample:** Term, low birth weight (TLBW): 33,507; Preterm, normal birth weight (PNBW): 19,905; Preterm, low birth weight (PLBW): 25,840; Term, normal birth weight: 83,756 **Birth years:** 1985-1989 **Exposure(s):** Gestational age: Preterm (<37) and/or LBW (<2500 g). SES: Paternal education (elementary or less, junior high, senior high, college and more). **Outcome(s):** Basic Competence Test, which includes tests of Mandarin (verbal, reading, and writing ability), mathematics (ability in calculation and logical inference), and science (knowledge of biology, chemistry, and physics) **Age at assessment:** 15-16 years **Findings:** TLBW, PNBW, PLBW and lower paternal education (compared with college or more) were independently associated with lower BCT scores in Mandarin, mathematics, and science, after adjusting for sex, birth order, singleton/multiple birth, month of birth, parental age, maternal marital status, and current residence area. There was a dose response relationship between lower paternal education and lower BCT score. The effect sizes comparing TLBW and PLBW to TNBW (2-3 points) were larger than that comparing PNBW to TNBW (0.5 points). Interaction between PLBW category and paternal education was tested by including interaction terms in linear regression models for each BCT score. Interaction was significant, and deficits in scores between worse categories and TNBW decreased with increasing paternal education for Mandarin test scores. Interaction was significant for the mathematics and science test scores, but trends across paternal education were less apparent compared to that observed for Mandarin; significance of the interaction terms driven by an effect within PNBW, whereas there was no apparent difference in the effect of TLBW and PLBW across paternal education groups.
Koeppen-Schomerus et al. (2000)[80]	**Research question:** To investigate the roles of genetic and environmental factors in cognitive and language development for premature children. **Study type/location:** Cross-sectional twin study in England and Wales **Sample:** Target sample = 2223 twin pairs (1134 monozygotic pairs, 1089 dizygotic pairs). High-risk (<32 weeks): 5.0% of target sample; Moderate-risk (32-33 weeks): 8.6% of target sample; Low-risk (≥34 weeks): 86.4% of target sample

	Birth years: 1994 **Exposure(s):** Gestational age: N/A. SES: N/A. **Outcome(s):** MacArthur Communicative Development Inventory (verbal cognitive development); Parent Report of Children's Cognitive Abilities (non-verbal cognitive development) **Age at assessment:** 2 years **Findings:** Children in the higher risk prematurity groups had lower scores on the MCDI and PARCA than the low-risk group (gradient effect) but there was substantial variation in individual scores in each group. In the high-risk group, there was little difference in within-twin pair correlation between monozygotic and dizygotic pairs. Shared environment (84%) played a larger role in explaining the variance between twins at high risk, and genetic factors played no role (9%). Results were similar for MCDI and PARCA. In the moderate-and low-risk groups, there was more of a difference between the monozygotic and dizygotic pairs. Genetic factors played more of a role (33% for moderate, 22% for low), and shared environment played less of a role (65% for moderate, 73% for low), in explaining the variance between twins in these risk groups. Results were again similar for MCDI and PARCA.
Bendersky et al. (1994)[77]	**Research question:** To explore the relative contributory roles of biological and environmental variables to functional outcomes at age 2. **Study type/location:** Prospective cohort in the United States **Sample:** Cases only: 175 **Birth years:** 1985-1987 **Exposure(s):** Gestational age: <2000 g and treated in NICU. SES: Two environmental risk variables representing distal (social class) from proximal (family risk) variables, based on the following measurements: Parental education, parental occupation, minority status, number of children <18 years living in household, parents living together, positive and negative stressful life events, HOME scale, social support, and quality of mother-child interaction. **Outcome(s):** Bayley Scales of Infant Development (Mental Developmental Index, MDI & Psychomotor Development Index, PDI); Sequenced Inventory of Communication Development (receptive communication age, RCA & expressive communication age, ECA) **Age at assessment:** 2 years (18-24 months corrected age) **Findings:** Linear regression models tested associations of average family risk, increased or decreased family risk (dummy variables), average social class, IVH severity, medical complications score, and family risk x IVH with each cognitive outcome. The interaction term was significant in the models predicting MDI and the communication outcomes. For children with no or mild IVH, increasing family risk score was associated with worse MDI; however, MDI scores were similar across family risk categories among children with severe IVH. This result was similar for the RCA outcome, but for the ECA outcome, worsening family risk was associated with worsening score in the severe IVH and no IVH groups but not for the mild IVH group. It appeared that for MDI and RCA, for children at high biological risk, worsening family risk does not make an additional contribution to worsening their scores. The authors noted that the

	MDI and receptive language results suggest that infants at highest biological risk are least susceptible to environmental forces. For the MDI outcome, environmental and biological factors both contributed 17% to the variance, and an additional 3.6% of the variance was explained by their interaction. Receptive communication was explained more by environment (8.4%), and the ECA model accounted for only a small portion of variance in the outcome.
Weisglas-Kuperus (1993)[26]	**Research question:** To assess the contributions of biological and social factors to cognitive development of VLBW children at 1 to 3.6 years, to assess whether VLBW at high biological risk are more vulnerable to social factors compared with VLBW children at low biological risk, and to determine which elements in VLBW children's home environments are important for cognitive development and at what age. **Study type/location:** Prospective follow-up of NICU graduates from a regional tertiary intensive care unit in the Netherlands **Sample:** Cases only: 79 **Birth years:** 1985-1986 **Exposure(s):** Gestational age: <1500 g, <36 weeks; also, children were classified according to biological risk based on neonatal cerebral ultrasonographic findings (Group 0 = Normal through Group 4 = Highest Risk) and neurologic risk (normal, mildly abnormal, definitely abnormal). SES: Sociodemographic risk score based on occupational status of the family, maternal education, family support, and ethnic background; Home environment assessed with HOME (Home Observation for the Measurement of the Environment) at ages 1 and 3.6. **Outcome(s):** Bayley Scales of Infant Development Mental scale, Dutch version (corrected ages 1 and 2); Kaufman Assessment Battery for Children Mental and Achievement scales, Dutch version (corrected age 3.6) **Age at assessment:** 1, 2, and 3.6 years **Findings:** In models containing biological and social factors, only neurological score was significantly associated with cognitive score at age 1. In similar models for cognitive score at age 2, home environment and neurological score were significantly associated with cognitive score. In similar models at age 3.6, neurological score and home environment were significantly associated with mental and achievement scale cognitive scores. Interaction between biological and social factors tested by comparing mean scores between neurologically normal and abnormal children across levels of home environment stimulation. Findings suggest that cognitive outcomes remain relatively stable or even improved (for neurologically at-risk or abnormal) for children in highly stimulating environments, remained stable but lower for children in intermediately stimulating environments, and declined for children in low stimulation environments. The authors suggest that among VLBW infants, social disadvantage is associated with lower cognitive scores, but that a stimulating home environment may compensate for biological risk.
Hack et al. (1992)[91]	**Research question:** To determine whether VLBW children had poorer cognitive, academic, and behavior outcomes, after controlling for major neurologic impairment and social risk, and that social risk would modify the

	effect of VLBW (i.e., VLBW would have a larger effect among children of greater social risk). **Study sample/location:** Prospective follow-up of NICU graduates, with matching of controls from a geographically based sample of NBW term births in the United States **Sample:** Cases: 249 VLBW; Controls: 363 NBW term **Birth years:** 1977-1979 **Exposure(s):** Gestational age: <1500 g. SES: 4-category composite variable based on maternal race, maternal education, and marital status. **Outcome(s):** Wechsler Intelligence Scale for Children-Revised; speech and language tests; memory, visual-motor, and fine motor abilities tests; Woodcock Reading Mastery Test; mathematics sub-tests of Woodcock Johnson Psychoeducational Battery; spelling sub-test of Wide Range Achievement Test; and Child Behavior Checklist. **Age at assessment:** 8-9 years **Findings:** In multiple regression analyses, VLBW status was associated with worse IQ as well as performance in language, memory, academic achievement (math, spelling, reading), visual-motor skills, and behavior, after controlling for social risk and restricting to neurologically intact VLBW (but no other confounders). The effect size for social risk score was generally larger than that for VLBW. Interaction was tested by adding a social risk x birth weight variable in multiple regression for each of the outcomes. Interaction was only significant for verbal IQ, and this result suggested that the effect of VLBW was the largest in the lowest social risk group and its effect decreased as social risk increased.
Ross et al. (1991)[94]	**Research question:** To assess the developmental status and need for educational remediation among VLBW premature infants at school age, and to determine the separate effects and interactions of prematurity and social class on school age abilities, both overall and independent of neurologic abnormality and below normal intelligence. **Study type/location:** Prospective follow-up of NICU graduates, with matching (on sex, social class, ethnic group, and urban, suburban, or semirural) of controls from several mainstream schools in the geographic areas where the cases resided in the United States **Sample:** Cases: 88 VLBW; Controls: 80 full-term **Birth years:** 1978-1980 **Exposure(s):** Gestational age: ≤1500 g. SES: Social class (Hollingshead Scale); Controls were matched to cases on social class. **Outcome(s):** Full-scale IQ (Wechsler Intelligence Scale for Children-Revised); Four test groupings: Verbal, Performance, Academic achievement, Auditory memory **Age at assessment:** 7-8 years **Findings:** VLBW children were significantly more likely to have full-scale IQ in the borderline (71-84) or abnormal (≤70) range compared with full-term controls, although mean IQ scores for both groups were in the normal range. Children with higher SES scored significantly higher on full-scale IQ and all test groupings. Interaction between VLBW and SES was tested using two-way

	ANOVA. Significant interaction found for full-scale IQ, verbal tests, and achievement tests. There was a greater deficit between VLBW and full-term controls among children with low SES, compared to children with higher SES.
McGauhey et al. (1991)[174]	**Research question:** To assess whether LBW children are at greater risk for poor child health outcomes compared with NBW children regardless of their social environments; to determine if adverse sequelae of LBW are more likely for younger LBW children than for older LBW children; and to assess whether social environment risk factors operate differently for LBW and NBW children. **Study type/location:** Cross-sectional (1981 National Health Interview Survey) in the United States **Sample:** Cases: 767 LBW; Controls: 7985 NBW **Birth years:** Not stated **Exposure(s):** Gestational age: <2500 g. SES: Stressful life conditions (low, medium, high), and stressful life events (yes in past year/no). **Outcome(s):** Child health status, measuring restricted activity due to illness and functional status and role performance (including 2 measures of school achievement - maternal ranking of how the child is performing in school compared with peers, and having failed a grade at school) **Age at assessment:** 2-11 years **Findings:** Separate models were run in each birth weight group, for the association of SLE, SLC, and covariates with child health status. There was a larger effect of LBW compared with NBW on child health status (composite variable) in high-risk social environments. Stressful life conditions (i.e., increase in social environment risk) had a larger impact on school failure in the LBW group (OR=4.4, 95% CI: 1.9-9.9) than in the NBW group (OR=2.1, 95% CI: 1.6-2.8). These models included high-risk SLC, moderate-risk SLC, SLE, race, age, gender, and chronic medical conditions. There was no statistical test of interaction between SLC and preterm in their effects on school failure.