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ARTICLE

Early School-Age Outcomes of Late Preterm Infants

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What's Known on This Subject

Late preterm infants have increased risks for short-term morbidities when compared with term infants. Specifically, they are at risk for respiratory distress, hypoglycemia, temperature instability, and hyperbilirubinemia. Little is known about neurodevelopmental outcomes in this group of infants.

What This Study Adds

This study adds new information regarding school-related outcomes in the healthy late preterm infant as compared with the healthy term infant.

ABSTRACT

OBJECTIVE. Late preterm infants represent a significant portion of preterm deliveries. Until recently, these infants have received little attention because of assumptions that they carry minimal risk for long-term morbidities. The purpose of this study was to compare prekindergarten and kindergarten outcomes among healthy late preterm infants, 34$^{0}/_{7}$ to 36$^{6}/_{7}$ weeks' gestation at birth, and healthy term infants, 37$^{0}/_{7}$ to 41$^{6}/_{7}$ weeks' gestation at birth.

METHODS. The study sample consisted of singleton infants who were born in Florida between January 1, 1996, and August 31, 1997, with a gestational age between 34 and 41 weeks ($N = 161\,804$) with a length of stay ≤72 hours. Seven early school-age outcomes were analyzed. Outcomes were adjusted for 15 potential confounding maternal and infant variables. Unadjusted and adjusted relative risk with 95% confidence interval was estimated for each outcome by using Poisson regression modeling.

RESULTS. Risk for developmental delay or disability was 36% higher among late preterm infants compared with term infants. Risk for suspension in kindergarten was 19% higher for late preterm infants. The remaining 4 outcomes, disability in prekindergarten at 3 and 4 years of age, exceptional student education, and retention in kindergarten, all carried a 10% to 13% increased risk among late preterm infants. The assessment "not ready to start school" was borderline significant.

CONCLUSIONS. This study suggests that healthy late preterm infants compared with healthy term infants face a greater risk for developmental delay and school-related problems up through the first 5 years of life. *Pediatrics* 2009;123:e622–e629

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Key Words
late preterm, school performance, developmental outcomes

Abbreviations
LMP—last menstrual period
aRR—adjusted relative risk
CI—confidence interval

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LATE PRETERM INFANTS, formerly referred to as near-term infants, represent a significant portion of preterm deliveries in the United States.[1] It has been estimated that 70% of preterm births are born at 34 to 36 weeks' gestation.[2] In addition, births at 34 to 36 weeks' gestation increased 25% between 1990 and 2005, whereas births at <34 weeks' gestation remained unchanged.[3–5] Despite the growing number of late preterm births, most follow-up research has been directed at extremely preterm infants, those between 23 and 28 weeks' gestation, because of known risks for physical and mental disability and the high costs associated with their care.

Until recently, the late preterm infant has been overlooked because of assumptions that most of these infants have little to no risk for long-term morbidities; however, several recent studies of late preterm term infants have documented increased short-term medical risks during their birth hospitalizations (eg, respiratory distress, hypoglycemia, temperature instability, hyperbilirubinemia)[6–9] and higher rates of readmission to the hospital after the birth hospitalization compared with term infants.[6,10] Longer term outcomes are also affected by late preterm birth. Approximately 20% of late preterm infants have clinically significant behavioral problems at 8 years of age,[10] a rate much higher than comparable term cohorts.[11,12] Most recently, concerns have been raised about increased rates of learning difficulties in late preterm infants when they reach school age.[13]

In 2005, the National Institute of Child Health and Human Development of the National Institutes of Health convened a workshop entitled, "Optimizing Care and Outcome of the Near Term Pregnancy and the Near Term Newborn Infant." The workshop identified a significant knowledge gap in long-term outcomes of this large segment of the preterm population.[14] The purpose of this study was to compare prekindergarten and kindergarten outcomes

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among healthy singleton late preterm infants, 34⁰⁄₇ to 36⁶⁄₇ weeks' gestation with those of healthy singleton term infants, 37⁰⁄₇ to 41⁶⁄₇ weeks' gestation.

METHODS

Study Children

All infants who were born in Florida between January 1, 1996, and August 31, 1997 (N = 220 352), were matched to records in Children's Medical Services' Early Intervention Program (Florida Department of Health) and in the public school student database (Florida Department of Education). Children were excluded from the study when they met any of the following criteria: (1) gestational age <34 or ≥42 weeks (n = 9900; 4.5%); (2) length of hospital stay >3 days (n = 20 024; 9.1%); (3) missing information for any explanatory variable (n = 21 241; 9.6%); (4) major congenital anomaly (n = 2627; 1.2%); (5) transfers to another hospital after birth (n = 4111; 1.9%); and (6) multiple births (n = 2630; 1.2%). Gestational age was determined by using birth certificate data comparing last menstrual period (LMP) information with the clinical estimate of gestational age. When the LMP calculated gestational age was within 2 weeks of the clinical estimate, the LMP dating was used. Otherwise, the clinical estimate of gestational age was used.

The final study sample consisted of infants who had a gestational age between 34⁰⁄₇ and 41⁶⁄₇ weeks (N = 159 813) and were assumed to be healthy on the basis of the common length of stay of ≤72 hours and the aforementioned exclusions. The sample was divided into 2 groups: healthy late preterm infants (gestational age between 34⁰⁄₇ and 36⁶⁄₇ weeks, n = 7152) and healthy term infants (gestational age between 37⁰⁄₇ and 41⁶⁄₇ weeks, n = 152 661).

Outcome Measures

Seven early school-age outcomes were analyzed: developmental delay or disability (determined by participation in Florida's Early Intervention Program for infants and toddlers from birth to 36 months and administered by the Florida Department of Health's Children's Medical Services in accordance with Part C of the Individuals with Disabilities Education Act); Prekindergarten Program for Children with Disabilities at age 3; Prekindergarten Program for Children with Disabilities at age 5; the designation "not ready to start school" at the start of kindergarten; and exceptional student education, suspension, and retention. Table 1 provides the formal definitions used by the Florida Departments of Health and Education for assigning children to these categories.

TABLE 1 Definitions of Early School-Age Outcomes

Early School-Age Outcome	Definition
Developmental Delay or Disability	Developmental delay refers to a lag in the rate at which a child exhibits a functional level that is normal for his or her age. Delay may appear across the board or in specific areas: physical, language, cognitive, and socioemotional development. Delay is defined as scoring 1.5 SD below the mean on a standardized assessment instrument. Disability refers to an established medical condition that places a child at high risk for developmental delay. Such medical conditions include genetic or metabolic disorders, neurologic insults, and sensory impairment.
Prekindergarten Program for Children With Disabilities	A federally and state-funded program for children who have received a diagnosis of a learning problem as a result of a physical, cognitive, sensory, or behavioral impairment.
Not ready to start school	An assessment 6 weeks into the school year by a kindergarten teacher by using a 16-item checklist that covers such topics as physical health, language development, socioemotional development, and general knowledge, indicating that student does not yet exhibit preacademic and social skills needed to be a successful learner.
Exceptional student education	Services provided to children who have special learning needs because of a disability. These may include special teaching methods and materials, technology devices, therapy, special transportation, or other supports. Need is determined using a multidisciplinary diagnostic evaluation looking at academics, development, and functionality.
Suspension	A disciplinary code indicating temporary removal of a student from the school program not exceeding 10 days.
Retention	A student is retained in the same grade at the end of the school year for failing to meet levels of performance indicated in a school's pupil progression plan.

Control Variables

Information on 15 maternal and infant variables was obtained from Florida's Office of Vital Statistics and Agency for Health Care Administration and used to adjust for potential confounding as a result of their differential distribution in the late preterm and term groups: mother's age (<20 years, 20–34 years, >34 years); mother's race (black, white, other); mother's education (less than high school, high school, more than high school); mother's marital status (yes, no); tobacco use during pregnancy (yes, no); alcohol use during pregnancy (yes, no); mother's participation in Medicaid during pregnancy (yes, no); previous adverse pregnancy experience (stillbirths, spontaneous or induced abortion [yes, no]); parity (0, 1–2, >2); Kotelchuck index of adequacy of prenatal care use (yes, no); pregnancy complications (acute or chronic lung disease, anemia, cardiac disease, diabetes, hemoglobinopathy, hypertension, previous preterm or small-for-gestational-age infant, or re-

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nal disease [yes, no]); labor and delivery complications (cord prolapse, fetal distress, malpresentation, placenta previa, premature rupture of membranes, or seizures [yes, no]); cesarean section delivery (yes, no); mechanical ventilation (yes, no); and infant gender (male, female).

Data Sources

Data were extracted from Florida Office of Vital Statistics (birth certificate, late preterm and term annual delivery data), Florida Agency for Health Care Administration (Medicaid eligibility), Children's Medical Services' Regional Perinatal Intensive Care Centers Program and Minimum Data Set (birth defects identified at 17 NICUs and 14 medical subspecialty clinics), Early Intervention Program (diagnosis of developmental delay or disability), and Florida Department of Education (classroom assignment and behavioral records of students in public prekindergarten programs for 3- and 4-year-olds and kindergarten for 5- and 6-year-olds). The public school database is a repository of historical student records (demographics, enrollment, courses, test scores) as well as information on educational facilities, curriculum, and staff involved in instructional activities supplied by Florida's 67 school districts. A description of Florida's kindergarten through college Education Data Warehouse is available at http://edwapp.doe.state.fl.us/doe/.

Statistical Analysis

Poisson regression models were fitted using the GENMOD Procedure in SAS. This method modeled the log of the probability of a prekindergarten or kindergarten outcome as a linear function of late preterm or term group, sociodemographic variables, and medical variables. Stepwise model building was used considering only main effects. On the basis of the fitted model, unadjusted and adjusted relative risk (aRR) with a 95% confidence interval (CI) was estimated for each school-age outcome. Comparison of the unadjusted and adjusted risk provided an estimate of the effect of the control variables on each outcome.

χ^2 tests were used to test the null hypothesis that the outcomes for the 3 late preterm gestational age groups, 34, 35, and 36 weeks' gestation, were not different. When significant differences were found, pairwise testing was done using Bonferroni correction to control type 1 error.

RESULTS

The final study sample consisted of 7152 healthy late preterm infants (4%) and 152 661 healthy term infants (96%). Thirteen of the 15 potentially confounding variables were found to be statistically different between the 2 groups (Table 2). Three variables were not significantly different between the 2 groups: alcohol use during pregnancy, infant gender, and cesarean section rate. From a sociodemographic standpoint, mothers of late preterm infants were more likely adolescents (19% vs 15%), of black race (31% vs 21%), and not high school graduates (29% vs 24%) and had received Medicaid during pregnancy (59% vs 52%). Mothers of late preterm infants also had higher rates of complications of pregnancy or labor and delivery (34% vs 22% and 35% vs 28%, respectively).

Differences in early school-age outcomes between the late preterm and term groups were statistically significant in 6 of the 7 categories (Table 3). The adjusted risk for developmental delay or disability was 36% higher among late preterm infants compared with term infants (aRR: 1.36 [95% CI: 1.29–1.43]). The risk for suspension in kindergarten was 19% higher for late preterm infants. The remaining 4 outcomes, disability in prekindergarten at 3 and 4 years of age, exceptional student education, and retention in kindergarten, all carried a 10% to 13% increased risk among late preterm infants. "Not ready to start school" was borderline significant (aRR: 1.04 [95% CI: 1.00–1.09]).

Between 34 and 41 weeks' gestation, there was a gradual decline in the percentage of infants with poorer outcomes as gestational age increased (Fig 1). There does not seem to be a gestational age threshold at which risk is clearly increased for any of the 7 outcomes.

Within the late preterm group, 3 school-related outcomes were significantly different by gestational age week group: not ready to start school, retention in kindergarten, and exceptional student education. Additional analysis by using Bonferroni corrected pairwise comparisons found that infants who were born at 34 weeks' gestational age were more likely not be ready to start school when compared with infants who were born at 35 and 36 weeks. There was no difference between infants who were born at 35 and 36 weeks for this outcome. No pairwise differences were found for retention in kindergarten and exceptional student education when Bonferroni correction was used to maintain the type I error rate at $<5\%$.

DISCUSSION

Late preterm infants are at higher risk for adverse early school age outcomes than term infants. Multiple studies have found higher rates of short-term morbidities among late preterm infants, which led to increased hospitalizations and costs and increased mortality,[15–18] but few have looked at later developmental outcomes.[13] Many late preterm infants seem to do well after delivery and require no resuscitative measures beyond routine delivery room care provided to term infants. They are then cared for in the well-infant nursery and treated as though they are term infants. In fact, many are discharged from the hospital within 48 to 72 hours of delivery with routine care instructions.[10,19,20] Although this practice has led to higher readmission rates and short-term medical morbidities, long-term development of these infants has previously not been a concern.[19] The results of this study, however, indicate a significantly increased risk for developmental delay and school-related problems up to 5 years of age in a statewide population of healthy late preterm infants compared with term infants.

From an obstetric point of view, most deliveries at 34 to 36 weeks' gestation age are medically indicated

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TABLE 2 **Characteristics of Healthy Late Preterm and Term Infants Born Between January 1, 1996, and August 31, 1997, in Florida**

Factor	Healthy Late Preterm (n = 7152), n (%)	Term (n = 152 661), n (%)	χ^2	P
Mother's age				
<20	1351 (18.89)	22 701 (14.87)	92.06	<.0001
>34	818 (11.44)	16 890 (11.06)		
20–34	4983 (69.67)	113 070 (74.07)		
Mother's race				
Black	2234 (31.24)	32 553 (21.32)	394.44	<.0001
White	3464 (48.43)	85 024 (55.69)		
Other	1454 (20.33)	35 084 (22.98)		
Mother's education	2075 (29.01)	36 289 (23.77)	132.31	<.0001
<High school	2730 (38.17)	57 902 (37.93)		
High school or greater	2347 (32.82)	58 470 (38.30)		
Medicaid				
Yes	4206 (58.81)	79 076 (51.80)	134.54	<.0001
No	2946 (41.19)	73 585 (48.20)		
Tobacco use during pregnancy				
Yes	1432 (20.02)	26 875 (17.60)	27.41	<.0001
No	5720 (79.98)	125 786 (82.40)		
Alcohol use during pregnancy				
Yes	535 (7.48)	10 873 (7.12)	1.32	.2503
No	6617 (92.52)	141 788 (92.88)		
No. of live births				
1–2	3439 (48.08)	78021 (51.11)	61.05	<.0001
>2	846 (11.83)	14 123 (9.25)		
0	2867 (40.09)	60 517 (39.64)		
Adverse pregnancy experience				
Yes	2167 (30.30)	42 848 (28.07)	16.82	<.0001
No	4985 (69.70)	109 813 (71.93)		
Adequate prenatal care				
Yes	6162 (86.16)	137 260 (89.91)	104.60	<.0001
No	990 (13.84)	15 401 (10.09)		
Infant's gender				
Male	3730 (52.15)	78 278 (51.28)	2.11	.1467
Female	3422 (47.85)	74 383 (48.72)		
Mechanical Ventilation				
No	6968 (97.43)	149 713 (98.07)	14.64	<.0001
Yes	184 (2.57)	2948 (1.93)		
Complication of pregnancy				
Yes	2430 (33.98)	33 266 (21.79)	584.82	<.0001
No	4722 (66.02)	119 395 (78.21)		
Cesarean section				
Yes	1285 (17.97)	28 423 (18.62)	1.92	.1664
No	5867 (82.03)	124 238 (81.38)		
Complication of labor and delivery				
Yes	2536 (35.46)	42 532 (27.86)	194.80	<.0001
No	4616 (64.54)	110 129 (72.14)		
Marital status				
Married	3807 (53.23)	94 194 (61.70)	206.72	<.0001
Not married	3345 (46.77)	58 467 (38.30)		

and therefore no change in management need be considered; however, there is evidence from the state of California of significant cost savings of up to 40% for each week of gestation that a delivery can be delayed between 34 and 36 weeks.[21] Gilbert et al[21] demonstrated a potential annual savings of $49 million from delaying delivery of infants who were between 34 and 36 weeks' gestation and were not thought to require delivery for medical indications until 38 weeks' gestation. Traditionally, obstetricians have allowed preterm labor to progress among those at 34 to 36 weeks' gestation believing that the risks of tocolysis would outweigh the low mortality and morbidity risks of delivering at a late preterm gestation.[22,23] Higher risks for school delay, developmental delay, and early school-age problems, identified in this study, are important considerations when weighing the risks and benefits of late preterm delivery.

Late preterm infants also need close developmental follow-up despite their initial healthy presentation. Par-

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TABLE 3 **Percentage Occurrence and Risk (Unadjusted and Adjusted) of Adverse Early School-Age Outcome Among Healthy Late Preterm and Term Singleton Infants**

Early School-Age Outcome	Age	% Healthy Late Preterm (*N* = 7152)	% Term (*N* = 152 661)	Unadjusted Relative Risk [95% CI]	aRR [95% CI]
Developmental delay/disability	0–3	4.24	2.96	1.43 (1.36–1.51)	1.36 (1.29–1.43)
Disability in prekindergarten	3	4.46	3.89	1.15 (1.09–1.20)	1.13 (1.08–1.19)
Disability in prekindergarten	4	7.40	6.60	1.12 (1.08–1.16)	1.10 (1.05–1.14)
Not ready to start school	4	5.09	4.40	1.16 (1.11–1.21)	1.04 (1.00–1.09)
Exceptional student education	5	13.30	11.88	1.13 (1.09–1.16)	1.10 (1.07–1.13)
Retention in kindergarten	5	7.96	6.17	1.29 (1.24–1.34)	1.11 (1.07–1.15)
Suspension in kindergarten	5	1.80	1.22	1.48 (1.37–1.60)	1.19 (1.10–1.29)

ents, physicians, child development specialists, and education professionals need to be aware of the risks for possible school underachievement and behavioral problems so that prompt referrals to early intervention services are made. Pediatricians can play a crucial role by providing anticipatory guidance.

An epidemiologic consideration is related to individual risk and population impact. In the United States, from 1992 to 2002, late preterm infants represented 70% of preterm births and accounted for two thirds of the increase in the rate of preterm birth. Within Florida, the number of infants who were delivered late preterm steadily increased between 1993 and 2003. During the same period, the number of term deliveries steadily declined (Fig 2). Although the absolute risk for a poor outcome is relatively low for a healthy late preterm infant, ranging from 2% to 13%, the cumulative societal and medical costs are substantial as a result of the increasing number and proportion of late preterm deliveries, currently ~360 000 annually.

This study has several strengths. It comprises an entire statewide population; the construction of the late preterm cohort is novel because of its restriction to infants at 34 to 36 weeks' gestational age, who, like healthy term infants, were discharged from the hospital within 3 days of delivery; and it longitudinally links key neonatal, preschool, and kindergarten databases. Its findings are in response to a recent call by the American Academy of Pediatrics Committee on Fetus and Newborn: "Given that late preterm infants are born before their nervous systems have fully developed, large population studies that evaluate the long-term neurodevelopmental and behavioral outcomes of these children are needed."[24]

The limitations of the study center on the use of large retrospective data sets. Detailed medical information was not available in the statewide administrative databases consulted; therefore, the assumption was made that a hospital stay of ≤3 days for either a term or late preterm infant indicated a healthy prognosis. There may be infants who required early after discharge readmission that led to significant medical complications that was not captured in this analysis; however, studies of readmission among this late preterm population point to short-term minor medical issues such as jaundice and poor feeding.[9,10] Use of vital statistics in outcomes research is known to be problematic. For example, alcohol use during preg-

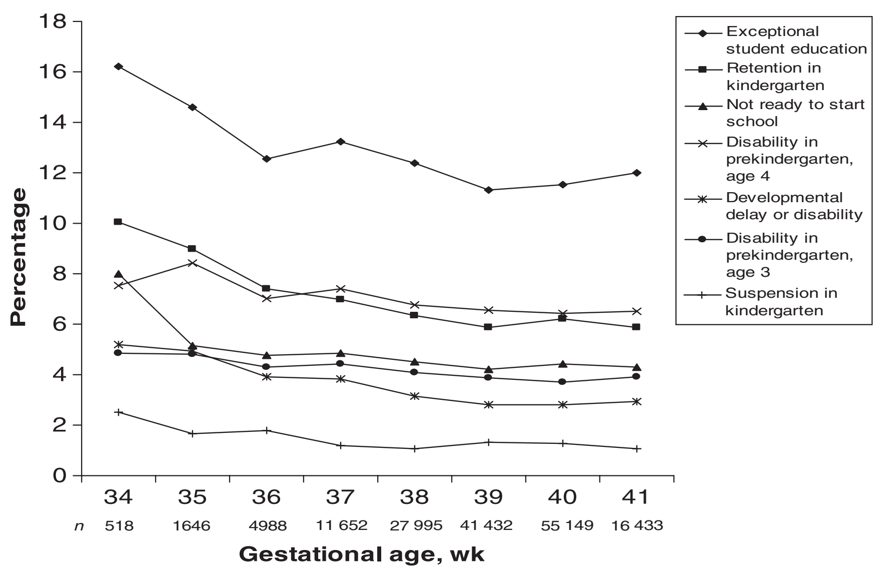

FIGURE 1
Percentage of children with adverse early school-age outcome by gestational age.

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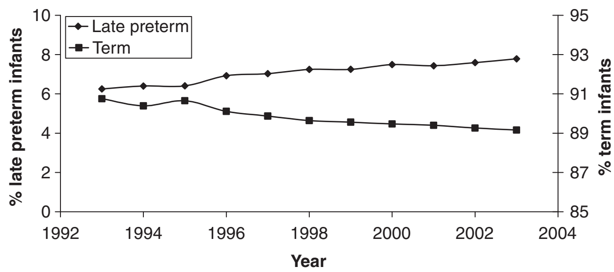

FIGURE 2
Changing proportions of term and late preterm deliveries in Florida 1993 to 2003.

nancy is not reliably reported on the birth certificate.[25,26] In this study, self-reported alcohol use was below published national estimates: 7% vs 16%[27] The observed rates of alcohol use during pregnancy in the late preterm and term groups, however, were nearly identical. Because there is no reason to assume that underreporting of this variable is different in the 2 groups, alcohol use during pregnancy has no effect on the comparison of school-age outcomes in healthy late preterm and term infants.

It is also widely known that there may be significant disagreement between date of LMP and clinical estimate of gestational age, especially among preterm births.[28–31] In cases in which discrepancies were >2 weeks, the clinical estimate of gestational age was used; however, the possibility of measurement error on this variable remains.

Multiple factors between birth and school age can influence developmental outcomes. This study controlled for commonly known factors that have an impact on developmental outcomes; however, other unknown or unmeasured factors may be present in our late preterm cohort biasing them to a more negative outcome. Approximately 10% of the initial sample of both the late preterm and term infants had missing data on hospital length of stay, which necessitated exclusion from the study. It is unknown whether these infants' outcomes would have changed the final results of this study. Last, the outcomes chosen were based on statewide surveillance programs that identify children at increased risk for developmental delay or disability. The inclusion of children not identified in these statewide surveillance programs could alter the final results; however, there is no reason to believe that this small sample of unobserved disabled or delayed children would be biased in its proportion of late preterm infants compared with the larger observed population. Although the overall incidence of each outcome may not have been estimated precisely, the significant difference between the 2 groups would not be expected to change.

Moreover, no routine referral process is in place for children who are born preterm in Florida to be evaluated for referral to a program that provides special services that would not also apply to children born at term. Preterm delivery is not itself an eligibility criterion for referral to Florida's Part C program for infants and toddlers with developmental delay or disability (birth to 36 months). In the event that an infant of any gestational age receives a diagnosis from a licensed physician as having an established condition (autism spectrum disorder, genetic/metabolic disorder, neurologic disorder, severe attachment disorder, and significant sensory impairment), written confirmation is needed to establish eligibility for special services.

Statistical adjustment by using multiple regression for covariate differences (eg, mother's race [black] was 31% in late preterm group compared with 21% in the healthy term group) may not be sufficient to create the needed balance between the 2 groups. The analysis was confined to main effects only and did not examine interactions between factor levels that might demonstrate different risk ratios among the subgroups.

Florida's public school database supplied information about how children were functioning in prekindergarten and kindergarten; however, it is widely known that many other factors influence children's educational performance, such as teachers' qualification and training, school resources, family involvement, neighborhood conditions, and peer effects.[32,33] Therefore, preterm birth cannot unequivocally be isolated as an independent factor predictive of future academic performance.

Although we found an association between late preterm birth and poorer early school-age outcomes, this study did not address the cause of this poorer outcome. Additional research is needed to elucidate the multiple factors that may be amenable to treatment soon after birth that would have a positive impact on neurodevelopmental outcome. Dramatic differences in brain maturation and growth at 35 weeks and term have been identified. At 35 weeks' gestation, there are significantly fewer sulci and the weight of the brain is 60% that of term infants.[34,35] In addition, during the final 4 weeks of gestation, significant growth is seen in the gyri, sulci, synapses, dendrites, axons, oligodendrocytes, astrocytes, and microglia.[36–41] These brain findings provide a clue to the causes of the poorer outcomes that we found in this study. Identifying how brain maturation in the final month of gestation influences later school performance is of paramount importance.

CONCLUSIONS

In light of the dearth of information currently available regarding the association between late preterm birth and early school-age outcomes, this study provides compelling information that healthy-appearing late preterm infants carry an increased risk for developmental delay and adverse early school-age outcomes compared with healthy term infants.

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