Published in final edited form as:

Early Hum Dev. 2012 September ; 88(9): 765–771. doi:10.1016/j.earlhumdev.2012.04.004.

Birth weight- and fetal weight-growth restriction: impact on neurodevelopment

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Abstract

Background—The newborn classified as growth-restricted on birth weight curves, but not on fetal weight curves, is classified prenatally as small for gestational age (SGA), but postnatally as appropriate for gestational age (AGA).

Aims—To see (1) to what extent the neurodevelopmental outcomes at 24 months corrected age differed among three groups of infants (those identified as SGA based on birth weight curves (B-SGA), those identified as SGA based on fetal weight curves only (F-SGA), and the referent group of infants considered AGA, (2) if girls and boys were equally affected by growth restriction, and (3) to what extent neurosensory limitations influenced what we found.

Study design—Observational cohort of births before the 28 week of gestation. Outcome measures: Mental Development Index (MDI) and Psychomotor Development Index (PDI) of the Bayley Scales of Infant Development II.

Results—B-SGA, but not F-SGA girls were at an increased risk of a PDI < 70 (OR=2.8; 95% CI: 1.5, 5.3) compared to AGA girls. B-SGA and F-SGA boys were not at greater risk of low developmental indices than AGA boys. Neurosensory limitations diminished associations among girls of B-SGA with low MDI, and among boys B-SGA and F-SGA with PDI < 70.

Conclusions—Only girls with the most severe growth restriction were at increased risk of neurodevelopmental impairment at 24 months corrected age in the total sample. Neurosensory limitations appear to interfere with assessing growth restriction effects in both girls and boys born preterm.

Introduction

Infants are considered growth restricted, or small for gestational age (SGA) if their birth weights are in the lowest decile on a gestational-age specific birth weight curve. Birth

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The authors have indicated that they have no financial relationships relevant to this article to disclose, nor do they have any conflict of interest to disclose.

weight distributions have lower means, medians and 10th centiles than estimated fetal weight distributions, especially among preterm newborns [1]. Some newborns whose birth weight is considered appropriate by neonatal standards are growth restricted by fetal standards (Figure 1). This phenomenon appears to reflect the preferential preterm birth of growth restricted infants [2].

We refer to infants who are SGA on birth weight curves as B-SGA, and to those who are SGA on estimated fetal weight curves, but appropriate for gestational age (AGA) on birth weight curves, as “F-SGA” [1]. Fetal weight estimates are considered reliable [3, 4].

Among children who had been born at an early gestational age or a low birth weight, those whose birth weight was in the lowest decile for gestational age tend to be at increased risk of cognitive limitations [5–10], but not always [11–14]. The authors of a recent report raised the possibility that their finding no association between fetal growth restriction and cognitive limitations might have been due to their excluding children who had neurosensory limitations. [14]. Recently, both the sex of the child [10] and the magnitude of the growth restriction [9] have been identified as factors that influence the relationship between growth restriction and development in children born at a low gestational age.

In this paper, we compare the development of extremely low gestational age newborns at age two years who were B-SGA (relatively severe growth restriction) and those who were F-SGA (less severe growth restriction) to their AGA peers. In addition, we explore the influence of the infant’s sex and neurosensory impairment on the relationship between growth-restriction and development.

Patients and Methods

The ELGAN study prospectively enrolled infants born between 23 0/7 and 27 6/7 weeks of gestation, from March 2002 until August 2004, at 14 institutions [15]. Institutional Review Board approval was obtained at each study site and written informed consent was obtained from every one of the 1249 mothers of the 1506 infants enrolled.

Study participants were assigned to a B-SGA, F-SGA or AGA group before data analysis. Even though all B-SGA infants are, by definition F-SGA, we restrict the term F-SGA to those children who were not classified as B-SGA. The three weight groups are mutually exclusive (Figure 1).

Of the three separate fetal-weight distributions [16–18], and the six birth-weight distributions [19–24] we evaluated, we chose the fetal [18] and the birth [23] distributions that were sex-specific and provided the most reasonable number of growth-restricted newborns. No newborn had a dysmorphic syndrome or congenital infection associated with growth restriction.

Maternal Characteristics/Delivery Characteristics

Maternal race was collected by maternal report. Details about factors associated with delivery and antenatal steroids are presented elsewhere [25]. The most reliable measure of gestational age is the timing of fertilization therapy or fetal ultrasound performed before the 14th week. When this information was not available, we accepted less reliable measures such as fetal ultrasound performed after the 14th week, the date of last menstrual period, and the gestational age as recorded by clinicians.

Newborn Characteristics

Anthropometric measures, including body weight, length and head circumference, were recorded throughout the hospitalization and at follow-up.

Newborn Morbidity and Mortality

The diagnoses of patent ductus arteriosus, pneumothorax, pulmonary interstitial emphysema, pulmonary hemorrhage and bacteremia were collected from the medical record. Modified Bell staging criteria were used to classify necrotizing enterocolitis [26].

Mode of ventilation and days of oxygen were noted. An infant was considered to have bronchopulmonary dysplasia if supplemental oxygen was provided at 36 weeks postmenstrual age. Retinal examinations were obtained in keeping with clinical guidelines and retinopathy of prematurity was diagnosed by ELGAN Study ophthalmologists [27]. Growth velocity (grams/kg/day) between days 7 and 28 was calculated using the formula $1000 * [(wt28 - wt7) / wt7] / 21$.

Ventriculomegaly and an echolucent lesion were identified by cranial ultrasound scans. The procedures for obtaining scans and interpreting them have been described elsewhere [28].

Neurodevelopmental Follow-up

Parents were invited to bring their infants for neurodevelopmental follow-up testing at approximately 24 months corrected age. Of the 1200 children who survived to 2 years, 1103 (92%) had a developmental assessment, with 75% of those children evaluated between 23.5 and 27.9 months corrected age.

Anthropometric measures, including body weight, length, and head circumference, were recorded at birth by members of the clinical staff in the intensive care nursery. The research-trained examiner (neurologist, development/behavior pediatrician, or psychologist) measured the head circumference at age 2 years corrected age [29].

The developmental assessment included the Bayley Scales of Infant Development – Second Edition (BSID) [30], a neurologic exam [29], and the Vineland Adaptive Behavior Scales (VABS). Those who conducted these assessments were not provided with any information about the child prior to the examination.

Motor impairment was classified with the Gross Motor Function Classification System (GMFCS) [31]. 1018 children had the full Bayley Scales of Infant Development assessment.

One set of analyses eliminated 122 children who had a major neurosensory limitation. This was defined as an inability to walk even with assistance (GMFCS 1), a significant hearing impairment (a parent report that the child required a hearing aid or needed special services for hearing impairment) or a significant vision impairment (a parental report that the child was considered legally blind in at least one eye).

Data analysis

We evaluated two separate hypotheses. The first hypothesis postulated that compared to children who were AGA, those who were classified as B-SGA and those classified as F-SGA were not at increased risk of developmental dysfunctions at 24 months corrected age. The second postulated that the relationships between intrauterine growth restriction and development dysfunctions at 24 months corrected age were not influenced by the child's sex or neurosensory impairment.

We created multivariable logistic regression models for each sex and each outcome that compared B-SGA and F-SGA infants to the referent group of AGA infants. Potential confounders, defined as variables associated with growth restriction and with an outcome were included in each model. The strengths of association of the SGA variables are presented as risk ratios with 95% confidence intervals.

We created the same models in the sample of children who had no major neurosensory disturbance (defined as a GMFCS score < 1, and no appreciable hearing or vision impairment).

Infants born of multi-fetal gestations were included in multivariable analyses that controlled for multiple gestations. We also conducted separate multivariable analyses of singletons only, which provided similar findings, but with a smaller sample.

Because cerebral palsy diagnoses are mutually exclusive and each is compared to the same referent group, we created multinomial multivariable logistic regression models for these diagnoses.

Results

Growth Categorization

In the total sample of 1506 newborns, 183 (12%) were classified as B-SGA (data not shown). An additional 109 (7%) infants, were classified as F-SGA only [17]. These 292 infants represent 19% of the total study population.

Of the 1103 infants who had a developmental assessment at approximately 2 years after term equivalent, 106 (10%) were B-SGA and 87 (8%) were F-SGA (Table 1). This is the sample for Tables 1–3.

In the sample of girls who had an MDI and PDI, 12% (N = 57) were B-SGA, 9% (N = 45) were F-SGA, 79% (N = 390) were AGA, while in the sample of boys who had an MDI and PDI, 8% (N = 42) were B-SGA, 7% (N = 35) were F-SGA, 85% (N = 449) were AGA. This is the sample for Table 4.

Among the girls in the restricted sample of children who had an MDI and PDI, but who did not have a major neurosensory limitation, 11% (N = 49) were B-SGA, 9% (N = 41) were F-SGA, and 79% (N = 346) were AGA. Among the boys in this restricted sample, 8% (N = 38) were B-SGA, and 7% (N = 34) were F-SGA, 84% (N = 388) were AGA. This is the sample for Table 5.

Maternal Characteristics/Delivery Characteristics (Table 1)

Race was the only maternal characteristic that was associated with SGA. Multi-fetal gestation was the only characteristic that was under-represented among B-SGA infants. Both SGA groups had higher Cesarean delivery rates than the AGA group. Preeclampsia and fetal indication were the disorders leading to preterm delivery for 9% of the AGA infants, but together they were the reason for delivery for 64% of B-SGA infants and 45% of F-SGA infants.

Newborn Characteristics (Table 1)

AGA infants were more likely than infants in both SGA groups to be born at 23–24 weeks. F-SGA infants had median head circumferences and birth weights intermediate between AGA and B-SGA infants.

No appreciable differences were noted in Apgar scores, delivery room resuscitation or SNAP–II scores (data not shown). The rate of death in the entire sample during the first 28 postnatal days was higher among B-SGA infants (22%) than among F-SGA (10%) and AGA infants (13%). The rate of death in the NICU after the 28th postnatal day was also higher among B-SGA infants (12%) than among F-SGA (6%) and AGA infants (4%).

Newborn Morbidity (Table 2)

AGA boys were more likely than AGA girls to have had moderate/severe ventriculomegaly on an ultrasound scan of the brain, and to a much smaller extent, an echolucent lesion. B-SGA boys were also more likely than B-SGA girls to be in the highest quartile of days on the ventilator and in the highest quartile of days receiving supplemental oxygen. F-SGA boys were more likely than F-SGA girls to have had bacteremia during the first postnatal week, and also surgical necrotizing enterocolitis. On the other hand, B-SGA girls were more likely than B-SGA boys to have had late bacteremia.

Growth and Neurodevelopmental Outcomes at 24 months corrected age (Table 3)

Since girls tend to differ from boys in their developmental trajectories [10, 32], we evaluated SGA relationships with developmental outcomes in girls separately from boys. Among girls, rates of MDI <70, PDI <70, and head circumference Z-score < -2 were highest in those who were B-SGA, while the rates of those who were F-SGA were only slightly higher than those who were AGA. Among boys, those born B-SGA and F-SGA had similarly elevated rates of MDI <70 and PDI <70 while only B-SGA boys were at increased risk of microcephaly.

At 24 months corrected age, 37% of B-SGA girls had an MDI below 70, while 40% of B-SGA boys had such a low MDI. This lack of male-female difference is in contrast to the rates of low MDIs among F-SGA and AGA children. 24% of F-SGA girls had an MDI below 70, while 40% of F-SGA boys had such a low MDI. Similarly, only 18% of AGA girls had an MDI <70, while 31% of AGA boys had such a low MDI.

B-SGA girls and boys tended to have low rates of quadriplegia and diplegia, but relatively high rates of hemiparesis. Both SGA groups of both sexes were more likely than their AGA peers to have a weight at age 2 years more than 2 standard deviations below the expected mean. B-SGA girls and boys had the highest rates of microcephaly at age 2 years, while F-SGA girls and boys tended to have rates that more closely approximated those of their AGA, rather than their B-SGA, peers.

Multivariable Models of Neurodevelopment in entire follow-up sample (Table 4)

For all multivariable analyses, we adjusted for race, gestational age, multi-fetal gestation, maternal and fetal indication for delivery, and route of delivery. The models for a head circumference Z-score < -2 also adjusted for head circumference < -2 at birth.

Compared to AGA girls, B-SGA girls were at significantly increased risk of a PDI < 70 [OR = 2.6 (1.4, 5.0)] and a 24-month weight Z-score < -2 [OR = 12 (2.1, 69)]. These girls were at a nearly significantly increased risk of an MDI < 70 [OR = 2.0 (1.00, 3.9)]. In contrast, B-SGA boys were at a significantly greater risk only of a head circumference Z-score < -2 [OR = 4.8 (1.7, 13)].

Multivariable Models of Neurodevelopment in among children who did not have a major neurosensory limitation (Table 5)

To evaluate to what extent what we saw in Table 4 reflected the influence of major neurosensory limitations, we again created multivariable models, but this time among children who were able to walk independently, who by parent report did not use a hearing

aid or receive special services for the hearing impaired, and who were not considered legally blind in either eye. This resulted in a loss of 56 girls (43 because of motor limitation, 15 for visual limitation and 10 for hearing limitation), and 66 boys (54 because of motor limitation, 14 for visual limitation and 12 for hearing limitation), some with multiple limitations.

In this sample, B-SGA girls were at increased risk of a score < 70 on both the MDI and PDI. In contrast, while they were not at increased risk of a PDI < 70 in the entire sample, both B-SGA boys and F-SGA boys were at increased risk in this restricted sample [B-SGA: OR = 2.6 (1.1, 5.8); F-SGA: OR = 2.2 (1.02, 4.7)]. The body weight and head circumference findings in Table 4 persisted. In addition, however, the modestly increased risk of a weight Z-score < -2 seen previously among B-SGA boys achieved statistical significance in this restricted sample [OR = 8.2 (1.6, 41)]

Discussion

Three of our findings are worthy of comment. First, among all girls, severe growth restriction (B-SGA) is associated with delayed development while less severe growth restriction (F-SGA) is not. Second, among all boys, neither severe, nor less severe fetal growth restriction is associated with developmental delay. Third, major neurosensory limitations appeared to obscure increased risks of low MDI in girls with severe growth restriction, and low PDI in boys with severe and less severe growth restriction.

Weaknesses and strengths of this study

The weaknesses of our study are those of all observational studies. We are unable to distinguish between causation and association as explanations for what we found. We were not able to assign growth-restricted infants to groups of uniform risk of developmental adversities based on the etiology of the growth restriction, or reason for delivery.

Our study has several strengths. We selected infants based on gestational age, and not birth weight. This minimizes confounding due to factors related to fetal growth restriction [33]. We collected all of our data prospectively. Also, at follow-up, examiners were not aware of the medical histories of the children they examined, thereby minimizing “diagnostic suspicion bias” [34]. We minimized observer variability as best we could in the assessments and classifications of neurodevelopmental functions. We studied more homogenous, and therefore more informative, outcomes than studies that have composite outcomes, such as any neurodevelopmental impairment (defined as impaired early cognitive function or cerebral palsy or sensory impairment). Our sample is sufficiently large to appreciate relatively small increases in the odds ratios in subgroups. For example, the 34 F-SGA boys were approximately twice as likely as their 388 AGA peers to have a PDI < 70 (odds ratio = 2.2, 95% CI: 1.02, 4.7). Finally, attrition was modest, with 92% of survivors having had a developmental assessment at approximately two years post-term equivalent.

Magnitude of growth restriction

Among children in the EPIPAGE Study born between the 29th and 32nd weeks of gestation, SGA children and “mildly”-SGA children (birth weight was at or above the 10th centile, but below 20th centile) were at comparably increased risk for minor cognitive and behavioral difficulties at age 5 years [9]. No gradient was found. SGA and mildly-SGA had similar increased risks of cognitive and behavioral limitations.

Among EPIPAGE Study children born between the 24th and 28th weeks of gestation, however, neither being born SGA nor “mildly”-SGA was associated with increased risks of cognitive “deficiency” [9]. Although a small percentage of our sample was born before 24 weeks, all the rest were born between the 24th and 27th weeks of gestation. Unlike the

EPIPAGE Study, we evaluated girls separately from boys. Thus, our finding that B-SGA girls, but not F-SGA girls, are at increased risk of developmental delay should not be viewed as discrepant with the findings of the EPIPAGE Study. Indeed, our finding that SGA boys (regardless of whether B-SGA or F-SGA) are at not at increased risk of developmental delay at 2 years can be seen as similar to the EPIPAGE Study findings of no increased risk of cognitive deficiency among SGA and mildly-SGA children at 5 years.

Several commentators have suggested that infants whose birth weight falls below the 10th centile for fetuses of the same gestational age, but above the 10th centile for live-born infants of the same gestational age be re-classified as F-SGA [1, 2, 35]. Our data for infants < 28 weeks indicate that this reclassification does not add much predictive power about neurodevelopmental outcomes. Unlike B-SGA infants, F-SGA infants were not more likely to die in the neonatal period, nor to suffer more neurodevelopmental impairments. Perhaps it is time to approach the definition of growth restriction in relation to the points along the birth weight distribution where adverse outcomes begin to increase, rather than at an arbitrary point that falls a certain distance below the mean [36–38].

Sex differences

In our cohort, B-SGA females were at a substantially increased risk of MDI < 70, PDI < 70 and 24-month weight Z-score < -2. Intrauterine growth did not predict neurodevelopment in male infants. It appears that the neurodevelopmental measures most influenced by restricted by processes associated with reduced *in-utero* growth are MDI and PDI, and that the smallest female infants are most affected by phenomena associated with disordered growth. In this cohort of infants 52% of survivors are male, whereas 57% of deaths were males. Consequently, preferential mortality is unlikely to account for much of what we see.

The difference in the association of growth restriction and poor neurodevelopmental outcome in girls and boys is not well understood. Another study found that this discrepancy could not be attributed to differences in neonatal disorders such as intraventricular hemorrhage, periventricular leukomalacia or bronchopulmonary dysplasia [39]. We, on the other hand, found that AGA boys were more likely than AGA girls to have ultrasound lesions indicative of focal and diffuse white matter damage were more common in AGA boys than in AGA girls, as well as impaired development at age 2 years. Others have also found that brain development in the male is more vulnerable than that in females [32].

Because these brain lesions are associated with heightened risk of developmental dysfunctions [40], the dysfunction in AGA boys probably has little, if anything, to do with intra-uterine growth restriction. Consequently, AGA boys, the most appropriate referent group for both B-SGA and F-AGA boys, might have been more similar to B-SGA and F-SGA boys, than AGA girls were to B-SGA and F-AGA girls. In part, this might have accounted for the relatively small effect on developmental function attributable to intra-uterine growth restriction in boys.

Neurosensory limitations

If the brain damage attributed to processes associated with fetal growth restriction was accompanied by major neurosensory limitations, then excluding children with major neurosensory limitations should result in our finding no association between growth restriction and cognitive impairment. Our excluding children with major neurosensory limitations, however, first revealed an association between growth restriction and PDI < 70 among boys that was not seen in the entire sample of boys.

A likely explanation is that low PDI among boys associated with a neurosensory limitation, most probably major motor limitation (i.e., GMFCS 1), is not associated with fetal growth

restriction. Indeed that is just what we found. 6% of B-SGA, 7% of B-SGA and 19% of AGA boys who had a PDI <70 were not able to walk independently, while all boys (regardless of fetal growth status) who had a PDI 70 could walk independently.

In summary, our data support the concept that growth restriction is far more complicated than simply identifying a ‘small’ infant or fetus. Gestational age, the degree of growth restriction, and now sex and neurosensory limitations, all need to be considered when appreciating the long-term impact of altered in-utero growth [37]. Unmeasured factors contribute to disordered growth, and these factors, not growth restriction itself, might influence development. Questions persist about how best to define growth restriction, especially in light of evidence that morbidity and mortality vary with birth weight above the 10th decile [36–38], and evidence that growth restriction effects/correlates vary with gestational age at birth [36, 41].

Acknowledgments

The study sponsors did not participate in, nor did they influence, the collection, analysis or interpretation of the data, the writing of the manuscript; or the decision to submit this manuscript for publication.

This study was supported by a cooperative agreement with the National Institute of Neurological Diseases and Stroke (5U01NS040069-05) and a center grant award from the National Institute of Child Health and Human Development (5P30HD018655-28). Dr. Streimish was supported by training grants from Eunice Shriver National Institute of Child Health and Human Development (T32 HD07094) and the Agency for Healthcare Research and Quality (2T32HS00006D-16). The authors gratefully acknowledge the contributions of their subjects, and their subjects’ families, as well as those of their colleagues.

List of abbreviations

AGA	Appropriate for gestational age
B-SGA	Birth weight defined small for gestational age
CI	95% confidence interval
BSID	Bayley Scales of Infant Development
ELGAN	Extremely low gestational age newborn
F-SGA	Fetal weight defined small for gestational age
GMFCS	Gross Motor Function Classification System
HC	Head circumference
MDI	Mental Development Index
OR	Odds ratio
PDI	Psychomotor Development Index
pPROM	Preterm premature rupture of membranes
SGA	Small for gestational age
VABS	Vineland Adaptive Behavior Scale

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Figure 1.

Distributions of birth weight and estimated fetal. Weights are along the X-axis and the proportion of the sample along the Y-axis. Weights to the left of the solid vertical line are SGA by BW and EFW. Weights falling between the vertical solid and dashed lines are SGA by EFW standards only (Fetal-SGA). BW-SGA weights are to the left of the solid vertical line and AGA weights fall to the right of the dashed vertical line.

Table 1

Percent of infants classified by their growth status who had the characteristics listed at the left. These are column percents.

Maternal, delivery and infant characteristics		Growth Status			Row N
		B-SGA	F-SGA	AGA	
Racial identity	White	50	55	63	660
	African American	29	34	26	291
	Other	21	10	12	135
Hispanic	Yes	16	11	11	129
Age (years)	< 21	17	10	13	143
	21–35	66	71	67	744
	> 35	17	18	20	216
Years of education	Less than college	47	40	43	460
	Some college	22	31	23	246
	College graduate/beyond	31	29	34	359
Marital status	Single	45	43	41	455
Multiple birth	Yes	25	32	35	371
Antenatal steroids	Any	92	97	89	988
	Complete course	68	72	63	708
Cesarean delivery	Yes	89	79	63	736
Initiator of delivery	PTL	16	31	50	499
	pPROM	13	16	23	240
	Preeclampsia	52	39	6	144
	Abrupt	7	3	12	118
	Cervical insufficiency	0	5	6	58
	Fetal indication	12	6	3	44
Male Infant	Yes	44	43	54	572
Gestational age	23–24	12	10	22	221
	25–26	50	38	46	508
	27	38	52	32	374
Birth weight	750	100	55	27	398

Maternal, delivery and infant characteristics		Growth Status			Row N
		B-SGA	F-SGA	AGA	
	751 – 1000	0	45	49	487
	> 1000	0	0	34	218
Birth weight Z-score*	< -2	54	1	0	58
	-2, < -1	46	69	4	145
	-1	0	30	96	900
Head circumference Z-score ^a	< -2	52	18	2	84
	-2, < -1	42	55	17	242
	-1	6	27	81	736
Maximum number of infants		106	87	910	1103

^aYudkin standard 15

Table 2

Percent of girls and boys classified by their growth status who have the newborn morbidities (ascertained or diagnosed during the NICU stay) listed at the left. These are column percents.

Newborn morbidities		Growth Status			Row N
		BW-SGA	Fetal-SGA	AGA	
<i>Growth</i>					
Lowest quartile growth velocity day 7-28 ^a	Girls	17	24	26	128
	Boys	19	28	24	133
<i>Neurologic</i>					
Any intraventricular hemorrhage ^b	Girls	12	16	17	87
	Boys	11	14	26	139
Ventriculomegaly ^b	Girls	8	4	8	41
	Boys	6	5	13	67
Echolucency ^b	Girls	2	4	6	30
	Boys	2	0	9	46
<i>Cardiovascular</i>					
Patent ductus arteriosus	Girls	32	42	34	182
	Boys	34	30	31	176
<i>Pulmonary</i>					
Pneumothorax	Girls	7	6	7	36
	Boys	11	8	7	44
Pulmonary interstitial emphysema	Girls	19	6	14	71
	Boys	13	22	18	100
Pulmonary hemorrhage	Girls	2	4	4	18
	Boys	0	3	4	19
Highest quartile days on ventilator	Girls	44	22	20	121
	Boys	45	38	26	161
Highest quartile days on oxygen	Girls	20	6	24	117
	Boys	28	27	30	169

Newborn morbidities		Growth Status			Row N
		BW-SGA	Fetal-SGA	AGA	
Postnatal steroid	Girls	25	12	9	59
	Boys	21	8	13	75
Chronic lung disease	Girls	78	46	45	258
	Boys	72	59	50	296
<i>Gastrointestinal</i>					
Surgical necrotizing enterocolitis	Girls	3	0	2	11
	Boys	4	11	5	28
Isolated bowel perforation	Girls	3	4	2	11
	Boys	4	3	4	22
<i>Infectious</i>					
Definite early bacteremia (postnatal week 1)	Girls	7	4	7	37
	Boys	6	11	5	32
Definite late bacteremia (postnatal week 2–4)	Girls	36	24	25	136
	Boys	26	32	24	140
<i>Ophthalmologic</i>					
Retinopathy of prematurity, Stage 3	Girls	49	28	25	147
	Boys	32	29	28	158
Maximum number of babies	Girls	59	50	422	531
	Boys	47	37	488	572

^a Growth velocity, day 7 to 28: $1000 * [(wt28 - wt7) / (wt7 / 21)]$

^b Finding on ultrasound sets obtained in the NICU

Table 3

Percent of infants classified by their growth status who have the growth measurements and neurodevelopmental outcomes at 24 months corrected age listed at the left. For each outcome, the top row presents column percents for girls and the bottom row presents column percents for boys.

Growth and neurodevelopmental outcomes at 24 months		Growth Status			Row N
		B-SGA	F-SGA	AGA	
MDI < 70	Girls	37	24	18	101
	Boys	40	40	31	168
PDI < 70	Girls	47	29	25	138
	Boys	40	40	32	176
GMFCS 1+	Girls	10	6	8	39
	Boys	4	3	11	53
Cerebral palsy:					
Quadriplegia	Girls	9	4	5	26
	Boys	2	3	8	38
Diparesis	Girls	2	2	3	16
	Boys	0	3	4	21
Hemiparesis	Girls	2	2	0.2	3
	Boys	4	0	3	16
Any	Girls	12	8	9	45
	Boys	7	6	15	75
Vision impairment ^a	Girls	5	6	3	17
	Boys	2	0	3	15
Hearing impairment ^b	Girls	5	0	1	9
	Boys	2	0	2	12
Weight Z-score ^d < -2	Girls	7	0	2	11
	Boys	7	3	3	19
Head circumference Z-score ^d < -2	Girls	26	8	6	42
	Boys	31	11	18	66
Maximum number of girls		59	50	422	531
Maximum number of boys		47	37	488	572

^a Legally blind in one or both eyes

^b Uses a hearing aid or receives special services for the hearing impaired

^c Among those with a GMFCS <1, and no major vision or hearing impairment

^d CDC standard

Table 4

Odds ratios (and 95% confidence intervals) of developmental outcomes at 2 years among children who had been B-SGA and F-SGA newborns compared to AGA infants, adjusted for confounders^a. The top row of each set presents odds ratios for girls. The bottom row presents odds ratios for boys. **Bolded items** are statistically significant.

Growth and neurodevelopmental outcomes at 24 months		Growth Status	
		B-SGA	F-SGA
MDI < 70	Girls	2.0 (1.00, 3.9)	1.3 (0.6, 2.8)
	Boys	1.2 (0.5, 2.5)	1.5 (0.7, 3.4)
PDI < 70	Girls	2.6 (1.4, 5.0)	1.2 (0.6, 2.5)
	Boys	1.8 (0.8, 3.9)	1.7 (0.8, 3.5)
GMFCS 1+	Girls	1.9 (0.6, 6.1)	0.9 (0.2, 4.5)
	Boys	0.4 (0, 3.1)	0.4 (0.1, 3.6)
Cerebral palsy:			
Quadriplegia	Girls	1.9 (0.6, 6.5)	1.0 (0.2, 4.9)
	Boys	0.3 (0, 2.4)	0.4 (0, 2.8)
Diparesis	Girls	0.7 (0.1, 6.1)	0.9 (0.1, 6.6)
	Boys	--- ^e	0.6 (0.1, 4.9)
Hemiparesis	Girls ^b	17 (0.8, 349)	13 (0.7, 222)
	Boys	1.7 (0.3, 9.9)	--- ^e
Any	Girls	1.9 (0.7, 5.2)	1.3 (0.4, 4.1)
	Boys	0.5 (0.1, 1.9)	0.3 (0.1, 1.6)
Weight Z-score ^d < -2	Girls	12 (2.1, 69)	--- ^e
	Boys	3.8 (0.9, 17)	1.4 (0.2, 11)
Head circumference Z-score ^d < -2	Girls	2.1 (0.7, 6.7)	0.9 (0.3, 3.3)
	Boys	4.8 (1.7, 13)	1.2 (0.4, 3.9)

^a race, gestational age, multi-fetal gestation, maternal indication for delivery (preeclampsia), fetal indication for delivery, and route of delivery. Head circumference Z-score < -2 is also adjusted for birth head circumference Z-score < -2.

^b multi-fetal gestation and route of delivery only

^c among children with GMFCS < 1 and no hearing or vision impairment

^d CDC standard

^e zero cell

Table 5

Odds ratios (and 95% confidence intervals) of developmental outcomes at 2 years among B-SGA and F-SGA children compared to AGA infants, adjusted for confounders^a. This table differs from Table 4 in excluding children who could not walk independently (i.e., had a Gross Motor Functional Classification System score 1) or had appreciable hearing or vision impairment. The top row of each set presents odds ratios for girls. The bottom row presents odds ratios for boys. **Bolded items** are statistically significant.

Growth and neurodevelopmental outcomes at 24 months		Growth Status	
		B-SGA	F-SGA
MDI < 70	Girls	2.6 (1.2, 5.6)	1.5 (0.6, 3.5)
	Boys	1.4 (0.6, 3.3)	1.8 (0.8, 4.1)
PDI < 70	Girls	3.2 (1.6, 6.5)	1.9 (0.9, 4.0)
	Boys	2.6 (1.1, 5.8)	2.2 (1.02, 4.7)
Weight Z-score ^c < -2	Girls	21 (2.5, 181)	--- ^e
	Boys	8.2 (1.6, 41)	2.6 (0.3, 24)
Head circumference Z-score ^c < -2	Girls	3.2 (0.8, 13)	1.3 (0.3, 6.2)
	Boys	5.0 (1.6, 15)	2.0 (0.6, 6.8)

^a race, gestational age, multi-fetal gestation, maternal indication for delivery (preeclampsia), fetal indication for delivery, and route of delivery. Head circumference Z-score < -2 is also adjusted for birth head circumference Z-score < -2.

^b multi-fetal gestation and route of delivery only

^c CDC standard

^e zero cell