

Long-Term Outcomes of Small for Gestational Age Twins Born at 34 Weeks or Later

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Abstract

Objective This article aims to compare long-term neurodevelopmental and health outcomes of twins born at 34 weeks or later, based on the presence of small for gestational age (SGA).

Study Design This study is a mail-based survey of twin gestations delivered by a single practice. We compared twins with and without SGA delivered at ≥ 34 weeks. There were two primary outcomes for this study: a composite of major adverse outcomes (death; cerebral palsy; necrotizing enterocolitis; chronic renal, heart, or lung disease) and a composite of minor adverse outcomes (learning disability, speech therapy, occupational therapy, physical therapy). Regression analysis was performed to control for clustering of outcomes within twin pairs.

Results A total of 712 children were included. Comparing twins with birthweights $<10\%$ to $\geq 10\%$, there were no significant differences in rates of composite major morbidities (3.2 vs. 1.4%, $p = 0.109$) or composite minor morbidities (43.6 vs. 39.3%, $p = 0.279$). Comparing twins with birthweights $<5\%$ to $\geq 5\%$, the rates of major morbidities were low in both groups, but significantly higher in the group with birthweights $<5\%$ (4.4 vs. 1.6%, $p = 0.046$). There were no significant differences seen in the composite minor morbidities (46.7 vs. 39.7%, $p = 0.134$). Twins with birthweights $<5\%$ were significantly more likely to have childhood cardiac disease (2.9 vs. 0.7%, $p = 0.041$).

Conclusion Twins with SGA $<10\%$ born at ≥ 34 weeks have similar long-term neurodevelopmental and health outcomes compared with twins with normal birthweights. Birthweight less than 5th percentile is associated with an increased risk of major morbidity, specifically cardiac disease, but the absolute risk is low.

Keywords

- ▶ twins
- ▶ delivery
- ▶ fetal growth restriction
- ▶ small for gestational age
- ▶ long term

Twin pregnancies have an increased risk of perinatal morbidity and mortality, mainly due to the increased rate of prematurity and growth abnormalities.¹ Fetal growth restriction (FGR) is a common complication of twin pregnancies, with prevalence as high as 25 to 50%, based on the

definition used.² There is no universally accepted definition for FGR, and it is frequently challenging to distinguish a fetus who is truly growth restricted and has not reached its full growth potential from one that is constitutionally small. A commonly accepted definition for FGR is an estimated fetal

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weight less than the 10th percentile for gestational age or a birthweight less than 10th percentile for gestational age, in which case it is usually referred to as small for gestational age (SGA).³

There are multiple causes of FGR and SGA that may be broadly categorized as maternal, fetal, or placental. Abnormal placentation that results in placental insufficiency is the most common contributor to FGR.⁴ Chronic hypoxia and limited nutrient supply lead to poor fetal growth in an asymmetric manner, as there is shunting of blood to vital organs such as the brain and the heart. Despite brain-sparing compensatory mechanism, studies have demonstrated decreased intracranial volume and gray matter in infants born with SGA.⁵

In utero alterations in brain development of SGA newborns may negatively affect childhood growth, cognitive, motor, and behavioral outcomes.^{6–11} Additionally, SGA has been associated with cardiovascular changes at 5 years of life, including abnormal cardiac morphology, decreased stroke volume, increased heart rate, and increased blood pressure.¹² However, existing outcome studies of SGA focus on singleton gestations in which SGA is often due to different pathophysiology from SGA in twin pregnancies. Furthermore, many studies include extremely preterm infants with SGA, in which gestational age is likely a confounding factor. Finally, existing outcome studies of SGA focus on specific outcomes of interest to investigators where differences may or may not be clinically apparent or important to families. It is currently unknown whether SGA is associated with long-term outcomes important to families among twins born at term or late preterm.

The objective of this study was to examine long-term neurodevelopmental and health outcomes of twins with SGA born at 34 weeks or later of gestation as compared with normally grown twins to estimate the association between SGA and long-term morbidity in twins.

Methods

After Institutional Review Board approval, we conducted a mail-based survey of all patients with twin pregnancies delivered by a single maternal–fetal medicine practice between June 2005 and March 2014. Surveys were mailed to mothers of twins in April 2016, such that all twins would be 2 to 10 years old. If clarification of any answers was needed, responders were contacted via phone or email. Nonresponders were followed up via phone or email as well, and patients who declined to participate were not contacted again. The survey questions were intended to be answerable by parents, and were designed to address outcomes clinically relevant to parents considering long-term outcomes for their twins.

For this analysis, inclusion criteria included all live births delivered at 34^{0/7} weeks of gestation or greater. We excluded pregnancies with deliveries prior to 34 weeks to exclude children with morbidities associated with prematurity. We excluded twin pregnancies with twin–twin transfusion syndrome, twins with fetal demise of the co-twin, and any twins

with major fetal anomalies or genetic abnormalities discovered before or after birth. In our practice, monochorionic–monoamniotic twins are delivered prior to 34 weeks; so, they were excluded as well. All patients in our practice have private health insurance.

We compared twins with and without SGA. For this study, outcomes were compared per child, as opposed to per pregnancy. We performed two separate analyses using two different definitions for SGA. The first analysis compared twins with birthweights <10% for gestational age to twins with birthweights ≥10%. The second analysis compared twins with birthweights <5% for gestational age to twins with birthweights ≥5%. To define birthweight percentiles for gestational age, we used standard tables for singleton pregnancies.¹³ We chose singleton tables, as they are the standard tables used for twins in the United States in defining SGA and determining neonatal outcomes.^{14–16}

In each analysis, we first compared baseline characteristics between the two groups. Baseline characteristics and birthweights were obtained from the medical record (not from the survey) and they included maternal age, chorionicity, in vitro fertilization, maternal race, corticosteroid exposure, gender, gestational age at delivery, mode of delivery, chronic hypertension, prepregnancy diabetes, preeclampsia, gestational diabetes, and neonatal intensive care unit (NICU) admission. We then compared outcomes between the groups. There were two primary outcomes for this study: a composite of major adverse outcomes (death; cerebral palsy; necrotizing enterocolitis; and chronic renal, heart, or lung disease) and a composite of minor adverse outcomes (learning disability, speech therapy, occupational therapy, and physical therapy). We also analyzed each individual outcome on the survey. For all analyses, we compared the groups using logistic regression. The long-term outcomes were independent variables and the birthweight percentile groups were categorical dependent variables, with robust clustering to control for nonindependence of observations, given that two twins were born to one mother.¹⁷ A *p*-value of <0.05 was considered significant.

Results

We identified 542 women who delivered live twin pregnancies at ≥34 weeks with no twin–twin transfusion. A total of 360 women responded to the outcome survey, for a response rate of 66.4%. There were no significant differences between responders and nonresponders in regard to maternal age, maternal race, prepregnancy body mass index, gestational age at delivery, birthweight of the larger or smaller twins, or steroid exposure (data not shown). However, the age of the children of responders was younger than nonresponders (5.9 ± 2.4 vs. 6.7 ± 2.6 years, *p* < 0.001), which was not unexpected given the greater difficulty in reaching women via survey who delivered longer ago.

After excluding infants with structural or genetic anomalies, there were 712 children eligible for analyses, 282/712 (39.6%) of who had a birthweight less than the 10th percentile, and 137/712 (19.2%) of who had a birthweight less than

the 5th percentile. The mean age of the children at the time of survey completion was 5.9 ± 2.4 years.

Our first analysis compared 282 twins with birthweights <10th percentile to 430 twins with birthweights \geq 10th percentile. Mean birthweights in these groups were $2,244 \pm 309$ g and $2,729 \pm 334$ g, respectively ($p < 0.001$). There were no significant differences in baseline characteristics between these two groups (►Table 1). Long-term outcomes are shown in ►Table 2. Age at the time of survey completion did not differ between the groups. There were no neonatal deaths in either group. The rates of major morbidity were low in both groups and did not differ between the groups (3.2 vs 1.4%, $p = 0.109$). There were also no significant differences seen in the composite minor morbidities (43.6 vs. 39.3%, $p = 0.279$). Twins with birthweights <10th percentile were significantly more likely to have colic, and more likely to have reported concerns over their height (too short), weight (too light), and motor skills. Otherwise, there were no differences between the two groups.

Our second analysis compared 137 twins with birthweights <5th percentile to 535 twins with birthweights \geq 5th percentile. Mean birthweights in these groups were $2,105 \pm 305$ g and $2,640 \pm 350$ g, respectively ($p < 0.001$). Twins with birthweights <5th percentile had younger mothers and were more likely to be female (►Table 3). Long-term outcomes are shown in ►Table 4. Age at the time of survey completion did not differ between the groups. There were no neonatal deaths in either group. The rates of major morbidity were low in both groups, but were significantly higher in the group with birthweights <5th percentile (4.4 vs. 1.6%, $p = 0.046$). There were no significant differ-

ences seen in the composite minor morbidities (46.7 vs. 39.7%, $p = 0.134$). Twins with birthweights <5th percentile were significantly more likely to have cardiac disease (2.9 vs. 0.7%, $p = 0.041$), and more likely to have reported concerns over their height (too short), weight (too light), and motor skills. Otherwise, there were no differences between the two groups.

In regard to the association of birthweight <5th percentile with long-term cardiac disease, there were four twins (from four pregnancies) with birthweights <5th percentile with reported long-term cardiac disease. In all four cases, fetal growth was normal prior to the third trimester. None had suspected cardiac disease after birth prior to discharge from the hospital, but each reported cardiac disease in childhood. The mothers of these children were contacted again to ascertain specific diagnoses. The cardiac diagnoses in the four children were as follows: (1) pulmonic valve stenosis that was corrected by the age of 3 years without treatment; (2) atrial septal defect with no complications or repair as of age 9 years; (3) ventricular septal defect with no complications or repair as of age 3 years; and (4) supraventricular tachycardia diagnosed at 6 weeks, requiring medical treatment for only 1 year and then no recurrences from age 1 (currently age 7).

Discussion

We studied the parent-reported neurodevelopmental and health outcomes of SGA twins born at 34 weeks or later to estimate the association of SGA with long-term outcomes evident to parents of twin gestations. Twins with SGA

Table 1 Pregnancy characteristics of twin births, based on birthweight less than the 10th percentile

	Birthweight <10% N = 282	Birthweight \geq 10% N = 430	p-Value
Maternal age	33.6 ± 6.4	34.3 ± 6.2	0.232
Chorionicity			0.151
Dichorionic–Diamniotic	243 (86.2%)	387 (90%)	
Monochorionic–Diamniotic	39 (13.8%)	43 (10.0%)	
In vitro fertilization	184 (65.2%)	284 (66.0%)	0.843
White race	254 (90.1%)	388 (90.2%)	0.954
Antenatal corticosteroid exposure	72 (25.5%)	92 (21.4%)	0.225
Gestational age at delivery	36.8 ± 1.1	36.7 ± 1.2	0.242
Gender			0.057
Female	151 (53.5%)	201 (46.7%)	
Male	131 (46.5%)	229 (53.3%)	
Cesarean delivery	162 (57.4%)	255 (59.3%)	0.657
Chronic hypertension	5 (1.8%)	11 (2.6%)	0.609
Prepregnancy diabetes	0.7%	4 (0.9%)	0.999
Preeclampsia	31 (11.2%)	53 (12.6%)	0.611
Gestational diabetes	20 (7.1%)	48 (11.3%)	0.076
Neonatal intensive care unit admission	55 (19.5%)	43 (10.0%)	<0.001

Table 2 Long-term outcome of twins, based on birthweight less than the 10th percentile

	Birthweight <10% N = 282	Birthweight ≥10% N = 430	p-Value ^a	OR (95% CI)
Age at the time of survey	5.9 ± 2.4	6.0 ± 2.4	0.795	
Neonatal death	0 (0%)	0 (0%)	NA	
Composite major adverse outcomes	9 (3.2%)	6 (1.4%)	0.109	2.3 (0.8, 6.6)
Composite minor adverse outcomes	123 (43.6%)	169 (39.3%)	0.279	1.2 (0.9, 1.6)
Has either twin been diagnosed with or treated for:				
Colic	30 (10.6%)	26 (6.0%)	0.042	1.9 (1.1, 3.2)
Asthma/Reactive airways	21 (7.4%)	39 (9.1%)	0.487	0.8 (0.5, 1.4)
Any other chronic lung disease	5 (1.8%)	0 (0%)	NA	
Gastrointestinal reflux	51 (18.1%)	58 (13.5%)	0.110	1.4 (0.9, 2.1)
Kidney (renal) disease	0 (0%)	2 (0.5%)	NA	
Heart (cardiac) disease	4 (1.4%)	4 (0.9%)	0.548	1.5 (0.4, 6.2)
Necrotizing enterocolitis	0 (0%)	0 (0%)	NA	
Cerebral palsy	1 (0.4%)	0 (0%)	NA	
Any learning disability	24 (8.5%)	34 (7.9%)	0.781	1.1 (0.6, 1.9)
Difficulty with hearing	6 (2.1%)	15 (3.5%)	0.375	0.6 (0.2, 1.6)
Diabetes	0 (0%)	0 (0%)	NA	
High blood pressure	0 (0%)	0 (0%)	NA	
Has your child ever required:				
Speech therapy	84 (29.8%)	119 (27.7%)	0.621	1.1 (0.8, 1.5)
Occupational therapy	68 (24.1%)	99 (23.0%)	0.764	1.1 (0.7, 1.5)
Physical therapy	71 (25.2%)	82 (19.1%)	0.073	1.4 (0.9, 2.0)
At or after the age of 2 y, has your pediatrician ever had any concerns regarding your child's:				
Height (too short)	19 (6.7%)	5 (1.2%)	0.001	6.1 (2.3, 16.6)
Weight (too light)	28 (9.9%)	13 (3.0%)	0.001	3.5 (1.8, 6.9)
Weight (too heavy)	5 (1.8%)	8 (1.9%)	0.923	0.9 (0.3, 2.9)
Vision	31 (11.0%)	41 (9.5%)	0.560	1.2 (0.7, 1.9)
Hearing	6 (2.1%)	14 (3.3%)	0.445	0.6 (0.3, 1.7)
Motor skills	32 (11.3%)	29 (6.7%)	0.044	1.8 (1.0, 3.0)
Has your child undergone any operations	57 (20.2%)	87 (20.2%)	0.995	0.9 (0.7, 1.5)
Does your child take any medications	26 (9.2%)	34 (7.9%)	0.557	1.2 (0.7, 2.0)
Is your child allergic to any foods	21 (7.4%)	35 (8.1%)	0.749	0.9 (0.5, 1.6)
Has your child ever been evaluated or treated by a psychologist or psychiatrist	30 (10.6%)	49 (11.4%)	0.735	0.9 (0.6, 1.5)
Does your child wear glasses	26 (9.2%)	53 (12.3%)	0.189	0.7 (0.4, 1.2)
Age when both twins were crawling (mo)	7.9 ± 2.0	8.3 ± 1.9	0.119	
Age when both twins were walking (mo)	13.7 ± 2.8	13.4 ± 2.3	0.247	
Age when both twins said their first word (mo)	13.7 ± 5.6	13.0 ± 4.0	0.195	

Abbreviations: CI, confidence interval; NA, not available; OR, odds ratio.

^aResults of logit regression. The long-term outcomes were independent variables and the birthweight percentile groups were categorical dependent variables, with robust clustering to control for nonindependence of observations given that two twins were born to one mother.

Table 3 Pregnancy characteristics of twin births, based on birthweight less than the 5th percentile

	Birthweight <5% N = 137	Birthweight ≥5% N = 575	p-Value
Maternal age	32.9 ± 6.3	34.3 ± 6.3	0.033
Chorionicity			0.276
Dichorionic–Diamniotic	117 (85.4%)	513 (89.2%)	
Monochorionic–Diamniotic	20 (14.6%)	62 (10.8%)	
In vitro fertilization	88 (64.2%)	380 (66.1%)	0.713
White race	125 (91.2%)	517 (89.9%)	0.669
Antenatal corticosteroid exposure	38 (27.7%)	126 (21.9%)	0.196
Gestational age at delivery	36.8 ± 1.0	36.8 ± 1.2	0.523
Gender			0.002
Female	84 (61.3%)	268 (46.6%)	
Male	53 (38.7%)	307 (53.4%)	
Cesarean delivery	78 (56.9%)	339 (59.0%)	0.696
Chronic hypertension	4 (2.9%)	12 (2.1%)	0.527
Prepregnancy diabetes	2 (1.5%)	4 (0.7%)	0.328
Preeclampsia	18 (13.5%)	66 (11.7%)	0.588
Gestational diabetes	11 (8.1%)	57 (10.0%)	0.560
Neonatal intensive care unit admission	37 (27.0%)	50 (10.4%)	<0.001

defined as birthweight <10th percentile for gestational age had similar outcomes compared with twins with birthweights ≥10th percentile. Twins with birthweights <5th percentile for gestational age had significantly higher rates of major morbidity, specifically cardiac disease, compared with twins with birthweights ≥5th percentile, but the absolute risk was low (<5%) and other outcomes were similar. Also, the specific cardiac diagnoses did not require surgery and as of the time of this survey were not affecting daily life for any of the children. There were no neonatal deaths among the entire cohort of twins born at 34 weeks or later. Our findings suggest that women with twins being followed up in pregnancy for FGR can be reassured that their children will have mostly normal long-term outcomes if delivery can be delayed to at least 34 weeks.

SGA is a common complication of twin pregnancies and occurs with greater frequency than in singleton gestations. In our study, twins with birthweights <10th percentile had similar outcomes as those with higher birthweights, which may indicate that SGA in twins reflects a different, less harmful pathophysiology than in singleton gestations. Most twins with severe growth restriction <5th percentile had low rates of long-term morbidity; however, our data suggest that childhood monitoring for cardiac disease may be warranted. This study was not designed to determine the optimal timing of delivery for twins with suspected FGR; however, we would suggest that twins with suspected FGR without a strong indication for delivery before 34 weeks be managed expectantly.

Much of the literature on twins with SGA focuses on twins born very premature. In 2004, Monset-Couchard et al demonstrated that SGA multiples born with extremely low

birthweight <1,000 g had higher rates of visual abnormalities, behavioral disturbances, and speech problems than their appropriate for gestational age (AGA) counterparts at 3 to 17 years of age.¹⁸ Goyen et al examined 21 pairs of discordant, very low-birth-weight twins born prior to 34 weeks and found that the smaller twins exhibited lower performance on assessment of locomotor, personal, hand-eye coordination, performance, and practical reasoning skills than the larger twins at 3 years of age.¹⁹

The studies that include twins born at >34 weeks mostly assess the effect of growth discordance on long-term outcomes. Edmonds et al analyzed 71 monozygotic twin pairs, 64 of which were born at >34 weeks, and found that within-pair differences in birthweight are related to within-pair differences in verbal IQ.²⁰ When growth discrepancy was greater, the smaller twin demonstrated lower verbal IQ scores, whereas when growth discrepancy was less, the larger twin demonstrated lower scores. In 2015, Halling et al studied 119 birthweight-discordant (>20%) twin pairs at 24 to 42 months of age and found that the smaller twin had significantly worse cognitive, language, and motor skills compared the larger twin.²¹ However, with multiple regression analysis, they found that prematurity below 33 weeks had a greater impact on cognitive outcomes than growth discordance. Vedel et al reported on 567 twin pairs and found that increased birthweight discordancy was not associated with adverse long-term developmental outcomes, defined in that study as lower scores on the “Ages and Stages Questionnaire.”²²

Our findings corroborate prior studies correlating SGA with an increased incidence of cardiac disease. In 1997, Rich-Edwards et al found an inverse relationship between birthweight and risk of nonfatal cardiovascular disease in a

Table 4 Long-term outcome of twins, based on birthweight less than the 5th percentile

	Birthweight <5% N = 137	Birthweight ≥5% N = 575	p-Value ^a	OR (95% CI)
Age at the time of survey	5.9 ± 2.3	5.9 ± 2.4	0.901	
Neonatal death	0 (0%)	0 (0%)	NA	
Composite major adverse outcomes	6 (4.4%)	9 (1.6%)	0.046	2.9 (1.1, 8.2)
Composite minor adverse outcomes	64 (46.7%)	228 (39.7%)	0.134	1.3 (0.9, 1.9)
Has either twin been diagnosed with or treated for:				
Colic	13 (9.5%)	43 (7.5%)	0.434	1.3 (0.7, 2.5)
Asthma/Reactive airways	8 (5.8%)	52 (9.0%)	0.225	0.6 (0.3, 1.3)
Any other chronic lung disease	2 (1.5%)	3 (0.5%)	0.257	2.8 (0.5, 17.1)
Gastrointestinal reflux	22 (16.1%)	87 (15.1%)	0.804	1.1 (0.6, 1.8)
Kidney (renal) disease	0 (0%)	2 (0.3%)	NA	
Heart (cardiac) disease	4 (2.9%)	4 (0.7%)	0.041	4.3 (1.1, 17.4)
Necrotizing enterocolitis	0 (0%)	0 (0%)	NA	
Cerebral palsy	1 (0.7%)	0 (0%)	NA	
Any learning disability	11 (8.0%)	47 (8.2%)	0.959	1.0 (0.5, 1.9)
Difficulty with hearing	4 (2.9%)	17 (3.0%)	0.983	1.0 (0.3, 3.0)
Diabetes	0 (0%)	0 (0%)	NA	
High blood pressure	0 (0%)	0 (0%)	NA	
Has your child ever required:				
Speech therapy	48 (35.0%)	155 (27.0%)	0.073	1.5 (0.9, 2.2)
Occupational therapy	35 (25.5%)	132 (23.0%)	0.548	1.2 (0.7, 1.8)
Physical therapy	35 (25.5%)	118 (20.5%)	0.235	1.3 (0.8, 2.1)
At or after the age of 2 y, has your pediatrician ever had any concerns regarding your child's:				
Height (too short)	10 (7.3%)	14 (2.4%)	0.017	3.2 (1.4, 7.3)
Weight (too light)	16 (11.7%)	25 (4.3%)	0.003	2.9 (1.5, 5.6)
Weight (too heavy)	1 (0.7%)	12 (2.1%)	0.269	0.3 (0.1, 2.7)
Vision	13 (9.5%)	59 (10.3%)	0.792	0.9 (0.5, 1.7)
Hearing	5 (3.6%)	15 (2.6%)	0.577	1.4 (0.5, 4.0)
Motor skills	19 (13.9%)	42 (7.3%)	0.021	2.0 (1.1, 3.6)
Has your child undergone any operations	22 (16.1%)	122 (21.2%)	0.210	0.7 (0.4, 1.2)
Does your child take any medications	7 (5.1%)	53 (9.2%)	0.132	0.5 (0.2, 1.2)
Is your child allergic to any foods	8 (5.8%)	48 (8.3%)	0.298	0.7 (0.3, 1.5)
Has your child ever been evaluated or treated by a psychologist or psychiatrist	18 (13.1%)	61 (10.6%)	0.421	1.3 (0.7, 2.2)
Does your child wear glasses	12 (8.8%)	67 (11.7%)	0.283	0.7 (0.4, 1.4)
Age when both twins were crawling (mo)	7.9 ± 2.0	8.2 ± 1.9	0.169	
Age when both twins were walking (mo)	13.8 ± 3.1	13.5 ± 2.3	0.260	
Age when both twins said their first word (mo)	13.1 ± 4.6	13.2 ± 4.7	0.814	

Abbreviations: CI, confidence interval; NA, not available; OR, odds ratio.

^aResults of logit regression. The long-term outcomes were independent variables and the birthweight percentile groups were categorical dependent variables, with robust clustering to control for nonindependence of observations given that two twins were born to one mother.

longitudinal cohort of 1,200 women.²³ Animal models of FGR show signs of cardiac disease already present in utero, with remodeling of sarcomere architecture that persists into the first year of life.²⁴ Crispi et al found evidence of compromised cardiac performance extending into childhood, with growth-restricted children demonstrating different cardiac shapes, more globular ventricles, and decreased stroke volume at 5 years of age.¹² Our study supports these findings, but our sample size was small with only four children with birthweights less than the 5th percentile having reported cardiac disease.

Our study has several strengths. First, we had an overall large sample size of 712 twins. All pregnancies were managed by a single maternal fetal medicine (MFM) group, reducing variation in prenatal care across the groups and ensuring accurate pregnancy records as opposed to using birth certificate data. We defined SGA as birthweight <10th percentile and <5th percentile as opposed to using estimated fetal weight, which is often inaccurate. Rather than using intelligence or performance quotients to assess outcomes, we used concrete, clinically meaningful outcomes that are understandable to parents. Finally, we followed up twins to an average of 5.9 years.

There are limitations of this study as well. The study design is retrospective; therefore, our results are subject to bias. It is possible that twins with SGA were followed up more closely and tested more frequently after birth than non-growth-restricted twins. Although the response rate was high at 66.4%, there could be selection bias. However, we did not observe any differences in maternal characteristics between responders and nonresponders, aside from the fact that nonresponders delivered longer ago, which was not unexpected. Since many of the outcomes were rare, we could have been underpowered to find differences in certain outcomes. All our outcomes were reported by parents and not verified with medical records, limiting the precision of our data. Furthermore, all patients delivered with an MFM group at a tertiary care hospital with 24-hour NICU coverage, and have private insurance. These patients' outcomes may not be generalizable to patients seeking care at other types of health care facilities or with limited access to subspecialty care. Greater access to care could lead to improved outcomes or conversely introduce bias due to increased rates of diagnosis from increased utilization of health care resources. Finally, with no standard definition of SGA aside from a birthweight percentile, it is difficult to distinguish truly growth-restricted twins from those who are constitutionally small. We chose to use birthweight percentiles as these are objective and reproducible. We repeated the analysis using two different definitions and found an association only with the more severe SGA (birthweight less than the 5th percentile), indicating a dose-dependent relationship between birthweight percentile and long-term outcomes.

In summary, we found that twins with SGA born at >34 weeks have similar long-term parent-reported neurodevelopmental and health outcomes compared with twins with normal birthweights. A birthweight percentile less than the 5th percentile is associated with an increased risk of major

morbidity, specifically cardiac disease, but the absolute risk is low and the cardiac diseases were not severe. Our findings may be used to reassure patients with twin pregnancies with suspected FGR that if delivery can be delayed until 34 weeks, their children will likely develop well and remain healthy through childhood. Twins with birthweight percentiles less than the 5th percentile may warrant close monitoring in childhood to detect and treat cardiac disease.

Conflict of Interest

None.

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