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Small for Gestational Age and Higher Birth Weight Predict Childhood Obesity in Preterm Infants

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Abstract

We sought to determine the association between small for gestational age (SGA), birth weight, and childhood obesity within preterm polysubstance exposed children. We sampled 312 preterm children with 11-year body mass index (BMI; age- and sex-specific) data from the Maternal Lifestyle Study (51% girls, 21.5% SGA, 46% prenatal cocaine, and 55% tobacco exposed). Multinomial regression analyzed the association between 11-year obesity (OBE) and overweight (OW) and SGA, birth weight, first-year growth velocity, diet, and physical activity variables. Overall, 24% were OBE (BMI for age ≥95th percentile) and 16.7% were OW (BMI ≥85th and <95th percentiles). In adjusted analyses, SGA was associated with OW (odds ratio [OR]=3.4, confidence interval [CI] 1.5 to 7.5). Higher birth weight was associated with OBE (OR = 1.8, CI 1.3 to 2.4) and OW (OR=1.4, CI 1.1 to 2.0). Growth velocity was associated with OBE (OR=2.7, CI 1.8 to 4.0) and OW (OR=1.6, CI 1.1 to 2.4). Low exercise was associated with OBE (OR=2.1, CI 1.0 to 4.4) and OW (OR=2.1, CI 1.0 to 4.5). There was no effect of substance exposure on obesity outcomes. Many (41%) of these high-risk preterm 11-year-olds were obese/overweight. Multiple growth-related processes may be involved in obesity risk for preterm children, including fetal programming as indicated by the SGA effect.

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Keywords

Childhood obesity; premature birth; infant SGA; birth weight; exercise; prenatal drug exposure

It is well established that childhood obesity is due to energy imbalance as a result of genetics, poor diet, and physical inactivity[1,2] and disproportionately affects children from low socioeconomic status (SES) and ethnic minority backgrounds and girls.[3–6] Before age 3, childhood obesity is more specifically related to parental (e.g., maternal prepregnancy weight) and early infancy factors (e.g., accelerated growth velocity).[7–9] Fetal Origins of Chronic Disease research suggests that in combination with accelerated growth velocity, low birth weight is also related to obesity.[10] Other research suggests that size at birth for gestational age, such as being small for gestational age (SGA), and not size at birth alone (e.g., low birth weight) is the most likely of the two early infancy factors associated with increased risk for later obesity.[11] The role of SGA or birth weight in predicting childhood obesity may be unclear given that SGA, low birth weight, and preterm birth are often studied interchangeably, as if they were synonymous.[12,13] Research on low birth weight and obesity in particular typically study full-term infants, or it is not clear whether these samples include preterm infants; and in some cases, samples include some combination of both term and preterm infants.[10] Postnatal growth trajectories are different for term and preterm infants.[14] Therefore, understanding the impact of SGA and birth weight on obesity may be further elucidated by examining the association between early infancy factors and obesity among preterm infants alone and not together with term infants.[14] Available research among preterm populations on fetal/early infancy risks for obesity is sparse and inconclusive, suggesting that preterm birth, low birth weight, and/or SGA are associated with both increased[15] and decreased risk of[16] childhood obesity. Further, much of this research has poorly controlled for the influence of confounders associated with preterm birth, SGA, low birth weight, and obesity. Preterm birth, low birth weight, and SGA similar to obesity are national health problems, disproportionately affecting ethnic minority and low SES children.[17,18] Maternal substance use, including illicit drug, tobacco, and alcohol use, is also associated with SGA, low birth weight, and preterm birth.[18–22] We have yet to fully understand the association between SGA, low birth weight, and childhood obesity for preterm children within the context of relevant obesity, low birth weight, and SGA risk factors, including fetal/early infancy factors (e.g., prenatal substance exposure and infant growth velocity), maternal factors (e.g., prepregnancy weight, diabetes history), and behavioral factors (e.g., physical activity and nutrition).[23,24]

We studied obesity and overweight at 11 years of age in preterm children participating in a longitudinal study. The sample is mostly African-American, polysubstance-exposed (cocaine, alcohol, tobacco, and marijuana) children from low-income environments at risk for poor health outcomes including obesity and overweight. We studied only preterm infants given the paucity of research on childhood obesity and overweight in this population and given differential growth trajectories for preterm versus term infants.[14] We examined SGA as a predictor of overweight and obesity given SGA is associated with nutritional deprivation[25] and therefore may be a marker for “fetal origins”[10] of physiological and metabolic alterations implicated in adult onset chronic disease including obesity.[26–29]

METHODS

Study Design

The Maternal Lifestyle Study (MLS) is a longitudinal study of children with prenatal cocaine exposure conducted in four sites: Brown University, University of Miami, University of Tennessee at Memphis, and Wayne State University. Institutional Review Board approval for MLS and a certificate of confidentiality from the National Institute on Drug Abuse were

obtained for each of the sites. Informed consent was obtained for all participants meeting enrollment criteria.

MLS was conducted in two phases. The acute outcome phase (1993 to 1995) extended through hospital discharge and enrolled mother-infant dyads within 24 hours of delivery from each hospital site. We recruited subjects across three birth weight groups, <1500 g, 1500 to 2500 g, and >2500 g, to ensure an adequate sample of preterm infants.[30] Gestational age was assessed via Ballard Examination.[31] Mothers consented to a brief interview of their drug use during pregnancy and a toxicology analysis of their infant's meconium. “Exposure” was defined as maternal admission of cocaine/opiate use during pregnancy and/or positive meconium assay of cocaine/opiate metabolites, confirmed with gas chromatography/mass spectroscopy.[32,33] “Comparison” was defined as maternal denial of prenatal cocaine/opiate use and negative cocaine/opiate enzyme-multiplied immunoassay technique. Maternal exclusion criteria were age <18 years, history of psychosis or institutionalization for retardation or emotional problems, and language barriers. Infant exclusion criteria included those infants born at another hospital, multiple gestation, birth weight <501 g, gestational age >42 weeks, or attending physician judgment of low infant survivability.[30]

The longitudinal follow-up phase began at the infant's first follow-up visit, at 1 month of age, corrected for prematurity.[34] Exposed children from the acute phase were group matched with “comparisons” within site on child race/ethnicity, gender, and gestational age. Exclusion criteria for the longitudinal phase were maternal intent to move out of her catchment area, chromosomal abnormality, or toxoplasmosis, other agents, rubella, cytomegalovirus, or herpes infection. Of the 1388 mother/infant dyads (658 exposed; 730 comparison) enrolled in the longitudinal phase, 577 were preterm infants <37 weeks' gestational age (318 exposed; 259 comparison). The uneven groups reflect the replacement of comparison mother/infant dyads if consent was withdrawn prior to the 1-month visit. This report includes preterm infants only.

Procedure

Follow-up was conducted at hospital sites at 1, 4, 8, 12, and 18 months, then annually through 11 years starting at 24 months and corrected for prematurity through the 3-year visit. Descriptive characteristics were obtained from child medical chart review and maternal interview. Prenatal tobacco, marijuana, and alcohol exposures were defined as maternal admission of use of these substances during pregnancy (yes/no); any prenatal substance exposure was calculated as a composite of cocaine/opiate, tobacco, alcohol, and marijuana variables. The Hollings-head Index of Social Position[35,36] was used to calculate SES at the 11-year visit based on education and occupation of primary contributors to the household. Maternal prepregnancy body mass index (BMI) was calculated according to Centers for Disease Control and Prevention (CDC)[37] and based on maternal report of height and prepregnancy weight during the postpartum recruitment interview. Maternal pregestational diabetes was based on maternal report of history diabetes (yes/no) and used as a proxy for gestational diabetes, which was not available in MLS.

EARLY GROWTH AND HEALTH BEHAVIOR PREDICTORS—Eight predictors were selected a priori based on previous literature: four early growth and four health behavior variables. Early growth variables were based on “fetal origins” literature and included gestational age (<32 weeks or 32 to 36 weeks), birth weight (g), SGA (<10th percentile birth weight for gestational age)[38] and growth velocity. Growth velocity was calculated as weight change per month from birth to 12 months (g/mo).[39] Health behavior variables were based on the childhood obesity literature and health behavior guidelines endorsed by the American Academy of Pediatrics (AAP) and included inadequate exercise, excessive television viewing, regular fruit and vegetable consumption, and regular grain and cereal consumption. Inadequate

exercise was based on national recommendations to accumulate 60 minutes of moderate to vigorous physical activity each day[40] and based on 8-, 9-, 10-, and 11-year visit data. Eight- and 9-year inadequate exercise variables were based on maternal report of her child exercising ≤30 minutes on a regular basis five or more times a week. Ten- and 11-year inadequate exercise variables were calculated from the Child Health and Illness Profile, parent report (CHIP-P) as maternal report of her child playing active games or sports, or playing hard enough to start sweating and breathing hard less than almost every day. Overall inadequate exercise was defined as a report of inadequate exercise in three or more of 8-, 9-, 10-, and 11-year visits. Excessive television viewing was based on AAP recommendations that sedentary behavior be limited to <2 hours daily[41] and based on 8-, 9-, 10-, and 11-year visit data. Eight- and 9-year excessive television viewing variables were calculated based on maternal report of her child watching television >2 hours a day during a school or weekend day. Ten- and 11-year excessive television viewing variables were calculated from the CHIP-P as maternal report of her child watching ≥2 hours of television on school days for the past 4 weeks. Overall excessive television viewing was defined as a report of excessive television viewing in three or more of 8-, 9-, 10-, and 11-year visits. Regular fruit and vegetable consumption and regular whole grain consumption variables were based on U.S. Department of Agriculture (USDA) recommendations that adolescents regularly consume appropriate quantities of fruits, vegetables, and whole grains[42] and calculated from the CHIP (adolescent edition) as adolescent report of eating fruits/vegetables and grains/cereals more than once a day in the past 4 weeks.

OVERWEIGHT AND OBESITY OUTCOMES—Study outcomes were childhood obesity and overweight calculated from child height and weight measurements from the 11-year visit. Outcomes were defined according to the CDC 2000 growth charts[43] and AAP recommendations.[44] Obesity was 11-year BMI for age >sex-specific 95th percentile (yes/no). Overweight was 11-year BMI for age >sex-specific 85th percentile but <95th percentile (yes/no).

Analyses

Descriptive statistics were analyzed using χ^2 for categorical variables and analysis of variance (ANOVA) for continuous variables. Post hoc comparisons for statistically significant descriptive variables were examined by adjusted standardized residuals in χ^2s and with Fisher's least significant difference in ANOVAs. Pearson correlation, Spearman correlation, or χ^2 tests were used during preliminary analyses to explore bivariate correlations between all predictors, covariates, and outcomes. Potential covariates were selected and included in the multinomial logistic regression modeling analysis if they were associated with the outcome variable at $p<0.10$. Multinomial logistic regression allows an outcome variable with greater than two levels. In this study, the outcome variable had three levels: obesity, overweight, and normal weight. Using multinomial logistic regression analysis, we generated odds ratios for predictor and covariate variables in the prediction of obesity and overweight in comparison to referent (e.g., normal weight). The final multinomial logistic regression model included the following predictors and covariates: birth weight, growth velocity, SGA, prepregnancy BMI, inadequate exercise, excessive television viewing, exercise, regular fruits and vegetable consumption, regular grain and cereal consumption, gender, race/ethnicity, site, SES, and maternal pregestational diabetic history. Additionally examined covariates not included in the final model were prenatal cocaine/opiate, tobacco, alcohol, and marijuana exposures. The SGA × cocaine/opiate exposure interaction resulted in inadequate sample numbers and was dropped from the final model. The SGA × substance exposure (cocaine/opiate, tobacco, marijuana, and alcohol), SGA × tobacco, SGA × birth weight, and SGA × - growth velocity interactions were not significantly associated with childhood overweight or obesity and were removed from the final model. Birth length and head circumference were also not included in the final model

given their high correlations with birth weight (Pearson r>0.70). All analyses were conducted using SPSS windows 15.0 (SPSS Inc., 2007).

RESULTS

MLS enrolled 577 preterm infants at longitudinal follow-up; 393 (68%) had height and weight data at the 11-year visit. Of these 393 children, 312 (79%) had complete data for all of the measures and were used as the final sample for this study. Comparison of medical and demographic characteristics between the 265 children not included and the 312 children included in this study showed more preterm births ≤32 weeks in the included (197, 63.1%) versus excluded (146, 55.1%) samples (p=0.001). Adolescents in the included sample were marginally more likely to have larger BMIs (p=0.05). There were no other differences between the two groups, including birth weight, SGA, head circumference, length at birth, exposure to drugs, gender, race/ethnicity, growth velocity, SES, or maternal prepregnancy BMI.

Descriptive Characteristics

The sample included 115 children born ≤32 weeks' gestational age (37%): 67 SGA children (21.5%), 158 girls (50.8%), and 249 African-Americans (81.1%). The sample also included 133 cocaine-exposed (42.6%), 170 tobacco-exposed (54.5%), 186 alcohol-exposed (59.6%) and 73 (23.4%) marijuana-exposed children (prenatal exposure). A total of 75 were obese (24%) and 52 (16.7%) were overweight at 11 years based on the 2000 CDC growth charts. Scatter plot observation showed two of five total large-for-gestational-age (LGA; >90th percentile birth weight for gestational age)[38] infants whose 11-year BMIs fell within the overweight/obesity categories (≥85th percentile). The mean BMI percentile for the obese group (97.8, standard deviation [SD]=1.5) was higher compared with the means for the overweight (89.9, SD=3.1) and normal weight (48.8, SD=23.4) categories defined by the 2000 CDC BMI growth charts (p<0.001).

Descriptive characteristics of the sample by BMI status (Table 1) showed that preterm children born SGA were more likely to be overweight than normal weight or obese at age 11 years. Preterm children who were obese at age 11 years had higher 12-month growth velocities and mothers with higher reported prepregnancy BMIs than their overweight and normal weight peers. Preterm children who were overweight versus normal weight at age 11 years had mothers who reported higher prepregnancy BMIs. Preterm 11-year-old children who reported inadequate exercise were more likely to be obese or overweight than normal weight.

Multivariable Analysis

The logistic regression model for obesity and overweight adjusting for confounders (Table 2) showed that SGA was a significant independent predictor of overweight at 11 years of age. Higher birth weight, higher 12-month growth velocity, and inadequate exercise were independently and significantly associated with increased odds for obesity and overweight at 11 years of age. Higher maternal prepregnancy BMI and female gender were also significantly associated with increased odds for obesity and overweight at 11 years.

DISCUSSION

It is surprising how little is known about childhood obesity and overweight in preterm infants. In this sample of prematurely born 11-year-old adolescents with prenatal polydrug and postnatal environmental risk factors, we did not find higher rates of obesity compared with national estimates. The 24% prevalence estimate for obesity in this sample is similar to national prevalence estimates of obesity for African-American youth (22%) from the National Health and Nutrition Examination Survey 2003 to 2004.[45] However, we did find that obese children

had higher BMIs compared with national estimates than did the overweight children, suggesting that obese children in this study are toward the upper end of the obesity curve, and therefore likely at greater risk for disease. The 16.7% prevalence estimate for overweight appeared to be lower than national estimates (40%) for African-Americans. National estimates are based on representative samples and include term and preterm infants.[6,43,45] Thus, it is possible that the distribution of weight is different in term and preterm infants. The results of regression analyses where we adjusted for covariates showed that typical factors relevant in the obesity literature among mostly term infant samples also predicted obesity and overweight in our preterm sample, although our SGA findings are unique.

SGA significantly predicted overweight in our study. Yet, SGA in preterm infants is rarely accounted for in the "fetal origins" literature. For example, a study showing increased risk of cardiovascular disease–related death given low birth weight found the highest standardized mortality ratios for preterm adults; SGA was not included.[46] We were unable to locate obesity studies of gestational age, birth weight, and SGA in preterm children.[15,16] Available studies often exclude relevant early growth variables, such as growth velocity.[16,47,48] Inconsistencies in the literature may be related to these methodological issues. For example, preterm birth, low birth weight, and SGA have been associated with increased risk for adolescent overweight[15] but not associated with BMI among 8-year-old children.[47] In nonobese populations, SGA preterm children were the lightest in weight,[16,47] and extremely low-birth-weight preterm infants were lighter compared with term infants.[48] Our study suggests that SGA is associated with increased risk for overweight at 11 years independent of both birth weight and postnatal growth velocity for children born preterm.

Contrary to our predictions, we found higher birth weight and not low birth weight was related to overweight and obesity at 11 years among preterm children. However, similar findings have been reported in term children at ages 3 to 6[13,49] and 7 years,[7] but not in preterm adolescents. The majority of evidence examines low-birth-weight and not other birth-weight categories, suggesting that low birth weight is associated with increased risk of childhood overweight and obesity.[50] In fact, among term children, some have found a stronger tracking effect for later adiposity among low-birth-weight versus normal or high-birth-weight children.[13] The landmark studies of men and women born during famine in England around the 1900s provided early evidence for the association between low birth weight and chronic disease,[51] but did not distinguish preterm from term births.[52,53] Our findings suggest that the mechanism that increases risk for obesity as birth weight increases in term children is similar among preterm children, and this risk extends into adolescents. Higher birth weight in this case is not synonymous with LGA, which has also been associated with overweight among term children.[49,54] Further, there were too few LGA children in this preterm sample overall and who later became overweight/obese to warrant further examination. Interestingly, the fact that there is increased obesity risk for normal-weight preterm children as birth weight increases suggests an interaction between the intrauterine and postnatal environment that warrants further investigation.

In adults, there is mixed evidence suggesting that both decelerated[52] and accelerated growth velocity[50] among low-birth-weight infants is associated with the highest risk of cardiovascular disease and overweight/obesity onset. In children, our findings are consistent with literature, suggesting that across different definitions of growth velocity (e.g., 12 to 24 months of infancy) and adiposity indicators (e.g., BMI and waist circumference), rapid weight gain during early life increases risk for adiposity.[55,56] Although the large majority of research is not limited to SGA infants, it has been established that low-birth-weight infants are more likely to show rapid infancy growth than normal and higher-birth-weight infants.[57] We did not find a significant SGA by growth velocity interaction. This finding is consistent with evidence suggesting that

outcomes related to rapid growth velocity are similar for SGA and normal-birth-weight populations.[56]

We found an association between inadequate exercise and adolescent overweight and obesity. This has been reported in some studies[44] but not others.[58] However, exercise has not been previously studied as a predictor for obesity in preterm infants. Our findings have implications for intervention, as physical exercise is increasingly being used to combat obesity in children.[40,59–61] We did not find an association between excessive television viewing and childhood adiposity, which is inconsistent with the term literature,[1,41] nor did we find an effect for regular health food consumption. Although evidence from the USDA suggests a modest effect for fruit and vegetable intake protecting against childhood adiposity,[62] other studies found no association between these two variables.[58]

The two studies of childhood overweight and obesity in preterm populations have used different methodological approaches to examine effects of gender.[7,63] Both studies were in term children; neither examined SGA status. One study found that female gender was associated with obesity at 7 years after controlling for birth weight, growth velocity, and other confounders.[63] The other study, also at age 7, stratified by growth velocity and birth weight found that accelerated growth velocity was more strongly associated with higher BMI among boys but not girls with lower birth weight.[7] Differences in methodological approaches could explain the discrepancy in findings. Findings from our study suggest that female gender is associated with 11-year overweight and obesity in preterm children.

Our finding that higher reported maternal prepregnancy BMI is associated with increased risk for childhood adiposity is consistent with previous literature.[8,64] Our study finding is unique from previous studies, which typically did not control for birth weight, SGA, and other relevant early growth variables among preterm infants.

The fact that MLS was not initially designed to examine overweight and obesity is a limitation. However, MLS provides a rare opportunity to longitudinally study childhood obesity and overweight in a sample of high-risk children. Although our findings are limited to preterm infants, this population is understudied in the field, and we were able to determine a unique effect for SGA. Although we found no main effect for in utero tobacco or cocaine exposures, we were unable to test SGA interaction effects due to small sample numbers. It may be that the association between SGA and adolescent obesity in this preterm sample is due to an interaction between SGA and prenatal cocaine or tobacco exposures. In utero tobacco exposure is associated with SGA,[65,66] and maternal smoking is associated with childhood obesity.[8,67] Evidence for SGA and prenatal cocaine exposure is limited and mixed.[20,68] The effect of prenatal cocaine exposure on childhood obesity is still unknown. In light of our unique findings for SGA and childhood obesity among preterm infants, the combined effect of SGA and tobacco and cocaine exposure on obesity warrant further exploration.

The use of BMI is this study is both a limitation and strength. The limitation of BMI is that it is an indirect measure for adiposity that may reflect lean body mass rather than body fatness.[69] As such, BMI as a measure of overweight and obesity tends to have high specificity for identifying adolescents with a high percentage of body fat, but low sensitivity.[70] The utility of BMI is that it correlates with more direct measures of body fatness, is the most widely used adiposity measure,[71] and has been used with youth born prematurely.[7,72]

Our findings extend to preterm children evidence that SGA, accelerated growth velocity, and higher birth weight[7,13,50] are independently associated with increased risk of childhood adiposity. This suggests that multiple growth-related processes are involved in the risk of childhood adiposity for preterm infants, one of which may be fetal programming as indicated by the SGA effect. The findings also indicate that both prenatal and postnatal processes

(inadequate exercise) are involved, providing opportunities for prenatal and postnatal behavioral interventions.

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Data collected at participating sites of the NICHD Neonatal Research Network (NRN) were transmitted to RTI International, the data coordinating center (DCC) for the network, which stored, managed, and analyzed the data for this study. On behalf of the NRN, Drs. Abhik Das (DCC Principal Investigator) and Jing Liu (MLS Statistician) had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

REFERENCES

1. Berkey CS, Rockett HR, Field AE, et al. Activity, dietary intake, and weight changes in a longitudinal study of preadolescent and adolescent boys and girls. Pediatrics 2000;105:E56. [PubMed: 10742377]
2. Maes HH, Neale MC, Eaves LJ. Genetic and environmental factors in relative body weight and human adiposity. Behav Genet 1997;27:325–351. [PubMed: 9519560]
3. Miech RA, Kumanyika SK, Stettler N, Link BG, Phelan JC, Chang VW. Trends in the association of poverty with overweight among US adolescents, 1971–2004. JAMA 2006;295:2385–2393. [PubMed: 16720824]
4. Gordon-Larsen P, Adair LS, Popkin BM. The relationship of ethnicity, socioeconomic factors, and overweight in US adolescents. Obes Res 2003;11:121–129. [PubMed: 12529494]
5. Freedman DS, Khan LK, Serdula MK, Ogden CL, Dietz WH. Racial and ethnic differences in secular trends for childhood BMI, weight, and height. Obesity (Silver Spring) 2006;14:301–308. [PubMed: 16571857]
6. Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999–2002. JAMA 2004;291:2847–2850. [PubMed: 15199035]
7. Hui LL, Schooling CM, Leung SS, et al. Birth weight, infant growth, and childhood body mass index: Hong Kong's children of 1997 birth cohort. Arch Pediatr Adolesc Med 2008;162:212–218. [PubMed: 18316657]
8. Salsberry PJ, Reagan PB. Dynamics of early childhood overweight. Pediatrics 2005;116:1329–1338. [PubMed: 16322155]
9. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH. Predicting obesity in young adulthood from childhood and parental obesity. N Engl J Med 1997;337:869–873. [PubMed: 9302300]
10. Barker DJ, Eriksson JG, Forsén T, Osmond C. Fetal origins of adult disease: strength of effects and biological basis. Int J Epidemiol 2002;31:1235–1239. [PubMed: 12540728]
11. Ong KK, Dunger DB. Birth weight, infant growth and insulin resistance. Eur J Endocrinol 2004;151 (Suppl 3):U131–U139. [PubMed: 15554898]
12. Ong KK. Catch-up growth in small for gestational age babies: good or bad? Curr Opin Endocrinol Diabetes Obes 2007;14:30–34. [PubMed: 17940416]
13. Mei Z, Grummer-Strawn LM, Scanlon KS. Does overweight in infancy persist through the preschool years? An analysis of CDC Pediatric Nutrition Surveillance System data Soz Praventivmed 2003;48:161–167.
14. Gibson AT, Carney S, Cavazzoni E, Wales JK. Neonatal and post-natal growth. Horm Res 2000;53 (Suppl 1):42–49. [PubMed: 10895042]

15. Abe Y, Kikuchi T, Nagasaki K, et al. Lower birth weight associated with current overweight status is related with the metabolic syndrome in obese Japanese children. Hypertens Res 2007;30:627–634. [PubMed: 17785931]
16. Chaudhari S, Otiv M, Hoge M, Pandit A, Mote A. Growth and sexual maturation of low birth weight infants at early adolescence. Indian Pediatr 2008;45:191–198. [PubMed: 18367763]
17. March of Dimes. Professionals and Researchers Quick Reference Fact Sheet: Preterm Birth. [Accessed January 28, 2009]. Available at: http://www.marchofdimes.com/professionals/14332_1157.asp. Up dated February 2007.
18. Bernstein PS, Divon MY. Etiologies of fetal growth restriction. Clin Obstet Gynecol 1997;40:723–729. [PubMed: 9429786]
19. Saenger P, Czernichow P, Hughes I, Reiter EO. Small for gestational age: short stature and beyond. Endocr Rev 2007;28:219–251. [PubMed: 17322454]
20. Bada HS, Das A, Bauer CR, et al. Low birth weight and preterm births: etiologic fraction attributable to prenatal drug exposure. J Perinatol 2005;25:631–637. [PubMed: 16107872]
21. Roquer JM, Figueras J, Botet F, Jiménez R. Influence on fetal growth of exposure to tobacco smoke during pregnancy. Acta Paediatr 1995;84:118–121. [PubMed: 7756793]
22. McDonald AD, Armstrong BG, Sloan M. Cigarette, alcohol, and coffee consumption and prematurity. Am J Public Health 1992;82:87–90. [PubMed: 1536341]
23. Petitt DJ, Bennett PH, Knowler WC, Baird HR, Aleck KA. Gestational diabetes mellitus and impaired glucose tolerance during pregnancy. Long-term effects on obesity and glucose tolerance in the offspring. Diabetes 1985;34(Suppl 2):119–122. [PubMed: 3996763]
24. McCowan L, Horgan RP. Risk factors for small for gestational age infants. Best Pract Res Clin Obstet Gynaecol 2009;23:779–793. [PubMed: 19604726]
25. Gluckman PD, Hanson MA. The consequences of being born small—an adaptive perspective. Horm Res 2006;65(Suppl 3):5–14. [PubMed: 16612108]
26. Chatelain P. Children born with intra-uterine growth retardation (IUGR) or small for gestational age (SGA): long term growth and metabolic consequences. Endocr Regul 2000;34:33–36. [PubMed: 10808251]
27. Eriksson JG, Forsén T, Tuomilehto J, Winter PD, Osmond C, Barker DJ. Catch-up growth in childhood and death from coronary heart disease: longitudinal study. BMJ 1999;318:427–431. [PubMed: 9974455]
28. Rich-Edwards JW, Kleinman K, Michels KB, et al. Longitudinal study of birth weight and adult body mass index in predicting risk of coronary heart disease and stroke in women. BMJ 2005;330:1115. [PubMed: 15857857]
29. Yang Z, Zhao W, Zhang X, et al. Impact of famine during pregnancy and infancy on health in adulthood. Obes Rev 2008;9(Suppl 1):95–99. [PubMed: 18307708]
30. Bauer CR, Shankaran S, Bada HS, et al. The Maternal Lifestyle Study: drug exposure during pregnancy and short-term maternal outcomes. Am J Obstet Gynecol 2002;186:487–495. [PubMed: 11904612]
31. Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard Score, expanded to include extremely premature infants. J Pediatr 1991;119:417–423. [PubMed: 1880657]
32. ElSohly MA, Stanford DF, Murphy TP, et al. Immunoassay and GC-MS procedures for the analysis of drugs of abuse in meconium. J Anal Toxicol 1999;23:436–445. [PubMed: 10517548]
33. Lester BM, ElSohly M, Wright LL, et al. The Maternal Lifestyle Study: drug use by meconium toxicology and maternal self-report. Pediatrics 2001;107:309–317. [PubMed: 11158464]
34. Lester BM, Tronick EZ, LaGasse L, et al. The Maternal Lifestyle Study: effects of substance exposure during pregnancy on neurodevelopmental outcome in 1-month-old infants. Pediatrics 2002;110:1182–1192. [PubMed: 12456917]
35. Cirino PT, Chin CE, Sevcik RA, Wolf M, Lovett M, Morris RD. Measuring socioeconomic status: reliability and preliminary validity for different approaches. Assessment 2002;9:145–155. [PubMed: 12066829]
36. Lagasse L, Seifer R, Wright L, Lester B, Tronick EZ, Bauer CR, et al. The Maternal Lifestyle Study (MLS): The caretaking environment of infants exposed to cocaine/opiates. Pediatr Res 1999;45:247A. [PubMed: 10022598]

37. US Department of Health and Human Services. Centers for Disease Control and Prevention. Healthy weight—it's not a diet it's a lifestyle: About BMI for adults. [Accessed January 28, 2009]. Available at: http://www.cdc.gov/nccdphp/dnpa/healthyweight/assessing/bmi/adult_BMI/about_adult_BMI.htm. Updated June 28, 2008.
38. Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. Obstet Gynecol 1996;87:163–168. [PubMed: 8559516]
39. Lagasse L, Shankaran S, Bada H, et al. Predictors of overweight at nine years in cocaine-exposed children. PAS 2005;57:2005.
40. Strong WB, Malina RM, Blimkie CJ, et al. Evidence based physical activity for school-age youth. J Pediatr 2005;146:732–737. [PubMed: 15973308]
41. American Academy of Pediatrics. Committee on Public Education. American Academy of Pediatrics: Children, adolescents, and television. Pediatrics 2001;107:423–426. [PubMed: 11158483]
42. United States Department of Agriculture. MyPyramidgov: Steps to a Healthier You. [Accessed January 28, 2009]. Available at: http://teamnutrition.usda.gov/resources/mpk_close.pdf. Updated January 22, 2009.
43. Ogden CL, Flegal KM, Carroll MD, Johnson CL. Prevalence and trends in overweight among US children and adolescents, 1999–2000. JAMA 2002;288:1728–1732. [PubMed: 12365956]
44. Barlow SE, Expert Committee. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics 2007;120(Suppl 4):S164–S192. [PubMed: 18055651]
45. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999–2004. JAMA 2006;295:1549–1555. [PubMed: 16595758]
46. Barker DJ, Osmond C, Simmonds SJ, Wield GA. The relation of small head circumference and thinness at birth to death from cardiovascular disease in adult life. BMJ 1993;306:422–426. [PubMed: 8461722]
47. Casey PH, Whiteside-Mansell L, Barrett K, Bradley RH, Gargus R. Impact of prenatal and/or postnatal growth problems in low birth weight preterm infants on school-age outcomes: an 8-year longitudinal evaluation. Pediatrics 2006;118:1078–1086. [PubMed: 16951001]
48. Kilbride HW, Thorstad K, Daily DK. Preschool outcome of less than 801-gram preterm infants compared with full-term siblings. Pediatrics 2004;113:742–747. [PubMed: 15060222]
49. Zhang X, Liu E, Tian Z, et al. High birth weight and overweight or obesity among Chinese children 3–6 years old. Prev Med 2009;49:172–178. [PubMed: 19632265]
50. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. BMJ 2005;331:929. [PubMed: 16227306]
51. Barker DJ. In utero programming of chronic disease. Clin Sci (Lond) 1998;95:115–128. [PubMed: 9680492]
52. Barker DJ, Winter PD, Osmond C, Margetts B, Simmonds SJ. Weight in infancy and death from ischaemic heart disease. Lancet 1989;2:577–580. [PubMed: 2570282]
53. Osmond C, Barker DJ, Winter PD, Fall CH, Simmonds SJ. Early growth and death from cardiovascular disease in women. BMJ 1993;307:1519–1524. [PubMed: 8274920]
54. Yu Z, Sun JQ, Haas JD, Gu Y, Li Z, Lin X. Macrosomia is associated with high weight-for-height in children aged 1–3 years in Shanghai, China. Int J Obes (Lond) 2008;32:55–60. [PubMed: 18193065]
55. Monteiro PO, Victora CG. Rapid growth in infancy and childhood and obesity in later life—a systematic review. Obes Rev 2005;6:143–154. [PubMed: 15836465]
56. Ong KK, Loos RJ. Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. Acta Paediatr 2006;95:904–908. [PubMed: 16882560]
57. Ong KK, Ahmed ML, Emmett PM, Preece MA, Dunger DB. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. BMJ 2000;320:967–971. [PubMed: 10753147]
58. Davis MM, Gance-Cleveland B, Hassink S, Johnson R, Paradis G, Resnicow K. Recommendations for prevention of childhood obesity. Pediatrics 2007;120(Suppl 4):S229–S253. [PubMed: 18055653]

59. Flynn MA, McNeil DA, Maloff B, et al. Reducing obesity and related chronic disease risk in children and youth: a synthesis of evidence with “best practice” recommendations. Obes Rev 2006;7(Suppl 1):7–66. [PubMed: 16371076]
60. Hebestreit H, Bar-Or O. Exercise and the child born prematurely. Sports Med 2001;31:591–599. [PubMed: 11475321]
61. Svien LR. Health-related fitness of seven- to 10-year-old children with histories of preterm birth. Pediatr Phys Ther 2003;15:74–83. [PubMed: 17057437]
62. American Dietetic Association. Childhood overweight evidence analysis project. [Accessed January 28, 2009]. Available at: www.adaevidencelibrary.com/evidence.cfm?evidence_summary_id=25. Published 2006. Updated January 2009.
63. Stettler N, Zemel BS, Kumanyika S, Stallings VA. Infant weight gain and childhood overweight status in a multicenter, cohort study. Pediatrics 2002;109:194–199. [PubMed: 11826195]
64. Agras WS, Hammer LD, McNicholas F, Kraemer HC. Risk factors for childhood overweight: a prospective study from birth to 9.5 years. J Pediatr 2004;145:20–25. [PubMed: 15238901]
65. Anderson GD, Blidner IN, McClemont S, Sinclair JC. Determinants of size at birth in a Canadian population. Am J Obstet Gynecol 1984;150:236–244. [PubMed: 6486191]
66. Pringle PJ, Geary MP, Rodeck CH, Kingdom JC, Kayamba-Kay's S, Hindmarsh PC. The influence of cigarette smoking on antenatal growth, birth size, and the insulin-like growth factor axis. J Clin Endocrinol Metab 2005;90:2556–2562. [PubMed: 15713720]
67. Bergmann KE, Bergmann RL, Von Kries R, et al. Early determinants of childhood overweight and adiposity in a birth cohort study: role of breast-feeding. Int J Obes Relat Metab Disord 2003;27:162–172. [PubMed: 12586995]
68. Schempf AH, Strobino DM. Illicit drug use and adverse birth outcomes: is it drugs or context? J Urban Health 2008;85:858–873. [PubMed: 18791865]
69. Gortmaker SL, Dietz WH Jr. Re: “Secular trends in body mass in the United States, 1960–1980.”. Am J Epidemiol 1990;132:194–197. [PubMed: 2356809]
70. Himes JH, Bouchard C. Validity of anthropometry in classifying youths as obese. Int J Obes 1989;13:183–193. [PubMed: 2744930]
71. Pietrobelli A, Faith MS, Allison DB, Gallagher D, Chiumello G, Heymsfield SB. Body mass index as a measure of adiposity among children and adolescents: a validation study. J Pediatr 1998;132:204–210. [PubMed: 9506629]
72. Euser AM, Finken MJ, Keijzer-Veen MG, Hille ET, Wit JM, Dekker FW, Dutch POPS-19 Collaborative Study Group. Associations between prenatal and infancy weight gain and BMI, fat mass, and fat distribution in young adulthood: a prospective cohort study in males and females born very preterm. Am J Clin Nutr 2005;81:480–487. [PubMed: 15699238]

Table 1

Descriptive Characteristics of 11-Year-Old Adolescents Born Premature by Weight Status

Characteristic	Obese (≥95%), *n*=75	Overweight (≥85 to <95%), *n*=52	Normal (>85%), *n*=185	P
Gestational age, *n* (%)				
≤32 wk	27 (36.0)	13 (25.0)	75 (40.5)	0.12
32–36 wk	48 (64.0)	39 (75.0)	110 (59.5)	
Birth weight (g), m (SD)	2096.7 (608.4)	2029.8 (646.6)	1921.3 (647.4)	0.11
Percentile birth weight adjusted for gestational age, mdn (min, max)	29.9 (5.0, 90.5)	24.7 (5.0, 94.3)	30.5 (5.0, 92.9)	0.53
12-mo growth velocity (g/mo), m (SD)*	655.4 (103.8)	610 (88.5)	600 (89.3)	<0.001
SGA, *n* (%)‡	13 (17.3)	18 (34.6)	36 (19.5)	0.04
Any prenatal substance exposure, *n* (%)	58 (77.3)	42 (80.8)	141 (76.2)	
Prenatal cocaine, *n* (%)	27 (36.0)	21 (40.4)	85 (45.9)	0.32
Prenatal tobacco, *n* (%)	35 (46.7)	28 (53.8)	107 (57.8)	0.26
Prenatal alcohol, *n* (%)	44 (58.7)	29 (55.8)	113 (61.1)	0.77
Prenatal marijuana, *n* (%)	16 (21.3)	9 (17.3)	48 (25.9)	0.38
Inadequate exercise, *n* (%)‡	49 (65.3)	36 (69.2)	96 (51.9)	0.03
>2 h TV watching, *n* (%)	37 (49.3)	26 (50.0)	97 (52.4)	0.88
Regular consumption fruits and vegetables, *n* (%)	22 (29.3)	14 (26.9)	69 (37.3)	0.25
Regular consumption grains and cereals, *n* (%)	36 (19.5)	15 (28.8)	18 (24.0)	0.32
Prepregnancy BMI, *m* (SD)§	28 (7.4)	24.5 (4.2)	22 (4.5)	<0.001
Female gender, *n* (%)	40 (53.3)	33 (63.5)	86 (46.5)	0.09
Race/ethnicity, *n* (%)				
Black	58 (77.3)	37 (71.2)	155 (83.8)	0.11
Hispanic	2 (2.7)	4 (7.7)	3 (1.6)	
Other	15 (20.0)	11 (21.2)	27 (14.6)	
Site, *n* (%)				
Detroit	39 (52.0)	29 (55.8)	93 (50.3)	0.61
Memphis	19 (25.3)	10 (19.2)	51 (27.6)	
Miami	6 (8.0)	4 (7.7)	22 (11.9)	
Providence	11 (14.7)	9 (17.3)	19 (10.3)	
Maternal pregestational diabetes, *n* (%)	4 (5.3)	1 (1.9)	4 (2.2)	0.35
Socioeconomic status, Hollingshead, m (SD)	31.4 (10.5)	29.2 (8.7)	29.4 (10.4)	0.32

Note: N=312; *p* values are based on chi-square tests for categorical variables and analysis of variance for continuous variables. BMI, body mass index; m, mean; mdn, median; max, maximum; min, minimum; SD, standard deviation; TV, television.

*Fisher's least significant difference in analysis of variance showed higher values for 12-mo growth velocity in the obese versus normal and overweight groups, both $p<0.001$.

†Results for adjusted standardized residuals from chi-square analyses showed greater than expected small-for-gestational-age children in the overweight group.

‡Results for adjusted standardized residuals from chi-square analyses showed fewer than expected for low exercise in the normal group and greater than expected for low exercise in the overweight and obese group.

[§]Fisher's least significant difference in analysis of variance showed higher maternal prepregnancy BMIs for obese versus normal and overweight groups, both $p<0.001$.

Table 2

Logistic Regression Modeling of the Association between Obesity and Overweight Compared with Normal Weight at 11 Years for Adolescents Born Premature, Adjusting for Confounders

Characteristic	Obese (≥95%), OR (95% CI)	Overweight (≥85 to <95%), OR (95% CI)
Birth weight, every 500-g increase	1.77 (1.32–2.38)	1.43 (1.05–1.95)
12-mo growth velocity (g/mo)	2.69 (1.80–4.00)	1.61 (1.07–2.43)
SGA	2.28 (0.95–5.46)	3.39 (1.53–7.51)
Inadequate exercise	2.13 (1.02–4.37)	2.12 (1.01–4.46)
>2 h TV watching	0.86 (0.42–1.73)	0.94 (0.45–1.97)
Regular consumption fruits and vegetables	1.36 (0.65–2.84)	1.63 (0.76–3.49)
Regular consumption grains and cereals	0.64 (0.28–1.44)	0.57 (0.26–1.28)
Prepregnancy BMI	1.28 (1.19–1.38)	1.15 (1.07–1.25)
Female gender	2.31 (1.13–4.75)	2.74 (1.30–5.77)
Race/ethnicity		
Black	1.27 (0.41–3.94)	1.26 (0.15–10.57)
Hispanic	0.54 (0.05–6.18)	0.56 (0.17–1.77)
Other*		
Site		
Detroit	0.47 (0.13–1.77)	0.99 (0.23–3.49)
Memphis	0.24 (0.06–1.05)	0.46 (0.10–2.09)
Miami	0.25 (0.05–1.30)	0.44 (0.08–2.34)
Providence*		
Maternal pregestational diabetes	0.24 (0.04–1.45)	0.97 (0.09–10.29)
Socioeconomic status, Hollingshead	1.01 (0.98–1.05)	0.99 (0.95–1.02)

Note: N=312; obese (*n*=75) and overweight (*n*=52) compared with normal weight. BMI; body mass index; CI, confidence interval; OR, odds ratio; SGA, small for gestational age; TV, television.

*Referent group within predictors.