Published in final edited form as:

J Dev Orig Health Dis. 2010 October ; 1(5): 338–346. doi:10.1017/S2040174410000401.

Weight gain in infancy and early childhood is associated with school age body mass index but not intelligence and blood pressure in very low birth weight children

L. Washburn¹, P. Nixon^{1,2}, B. Snively³, A. Tennyson^{2,4}, and T.M. O'Shea¹

¹Wake Forest University School of Medicine, Department of Pediatrics, Winston-Salem, NC, USA

²Wake Forest University, Department of Health and Exercise Science, Winston-Salem, NC, USA

³Wake Forest University School of Medicine, Division of Public Health Sciences, Winston-Salem, NC, USA

⁴Brody School of Medicine at East Carolina University, Greenville, NC, USA

Abstract

Rates of weight gain in infancy and early childhood can influence later neurocognitive, metabolic, and cardiovascular health. We studied the relationship of weight gain during infancy and early childhood to intelligence quotient (IQ), blood pressure (BP), and body mass index (BMI) at age 9 in children born with very low birth weight (VLBW). Sixty-five children born prematurely with VLBW were followed longitudinally and at 9 years IQ, BP, and BMI were measured. The mean weight z scores at birth, neonatal intensive care discharge, 1 year corrected for prematurity, 5, and 9 years were -0.17 , -2.09 , -1.3 , -0.68 , 0.06 , respectively. Weight gain during infancy (discharge to 1 year corrected for prematurity) and early childhood (1 year corrected age to 5 years) was expressed as rate of change in weight, rate of change in weight z score, and interval change in weight z score. In multiple regression analyses that adjusted for race, gender, maternal education, antenatal steroids, birth weight z score, major intracranial lesions on ultrasound, and chronic lung disease, rates of weight gain in infancy and early childhood were predictive of BMI z score at 9 years, regression coefficients (95% confidence intervals); 0.19 (0.02 , 0.36) and 0.37 (0.11 , 0.63), respectively, expressed as change in BMI z score per 10 g/week weight increase. Rates of weight gain were not predictive of systolic BP z score, Verbal IQ or Performance IQ. In VLBW infants, more rapid weight gain during infancy, and especially early childhood, is associated with higher BMI at school age.

Keywords

prematurity; growth; follow-up; outcomes

Introduction

In preterm infants postnatal growth is a potentially modifiable risk factor for neurodevelopmental impairment. Many prematurely born infants experience relative growth restriction in the neonatal intensive care unit (NICU) and at the time of hospital discharge, usually near term equivalent, many are small for gestational age (<10th percentile).^{1,2}

Correspondence to: L. Washburn.

Statement of Interest

None

Subsequently, these infants often exhibit accelerated growth in weight, length, and head circumference in the first 2–3 years of life, and this is associated with better neurodevelopmental outcomes at school age.^{3–5}

Although greater weight gain might be beneficial for preterm infants' developmental outcomes, it is also associated with higher blood pressure,⁶ lower insulin sensitivity,⁶ higher body mass index (BMI),⁷ and more abdominal fat,⁷ which are predictive of hypertension and metabolic syndrome later in life.^{8–10} Thus, the optimal rate of weight gain after premature birth is not known.

We are aware of no studies examining the relationship of rates of weight gain during early childhood to cognitive function as well as blood pressure and BMI at school age. The objective of this study was to evaluate the association of weight gain in the first 5 years of life with intelligence quotient (IQ), systolic blood pressure (SBP), and BMI at 9 years of age in very low birth weight (VLBW, <1501g) children.

Methods

Study Participants

Participants were born with VLBW between April 1992 and May 1995. As neonates, these individuals participated in a randomized placebo-controlled trial of dexamethasone to reduce the duration of ventilator dependence.¹¹ Eligibility criteria for the randomized trial were: 1) birthweight <1501g; 2) age 15 to 25 days; 3) lack of weaning of ventilator settings; 4) absence of clinical signs of sepsis; 5) absence of patent ductus arteriosus by echocardiography; and 6) parental informed consent.¹¹ Of the 118 children who were randomized, 95 survived to one year of age corrected for prematurity (subsequently referred to as 1 year CA), and all 95 survivors were examined at least once, at or beyond 1 year CA. From hospital records we collected data on birth weight and weight on the day of discharge from neonatal intensive care. Additional anthropometric measurements were collected by research staff on 93 children (98%) at 1 year CA age, 74 (78%) at or around 5 years, and 68 (72 %) at or around 9 years of age. A convenience sample of 65 surviving participants in the trial of dexamethasone had outcome data collected at the 9 year visit, measurement of weight at 1 year CA, and measurement of weight at either discharge or the 5 year visit and were included in this analysis. Post-hoc power calculations based on a significance level of 0.05 and 2-sided testing indicate that the study sample provided about 80% power to detect a 0.7 standard deviation difference in 9 year outcomes (i.e. 8 mm Hg in SBP, 14 points in Verbal IQ) between children with rates of weight gain above the median and those with rates of weight gain below the median.

This study was approved by the Institutional Review Board and the General Clinic Research Center (GCRC) of the Wake Forest University Baptist Medical Center and Forsyth Medical Center. Parents gave written informed consent and children over the age of 7 years gave assent.

Definitions and Measurements

Infancy was defined as the interval from NICU discharge until 1 year CA. Early childhood was defined as the period from 1 year CA to 5 years of age. The following measures of weight gain during infancy and early childhood were of primary interest: 1) change in weight from the beginning to end of the interval of interest, divided by elapsed time between measurements; 2) change in weight z score during the interval of interest; and 3) change in weight z score divided by the elapsed time. To evaluate the possible effects of differences among participants with respect to ages at NICU discharge and during observed intervals of infancy and childhood, results of analyses were compared to an approach that statistically

estimates weight gain per unit time in each participant at two fixed ages, 6 months and 2.5 years adjusted for prematurity (refer to Statistical Methods).

Data on neonatal characteristics and diagnoses were obtained by a research nurse from medical records. The estimate of gestational age in completed weeks was based on a hierarchy of the quality of information available. Most desirable was last menstrual period, followed sequentially by an obstetrician's estimate from ultrasound measurements and an assessment of the neonate. Infants whose mothers were treated with betamethasone or dexamethasone (any number of doses) prior to delivery were considered to have had antenatal steroid exposure. Whether the obstetrician diagnosed maternal hypertension during pregnancy was ascertained from review of the medical record. Chronic lung disease (CLD) was defined as the use of supplemental oxygen at 36 weeks postmenstrual age.¹² Severe cranial ultrasound abnormality was defined as 1) subependymal or intraventricular hemorrhage with post hemorrhagic hydrocephalus requiring placement of a shunt, 2) persistent but non-progressive ventricular dilation, or 3) intraparenchymal echodensity or echolucency in the periventricular white matter on the basis of the last cranial ultrasound obtained during the neonatal hospitalization.¹³ Race of the child was obtained from the medical records and categorized for analysis as Caucasian versus African American. Maternal education was assessed via questionnaire when the infant was 1 year CA and was categorized for analysis as less than 12 versus 12 or more completed years of education.

Birth weight and discharge weight were measured as part of clinical care; measurements at 1 year CA and 5 years of age were made by research nurses. Anthropometric measurements at 9 years were made in triplicate by GCRC nutritionists and averaged for analyses. Weight was measured without shoes using a digital platform scale and height was measured using a wall-mounted stadiometer. Children with BMI (kg/m^2) 85th to less than 95th percentile were considered overweight and those with BMI $\geq$ 95th percentile were considered obese.¹⁴ Blood pressure at 9 years of age was determined using the average of three measurements made with an automated oscillometric device (Alaris medical systems, Model #4410) by General Clinical Research Center nursing staff certified in blood pressure measurement following guidelines established by the National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents.¹⁵ Child psychologists administered The Wechsler Intelligence Scale for Children, 3rd Edition (WISC-III) to assess Verbal and Performance IQ¹⁶ as previously described.^{17,18}

Gender specific birth weight and discharge weight z scores were determined using United States natality data.¹⁹ Weight z scores at 1 year CA were determined using Epi info 2000 (Centers for Disease Control, Atlanta, GA) by entering the expected date of confinement as the birth date.²⁰ Age- and gender-specific weight z scores at 5 and 9 years and BMI z scores at 9 years were derived from the 2000 reference data using the birth date. Age- and gender-specific oscillometric blood pressure standards for children were used to determine systolic blood pressure z scores.²¹

Statistical Methods

Characteristics of study participants and their mothers were summarized using counts, percentages, sample means, and standard deviations. Between-group differences were tested for statistical significance using Fisher exact test (categorical measures) and two-sample t-test (continuous measures).

Primary modeling analyses of the 9 year outcome measures (dependent variables) -- Verbal IQ, Performance IQ, SBP, and BMI -- were performed using multiple linear regressions. For models of SBP and BMI, a natural logarithmic transformation was applied to each outcome measure first, and results were compared using SBP z score and BMI z score, respectively.

To address our main hypotheses, the weight gain measures were evaluated as potential independent predictors in the multivariate modeling, including rate of change in weight, rate of change in weight z score, and interval change in weight z score. These independent variables, measured during the two time intervals, infancy and early childhood, were evaluated using separate models. Additional independent variables were selected a priori for multivariate adjustment from among known predictors and potential confounders: age (at the 9 year visit), gender, exposure to antenatal steroids (yes/no), birth weight, CLD (yes/no), severe cranial ultrasound abnormality (yes/no), and level of maternal education (included in models for IQ only). Modification of the predictive effect of weight gain by weight at the start of the interval (initial weight) was tested using an interaction model with main effects for weight gain and initial weight, and the interaction, weight gain $\times$ initial weight, adjusting for the other covariates. Prior to evaluation of weight gain as a potential predictor, the interaction term was dropped from the model if not statistically significant; if the interaction term was dropped, then the main effect for initial weight was evaluated (under the no-interaction model) and was similarly dropped if not significant.

The multivariate regression modeling just described assumes no correlation between age of the child at the beginning and end of the interval of interest (i.e., infancy or early childhood) and rate of weight gain. Since the age of children differed at discharge and at the follow up visits at 1 year adjusted age and 5 years, we compared the results of the multivariate modeling described above with results obtained using estimates of what each child's rate of weight gain was at 6 months of age (an estimate of the rate of weight gain during infancy) and 2.5 years of age (an estimate of the rate of weight gain during early childhood). First, we estimated weight and change in weight per unit time (slope in the weight-by-age curve) for each participant at pre-specified ages. This estimation procedure was then followed up with the same multivariate modeling as described above, except the estimates were used as independent variables in place of the observed initial weights and weight changes. The estimated intercepts and slopes were calculated under random intercept and slope mixed models of weight as a function of age and age squared.

We used locally weighted regression curves (i.e. lowess curves) to describe patterns in weight z scores for three groups of study participants, defined by tertiles of outcomes at 9 years of age. These curves can be used to visually compare the pattern of weight gain for the upper, middle, and lower third of the study sample for each of the four outcomes assessed at 9 years. All analyses were performed using either SAS statistical software, version 9.1 (SAS Institute Inc., Cary, NC), or S-PLUS software, version 8.0 (Insightful Corp., Seattle, WA). P-values ≤ 0.05 were considered statistically significant.

Results

Study participants

Neonatal and maternal characteristics of study participants are shown in Table 1. Children whose data are included in this study were similar to participants in the original randomized trial except that children not included in this study were more likely to have CLD. Postnatal dexamethasone treatment was unrelated to the outcomes assessed at 9 years in the neonatal trial and in the subset described in this study (results not shown), thus, dexamethasone- and placebo-treated children were combined for the analyses reported here.^{17,18}

Weight and weight gain through 9 years

As shown in Table 1, the mean birth weight z score was -0.17 , indicating that the birth weights for gestational age among study participants were on average similar to the U.S. population reference sample. In contrast, at the time when study participants were

discharged from the neonatal intensive care unit, mean weight z score was -2.09 , indicating that the average growth rate during the initial hospitalization was well below intrauterine rates of weight gain.

As shown in Table 2, mean change in weight z scores between one year CA and 5 years increased by 0.83 and 0.53 , respectively, indicating that in the intervals between follow up visits, the study participants' average rate of weight gain (117 grams/week from NICU discharge to the visit at 1 year CA, and 43 grams per week from 1 year CA to the visit at year 5) exceeded that of the reference sample. Thus by 9 years of age, the average weight z score for study children was 0.06 , similar to the reference sample.

Outcomes at 9 years

Data for the three outcomes of primary interest are summarized in Table 3. The average systolic blood pressure was 1 standard deviation higher than age- and gender-specific SBP reference values. Eighteen percent of participants at the 9 year visit were obese, (BMI 95th percentile), 11% were overweight (BMI 85th to less than 95th percentile), and 9% were under weight (BMI < 5th percentile). The mean Verbal IQ was 0.5 standard deviation below the normative sample and the mean Performance IQ was almost 1 standard deviation below that of the normative sample.

Weight gain in infancy and early childhood and outcomes at 9 years

Verbal and Performance IQ—In bivariate analyses, exposure to antenatal steroids was associated with higher Verbal IQ ($p=0.02$) and the diagnosis of chronic lung disease was associated with lower Verbal IQ ($p=0.004$). Severe cranial ultrasound abnormality was associated with a lower Performance IQ ($p=0.02$). Although not quite statistically significant, Verbal IQ was higher among children with higher birth weight z score ($p=0.07$), higher weight z score at 1 year CA ($p=0.09$), and greater rate of weight gain (expressed as grams per week) from NICU discharge to 1 year CA ($p=0.06$). In multivariate models that included antenatal steroid exposure, gender, race, birth weight z score, CLD, severe cranial ultrasound, and level of maternal education, no association was found between rates of weight gain and either Verbal or Performance IQ (Table 4).

SBP z score—None of the rates of weight gain were associated with SBP z score at 9 years of age (Table 4). SBP z score was not associated with BMI z score at age 9 years.

BMI z score—In bivariate analyses, higher BMI at 9 years was associated with African American race ($p=0.0007$), higher weight at 1 year CA ($p=0.003$), and greater rates of weight gain during infancy ($p=0.004$) and early childhood ($p<0.0001$). In multivariate analyses adjusting for birth weight z score, race, antenatal steroid exposure, severe cranial ultrasound abnormality, and chronic lung disease, rates of weight gain during infancy ($p<0.03$) and early childhood ($p<0.006$) were positively associated with BMI z score at 9 years. As shown in Table 4, the magnitude of the association was about 2-fold greater for weight gain during early childhood compared to weight gain during infancy. The interaction term for weight at 1 year CA $\times$ weight gain in early childhood was significant ($p=0.02$) with a beta coefficient of -0.07 indicating that the lower the weight at 1 year CA, the steeper the slope of the line relating weight gain during early childhood and BMI z score at age 9 years. When weight gain was expressed as change in weight z score, only weight gain during early childhood was associated with BMI z score at 9 years of age ($p<0.0001$).

Patterns of weight gain in infancy and early childhood and outcomes at 9 years

In Figs. 1 and 2 we present lowess curves showing patterns of weight gain for children classified according to tertiles of BMI z score and Verbal IQ at school age. Weight z score is

plotted versus age in years (corrected for prematurity) at NICU discharge and three follow-up visits. The curves in Fig. 1 suggest that children in the highest tertile of BMI z score at 9 years tended to have higher rates of change in weight z score beginning at NICU discharge and persisting through childhood, while those in Fig. 2 suggest that children in the upper tertile for Verbal IQ tended to have more rapid weight gain through 1 year CA, but not after that age. Lowess curves for weight z score were nearly identical for tertiles of Performance IQ and SBP z score (not shown).

Discussion

The aim of our study was to examine the relationships of weight gain in infancy and early childhood to IQ, BP, and BMI in school age VLBW children. Our findings suggest that the rate of weight gain in infancy and especially in early childhood is positively associated with BMI z score at age 9 years. We did not find a relationship between early weight gain and Verbal or Performance IQ or SBP z score at 9 years of age.

We found that weight gain in infancy and early childhood was predictive of BMI at school age. Similarly, Euser et al reported that in premature infants, rates of weight gain between birth and 3 months post term and between 3 months and 1 year post term were positively correlated with BMI at 19 years of age.⁷ We found that the association of weight gain during early childhood and school age BMI was twice as strong as the association with weight gain during infancy. Similarly, among individuals born small for gestational age at term, adult BMI was correlated with the magnitude of gain in BMI during childhood only when the gain persisted after the first year of life.²² Our study subjects were also small for gestational age at term because they experienced growth failure relative to intrauterine growth rates while in the NICU.

The VLBW children whom we studied, born 1992–95, have already attained a BMI comparable to the reference population at age 9 years. In contrast, the VLBW cohort studied by Hack et al, born 1977–79,²³ did not attain a mean BMI equal to the mean of the reference sample until young adulthood. Similarly, Doyle et al reported longitudinal follow up on a cohort of prematurely born infants whose weight was lighter than average at 8 years but not different from the population mean by ages 14 and 20 years. Interestingly, one third of the 20 year old participants whom Doyle et al studied had BMI >25.²⁴ It is concerning that 29% of our cohort are overweight or obese (BMI ≥ 85th percentile for age and gender) at age 9 years in view of the fact that the mean weight at about term age equivalent was 2 standard deviations below the mean in the reference sample. Findings of the Minneapolis Blood Pressure Study suggest that childhood weight gain rather than the actual weight at school age is the factor related to young adult risk factors for cardiovascular disease.¹⁰

In contrast to our findings of no association between rates of weight gain in infancy and early childhood to systolic blood pressure z score at school age, Rotteveel et al reported that weight gain during infancy or childhood was positively associated with blood pressure in young adults born prematurely.⁶ Perhaps this is due to the differences in the age of the participants (21 years versus 9 years). Further study of our cohort is warranted because an association of weight gain and blood pressure might become evident when our study participants reach adulthood as the blood pressure elevation associated with low birth weight is thought to amplify with age.²⁵

Although we did not detect an association between the rate of weight gain after discharge from neonatal intensive care and school age IQ, larger studies of premature infants have described better neurocognitive outcome among those with greater post-NICU weight

gain.^{3–5} In studies that include measurements of head circumference, head growth is more strongly related to improved outcome than weight gain.^{3,4,26}

Our finding that the mean SBP z score of our cohort was higher than the reference population is consistent with the findings of other studies of premature infants during childhood.^{27–32} We did not find the expected correlation between blood pressure z score and BMI z score at age 9 years. Although the etiology of elevated blood pressure among children born prematurely is unknown, it seems to be mediated by factors other than elevated BMI.

Our failure to detect an association of rate of weight gain with school age IQ or SBP z score might have resulted from insufficient power provided by our relatively small sample. The generalizability of our results may be limited because our study included only infants requiring mechanical ventilation for at least 2 weeks. For example, we would expect that a more representative sample of VLBW infants (lower rate of CLD than that of our study cohort) would have exhibited better weight gain.^{33,34} We also recognize that including measurements of head circumference and length or height would allow for a more complete assessment of postnatal growth and body composition.³⁵ While weight gain during intensive care can influence later outcomes,^{7,36} we restricted our analysis to post NICU discharge changes in weight because all of the infants in our cohort experienced slowed growth during their initial hospitalization.

Infants born prematurely are at risk for cognitive impairment, elevated blood pressure,^{27–32} insulin resistance,^{6,37,38} and abdominal adiposity.^{7,39} Evidence is accumulating that growth rates in infancy and early childhood are important for later neurocognitive, metabolic, and cardiovascular health. Follow up studies of prematurely born infants suggest that neurodevelopment is improved when post discharge growth failure is prevented and growth in head circumference occurs.^{3–5,26,40–46} Increased rates of weight gain, however, are associated with elevated blood pressure, insulin resistance, and increased abdominal adiposity in young adults.^{6,7}

Our findings suggest that among VLBW infants, weight gain during infancy is predictive of higher BMI at school age but rapid weight gain in early childhood is an even stronger predictor of increased school age BMI. The optimum pattern of weight gain for infants born prematurely to promote adequate brain growth and prevent obesity or excessive abdominal adiposity is not known. More detailed study of growth patterns to identify critical periods of growth, and mechanisms associated with growth, in VLBW infants, might provide strategies for improving neurodevelopmental outcomes and decreasing the risk of obesity and cardiometabolic disease in adulthood.

Acknowledgments

This research was supported by the General Clinical Research Center of Wake Forest University Baptist Medical Center grant MO1-RR07122, NICHD PO1 HD047584, and the Brenner Center for Child and Adolescent Health. We thank Alice Scott, RN, the GCRC staff, and the participants and their families for their dedication to the study.

References

1. Clark RH, Thomas P, Peabody J. Extrauterine growth restriction remains a serious problem in prematurely born neonates. *Pediatrics*. 2003; 111:986–990. [PubMed: 12728076]
2. Ehrenkranz RA, Younes N, Lemons JA, et al. Longitudinal growth of hospitalized very low birth weight infants. *Pediatrics*. 1999; 104:280–289. [PubMed: 10429008]

3. Kan E, Roberts G, Anderson PJ, et al. The association of growth impairment with neurodevelopmental outcome at eight years of age in very preterm children. *Early Human Development*. 2008; 84:409–416. [PubMed: 18096332]
4. Cooke RWI, Foulder-Hughes L. Growth impairment in the very preterm and cognitive and motor performance at 7 years. *Arch Dis Child*. 2003; 88:482–487. [PubMed: 12765911]
5. Casey PH, Whiteside-Mansell L, Barrett K, et al. 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]
6. Rotteveel J, van Weissenbruch MM, Twisk JWR, et al. Infant and Childhood Growth Patterns, Insulin Sensitivity, and Blood Pressure in Prematurely Born Young Adults. *Pediatrics*. 2008; 122:313–321. [PubMed: 18676549]
7. Euser AM, Finken MJ, Keijzer-Veen MG, et al. 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]
8. Sun SS, Grave GD, Siervogel RM, et al. Systolic blood pressure in childhood predicts hypertension and metabolic syndrome later in life. *Pediatrics*. 2007; 119:237–246. [PubMed: 17272612]
9. Rademacher ER, Jacobs DR Jr, Moran A, et al. Relation of blood pressure and body mass index during childhood to cardiovascular risk factor levels in young adults. *J Hypertens*. 2009; 27:1766–1774. [PubMed: 19633567]
10. Sinaiko AR, Donahue RP, Jacobs DR Jr, et al. Relation of weight and rate of increase in weight during childhood and adolescence to body size, blood pressure, fasting insulin, and lipids in young adults. The Minneapolis Children's Blood Pressure Study. *Circulation*. 1999; 99:1471–1476. [PubMed: 10086972]
11. Kothadia JM, O'Shea TM, Roberts D, et al. Randomized placebo-controlled trial of a 42-Day tapering course of dexamethasone to reduce the duration of ventilator dependency in very low birth weight infants. *Pediatrics*. 1999; 104:22–27. [PubMed: 10390255]
12. Shennan AT, Dunn MS, Ohlsson A, et al. Abnormal pulmonary outcomes in premature infants: prediction from oxygen requirement in the neonatal period. *Pediatrics*. 1988; 82:527–532. [PubMed: 3174313]
13. Stewart AL, Reynolds EO, Hope PL, et al. Probability of neurodevelopmental disorders estimated from ultrasound appearance of brains of very preterm infants. *Dev Med Child Neurol*. 1987; 29:3–11. [PubMed: 2435593]
14. Barlow SE. the Expert Committee. Expert Committee Recommendations Regarding the Prevention, Assessment, and Treatment of Child and Adolescent Overweight and Obesity: Summary Report. *Pediatrics*. 2007; 120:S164–S192. [PubMed: 18055651]
15. National High Blood Pressure Education Program Working Group on Hypertension Control in Children and Adolescents. Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents: a working group report from the National High Blood Pressure Education Program. *Pediatrics*. 1996; 98:649–658. [PubMed: 8885941]
16. Wechsler, D. Wechsler Intelligence Scale for Children. New York, NY: Psychological Corporation; 1999.
17. O'Shea TM, Washburn LK, Nixon PA, et al. Follow-up of a randomized, placebo-controlled trial of dexamethasone to decrease the duration of ventilator dependency in very low birth weight infants: neurodevelopmental outcomes at 4 to 11 years of age. *Pediatrics*. 2007; 120:594–602. [PubMed: 17766533]
18. Washburn LK, Nixon PA, O'Shea TM. Follow-up of a randomized, placebo-controlled trial of postnatal dexamethasone: blood pressure and anthropometric measurements at school age. *Pediatrics*. 2006; 118:1592–1599. [PubMed: 17015551]
19. Oken E, Kleinman KP, Rich-Edwards J, et al. A nearly continuous measure of birth weight for gestational age using a United States national reference. *BMC Pediatr*. 2003; 3:6. [PubMed: 12848901]
20. Kuczmarski RJ, Ogden CL, Grummer-Strawn LM, et al. CDC Growth Charts: United States. *Adv Data*. 2000; 314:1–27. [PubMed: 11183293]

21. Park MK, Menard SW, Schoolfield J. Oscillometric Blood Pressure Standards for Children. *Pediatr Cardiol.* 2005; 26:601–607. [PubMed: 16151689]
22. Ezzahir N, Alberti C, Deghmoun S, et al. Time course of catch-up in adiposity influences adult anthropometry in individuals who were born small for gestational age. *Pediatr Res.* 2005; 58:243–247. [PubMed: 16055935]
23. Hack M, Schluchter M, Cartar L, et al. Growth of very low birth weight infants to age 20 years. *Pediatrics.* 2003; 112:e30–e38. [PubMed: 12837903]
24. Doyle LW, Faber B, Callanan C, et al. Extremely low birth weight and body size in early adulthood. *Arch Dis Child.* 2004; 89:347–350. [PubMed: 15033844]
25. Davies AA, Smith GD, May MT, et al. Association between birth weight and blood pressure is robust, amplifies with age, and may be underestimated. *Hypertension.* 2006; 48:431–436. [PubMed: 16880348]
26. Franz AR, Pohlandt F, Bode H, et al. Intrauterine, early neonatal, and postdischarge growth and neurodevelopmental outcome at 5.4 years in extremely preterm infants after intensive neonatal nutritional support. *Pediatrics.* 2009; 123:e101–e109. [PubMed: 19117831]
27. Bonamy AK, Martin H, Jorreskog G, et al. Lower skin capillary density, normal endothelial function and higher blood pressure in children born preterm. *J Intern Med.* 2007; 262:635–642. [PubMed: 17986202]
28. Mikkola K, Leipala J, Boldt T, et al. Fetal growth restriction in preterm infants and cardiovascular function at five years of age. *Journal of Pediatrics.* 2007; 151:494–499. [PubMed: 17961692]
29. Doyle LW, Faber B, Callanan C, et al. Blood pressure in late adolescence and very low birth weight. *Pediatrics.* 2003; 111:252–257. [PubMed: 12563047]
30. Hack M, Schluchter M, Cartar L, et al. Blood pressure among very low birth weight (<1.5 kg) young adults. *Pediatr Res.* 2005; 58:677–684. [PubMed: 16192252]
31. Evensen KA, Steinshamn S, Tjonna AE, et al. Effects of preterm birth and fetal growth retardation on cardiovascular risk factors in young adulthood. *Early Hum Dev.* 2009; 85:239–245. [PubMed: 19013031]
32. Keijzer-Veen MG, Finken MJ, Nauta J, et al. Is blood pressure increased 19 years after intrauterine growth restriction and preterm birth? A prospective follow-up study in The Netherlands. *Pediatrics.* 2005; 116:725–731. [PubMed: 16140714]
33. deRegnier RA, Guilbert TW, Mills MM, et al. Growth Failure and Altered Body Composition Are Established by One Month of Age in Infants with Bronchopulmonary Dysplasia. *J Nutr.* 1996; 126:168–175. [PubMed: 8558298]
34. Ehrenkranz RA, Walsh MC, Vohr BR, et al. Validation of the National Institutes of Health consensus definition of bronchopulmonary dysplasia. *Pediatrics.* 2005; 116:1353–1360. [PubMed: 16322158]
35. Olsen IE, Lawson ML, Meinzen-Derr J, et al. Use of a body proportionality index for growth assessment of preterm infants. *J Pediatr.* 2009; 154:486–491. [PubMed: 19041096]
36. Ehrenkranz RA, Dusick AM, Vohr BR, et al. Growth in the neonatal intensive care unit influences neurodevelopmental and growth outcomes of extremely low birth weight infants. *Pediatrics.* 2006; 117:1253–1261. [PubMed: 16585322]
37. Hovi P, Andersson S, Eriksson JG, et al. Glucose regulation in young adults with very low birth weight. *N Engl J Med.* 2007; 356:2053–2063. [PubMed: 17507704]
38. Hofman PL, Regan F, Jackson WE, et al. Premature Birth and Later Insulin Resistance. *N Engl J Med.* 2004; 351:2179–2186. [PubMed: 15548778]
39. Uthaya S, Thomas EL, Hamilton G, et al. Altered adiposity after extremely preterm birth. *Pediatr Res.* 2005; 57:211–215. [PubMed: 15611357]
40. Latal-Hajnal B, von Siebenthal K, Kovari H, et al. Postnatal growth in VLBW infants: significant association with neurodevelopmental outcome. *J Pediatr.* 2003; 143:163–170. [PubMed: 12970627]
41. Lorenz JM, Whitaker AH, Feldman JF, et al. Indices of body and brain size at birth and at the age of 2 years: relations to cognitive outcome at the age of 16 years in low birth weight infants. *J Dev Behav Pediatr.* 2009; 30:535–543. [PubMed: 19901846]

42. Powers GC, Ramamurthy R, Schoolfield J, et al. Postdischarge Growth and Development in a Predominantly Hispanic, Very Low Birth Weight Population. *Pediatrics*. 2008; 122:1258–1265. [PubMed: 19047243]
43. Connors JM, O’Callaghan MJ, Burns YR, et al. The influence of growth on development outcome in extremely low birthweight infants at 2 years of age. *J Paediatr Child Health*. 1999; 35:37–41. [PubMed: 10234633]
44. Brandt I, Sticker EJ, Lentze MJ. Catch-up growth of head circumference of very low birth weight, small for gestational age preterm infants and mental development to adulthood. *J Pediatr*. 2003; 142:463–468. [PubMed: 12756374]
45. Powls A, Botting N, Cooke RW, et al. Growth impairment in very low birthweight children at 12 years: correlation with perinatal and outcome variables. *Arch Dis Child Fetal Neonatal Ed*. 1996; 75:F152–F157. [PubMed: 8976679]
46. Kuban KC, Allred EN, O’Shea TM, et al. Developmental correlates of head circumference at birth and two years in a cohort of extremely low gestational age newborns. *J Pediatr*. 2009; 155:344–349. [PubMed: 19555967]

Figure 1.

Weight z scores through early childhood as a function of BMI z score at study year 9: Time plot of weight z score versus age in years (corrected for prematurity) at hospital discharge and three follow-up visits. Locally weighted regression (lowess) curves are displayed for comparison of patterns in weight z scores between participants grouped by BMI z score tertile.

Figure 2.

Weight z scores through early childhood as a function of Verbal IQ at study year 9: Time plot of weight z score versus age in years (corrected for prematurity) at hospital discharge and three follow-up visits. Locally weighted regression (lowess) curves are displayed for comparison of patterns in weight z scores between participants grouped by Verbal IQ tertile.

Table 1

Comparison of attributes in children included in the current study (Participants), and children who were members of the original study cohort but were not included in the present study (Non-participants)

Attribute	Mean (SD) or Count (%)		P-value*
	Participants	Non-participants	
Gestational age, wks	25.6 (1.6)	25.6 (1.3)	1.0
Birth weight, g	796 (195)	784 (130)	0.72
Birth weight z score	-0.17 (0.63)	-0.18 (0.55)	0.95
Female	33 (51)	14 (47)	0.83
Caucasian	37 (57)	20 (67)	0.50
Maternal hypertension	12 (19)	N/A	N/A
Maternal education > high school	19 (30)	10 (37)	0.62
Antenatal steroids	22 (35)	6 (23)	0.32
Postnatal steroids	35 (54)	15 (50)	0.83
Chronic lung disease	39 (60)	24 (80)	0.07
Severe cranial ultrasound abnormality [†]	11 (18)	7 (23)	0.58
Sepsis [‡]	13 (20)	6 (20)	1.0
Necrotizing enterocolitis [§]	4 (6)	2 (7)	1.0
Gestational age at discharge, wks	38.7 (2.6)	39.1 (2.5)	0.45
Discharge weight, g	2261 (437)	2391 (521)	0.21
Discharge weight z score	-2.09 (0.55)	-1.84 (1.00)	0.21

* P-values are for comparison of participant and non-participant attributes using two-sample t-test or Fisher's exact test.

[†] Severe cranial ultrasound abnormality: post-hemorrhagic hydrocephalus, persistent ventricular enlargement, or periventricular echolucency

[‡] Positive blood culture

[§] Bell's stage II or higher

N/A – data not available

Table 2

Observed weights and rates of weight gain during infancy and early childhood.

	Mean (SD)
Age (years)	
1 year corrected age, n=65	1.1 (0.1)
5 years, n=59	4.8 (0.7)
9 years, n=65	9.4 (0.9)
Weight (kg)	
at 1 year corrected age	9.0 (1.3)
at 5 years	17.0 (4.0)
at 9 years	33.7 (12.1)
Weight z score	
at 1 year corrected age	-1.26 (1.29)
at 5 years	-0.68 (1.43)
at 9 years	0.06 (1.51)
Change in weight (grams per week)	
Birth - NICU discharge	112 (24)
NICU discharge to 1 year corrected age	117 (21)
1 year corrected age to 5 years of age	43 (15)
Change in weight z score	
Birth-NICU discharge	-1.92 (0.66)
NICU discharge to 1 year corrected age	0.83 (1.18)
1 year corrected age to 5 years of age	0.53 (1.37)

NICU-neonatal intensive care unit

Table 3

Outcomes at 9 year visit (n = 65)

Outcome	Mean (SD)
SBP, mmHg	113 (11)
DBP, mmHg	64 (8)
SBP z score	1.18 (1.02)
DBP z score	0.35 (0.70)
BMI, kg/m ²	18.2 (4.4)
BMI z score	0.19 (1.34)
Verbal IQ	92 (19)
Performance IQ *	86 (16)

SBP – systolic blood pressure; DBP – diastolic blood pressure; BMI – body mass index; IQ – intelligence quotient

*
n=64

Table 4

Regression coefficients (95% confidence intervals) for final models relating rates of weight gain during infancy (discharge to 1 year corrected age) and early childhood (1 year corrected age to 5 years of age) to systolic blood pressure, body mass index, and intelligence quotient (IQ) at 9 years of age.

	Outcome			
	BMI z score ^a	Verbal IQ ^b	Performance IQ ^b	SBP z score ^a
Infancy				
Change in weight z score	0.29 (−0.03, 0.62)	1.50 (−3.4, 6.39)	0.65 (−3.77, 5.07)	−0.01 (−0.29, 0.27)
Change in weight (10 g/week) **	0.19 (0.02, 0.36) *	0.38 (−2.24, 2.99)	0.07 (−2.29, 2.43)	0.04 (−0.11, 0.18)
Early Childhood				
Change in weight z score	1.59 (0.72, 2.46) *	3.17 (−11.53, 17.87)	2.45 (−10.94, 15.83)	−0.13 (−0.99, 0.73)
Change in weight (10 g/week) **	0.37 (0.11, 0.63) * [†]	0.68 (−3.07, 4.43)	−0.28 (−3.62, 3.06)	−0.13 (−0.34, 0.09)

^a adjusted for race, antenatal steroids, birth weight z score, major intracranial lesions on ultrasound, and chronic lung disease

^b adjusted for race, gender, maternal education, antenatal steroids, birth weight z score, major intracranial lesions on ultrasound, and chronic lung disease

* p < 0.05

** estimates are calculated assuming the model described in Statistical Methods for mixed modeling; confidence intervals are approximate

[†] regression coefficient for interaction term (weight at 1 year CA × early childhood weight gain) = −0.07 (−0.14, −0.01)

BMI- body mass index; SBP- systolic blood pressure