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Gender-specific differences in birthweight and the odds of puberty: NHANES III, 1988–94

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Summary

The association between birthweight and the odds ratio (OR) of pubertal status in girls aged between 8 and 11 and in boys aged between 8 and 12 was examined using the 1988–94 Third National Health and Nutrition Examination Survey (NHANES III). Girls ($n = 956$), and boys ($n = 1199$), who had data on birthweight and Tanner staging were included. Maternal-reported birthweight, smoking in pregnancy and other information were provided in a home interview, while Tanner staging to assess pubertal status was part of a medical examination. Multiple logistic regression models were computed for the endpoints of the OR [95% confidence interval (CI)] of being Tanner Stage 2+ vs. 1 or being 2+ vs. 1 in an asynchronous pubertal pathway after adjustment for the complex sampling design of NHANES, age, race, height and body mass index (BMI).

Birthweight was not associated with the OR of Tanner stage 2+ among girls; however, boys who were low birthweight (<2500 g) and boys born higher than average birthweight (3500–3999 g) were more likely to be Tanner stage 2+ than 1. Childhood BMI was associated with the OR of having entered puberty among girls, but not boys. In an analysis of asynchronous maturation, girls born at high birthweight (>4000 g) were more likely to have breast development 3+ than girls of normal birthweight, OR = 3.18 [95% CI 1.39, 8.25]. Thus, the birthweight–puberty association varies by gender and by pubertal pathway. Our findings need replication in prospective longitudinal studies, and research to understand the mechanisms underlying the relation of early life exposures to cancer risk.

Keywords

puberty; birthweight; childhood BMI; NHANES

Introduction

Birthweight has been associated with risk of chronic diseases, including coronary heart disease, diabetes, hypertension and cancer.¹⁻³ Specifically, low birthweight and subsequent catch-up in weight gain before 2 years of age is associated with increased risk of diabetes, coronary heart disease and insulin resistance.⁴ These findings relate to the Developmental Origins Hypothesis, which proposes that events early in life, including *in utero*, and weight gain in early life, affect risk of disease during adulthood.⁵ Development *in utero*, infancy and childhood is rapid, so specific exposures and insults could have a significant impact on later disease risk. Furthermore, birthweight is considered to be an indicator for the predictive adaptive responses,^{6,7} where exposures *in utero* and during the early neonatal period establish biosystemic responses that can result in maladaptive long-term effects.⁸ However, birthweight may also serve as a proxy for differences in fetal growth.

Pubertal onset is occurring earlier in children in the United States over time.^{9,10} This phenomenon of maturing at earlier ages has recently been reported in a cohort of British girls as well.¹¹ The mean age for Tanner Stage 2+ decreased from 11 years of age in the 1950s and 1960s to 10 years of age in white girls and to 9.5¹² or <9 years of age in black girls in the 1990s.¹³ Using nationally representative data from the third National Health and Nutrition Examination Survey (NHANES III) conducted from 1988 to 1994, the median age of Tanner Stage 2+ among girls and boys was 10 years old in white and Mexican Americans and 9 years old in Blacks.¹² In a more recent study in 2006, the median age of 10.2 years for Tanner Stage 2+ was reported in white girls and 9.6 years in Black girls.¹⁴ The earlier age of pubertal onset leads to a longer cumulative exposure to hormones, and may therefore have potential implications for risk of breast and other hormonal cancers.

Pubertal onset is typically assessed using Tanner stages which evaluate pubic hair in males and females, genitalia development in males and breast development in females.^{15,16} Tanner stage 1 constitutes prepuberty for that specific aspect of development. Tanner stages 2 to 5 constitute increasing stages of physical development of pubic hair growth, genitalia development or breast development.^{15,16} Biro *et al.* examined asynchronous pubertal development among girls in the National Heart, Lung, and Blood Institute Growth and Health Study using Tanner stages to assess breast development and pubic hair development.¹⁷ In this study, girls who displayed breast development as the initial manifestation of pubertal development were in the thelarche pathway, while girls who displayed pubic hair development as the initial manifestation of pubertal development were in the adrenarche pathway.¹⁷ The authors observed that the majority of girls had asynchronous pubertal maturation with most of them experiencing thelarche first.¹⁷

In this study, we examine whether birthweight is associated with current pubertal status. This interest initially arose from the associations between high birthweight and increased breast cancer risk, and earlier pubertal onset and increased breast cancer risk^{2,18,19} Although the biological mechanisms underlying these associations are unknown, it has been hypothesised that increased exposure to hormones, such as oestrogen, occurs *in utero*.^{2,20} Interestingly, there are also epidemiological studies observing a U-shaped relationship among birthweight and testicular cancer in men.²¹⁻²² Men who weighed <2500 g or >4000 g

at birth had an increased risk of testicular cancer compared with those with a normal birthweight.²¹ However, there are few, if any, studies investigating the role of birthweight on pubertal status in boys. Some studies have examined the association of age at puberty with risk of testicular cancer and have observed increased risk of testicular cancer with early age of puberty²³⁻²⁵ while others observe no association.^{22,26,27}

The aims of the present analysis were to investigate the association between birthweight and a child's pubertal status among 2155 children aged 8–12 years who participated in the 1988–94 NHANES survey, taking into consideration potential covariates such as age, race/ethnicity, height and body mass index (BMI). We contrast two approaches: Tanner staging, which classifies development based on the combination of assessing breast and pubic hair in girls and genital and pubic hair in boys, vs. asynchronous maturation,¹⁷ that classifies children on the individual pathways of Tanner Stage as described by Biro, to identify whether birthweight is associated with one approach to pubertal assessment.

Materials and methods

Sample

The study utilised cross-sectional data collected in the 1988–94 NHANES III survey²⁸ from 33 994 civilian non-institutionalised individuals in the United States aged 2 months to 80+ years. For the current study, we focused on all girls aged 8–11 and boys aged 8–12 years. This age range corresponds to the ages for Tanner staging since 8 years is considered the lower limit of a normal age for onset of puberty among girls, and 9 years is considered the lower limit of a normal age for onset of puberty for boys.¹² Analysis of Tanner staging by NHANES physicians was completed on all participants aged 8–18 years, therefore, we included boys that were 8 years of age to ensure we did not miss any boys with onset of puberty. Additionally, this age range should incorporate the majority of children undergoing pubertal onset (Tanner Stage 2) at a minimum because by age 12, approximately 91% of boys and 94% of girls are Tanner stage 2 or higher.²⁹ A total of 1476 girls and 1705 boys in these age ranges had a medical examination; however, 200 girls and 134 boys were missing birthweight and 320 girls and 372 boys were missing Tanner staging and thus were excluded from this analysis. The final analytical sample had 956 girls aged 8–11 and 1199 boys aged 8–12.

The NHANES III sample weights reflect the differential rates of sample selection which include oversampling of Blacks and Mexican Americans and adjusts for survey and medical examination non-response; therefore, sampling weights were used in all analyses to calculate estimates for the US population (see the data analysis section). Demographic (age, gender, race/ethnicity), socio-economic (poverty level, geographical area) and medical history information (birthweight, diabetes in the mother and maternal smoking in pregnancy) were collected from the mother during household interviews for the NHANES III children. After the household interview, participants were invited to go to Mobile Examination Centers (MEC) where they underwent physical examination. Height and weight were measured to calculate BMI during the physical examination, and pubertal stage was classified into one of five Tanner stages by trained clinicians.^{15,28} Physicians underwent extensive specialised training in pubertal assessment.³⁰

Categories of BMI-for-age were based on the Centers for Disease Control and Prevention guidelines for children³¹ using: underweight for those individuals whose BMI was less than the fifth percentile; healthy weight for a BMI between the fifth and 85th percentile; at risk of overweight for the 85th to 95th percentile; and overweight for a BMI over the 95th percentile for their age-gender-specific groups.³¹ Poverty index was calculated from family income and family size, and was categorised as below, or at and above poverty level as suggested in Section 1: Key Variables for Analysis in the Analytic and Reporting Guidelines of NHANES III.²⁸ Other variables were age [8, 9, 10, 11 years (for girls) plus 12 years (for boys)], maternal smoking exposure (no/yes), maternal diabetes status (no/yes) and race/ethnicity (white, Black and Mexican American).

Pubertal stage was classified using Tanner stage by physicians who were trained in a standardised method for the NHANES examination.¹⁵ Tanner staging has two classifications by breast and pubic hair development in girls, and by genital and pubic hair development in boys.¹⁵ For breast (B), genitalia (G) and pubic hair (PH) development, the subjects were classified as Stage 1 (prepubertal) up to Stage 5 (full maturity) based on well-documented criteria.¹⁵ Tanner staging was classified by observation only; no palpation was involved.²⁸

In this study, two different approaches for pubertal assessment were used: Tanner staging and asynchronous maturation.¹⁷ For Tanner staging, prepubertal included all classified as Stage 1 for both pubic hair and breast development for girls (PH1/B1), and Stage 1 for both pubic hair and genitalia development for boys (PH1/G1). All others were classified as Tanner stage 2 or more since they had breast, genitalia, and/or pubic hair development and had therefore experienced pubertal onset at a minimum in at least one facet of development. We applied Biro's classification for asynchronous pubertal development.¹⁷ Specifically, Biro reported that girls often underwent breast development (thelarche) earlier than pubic hair development (adrenarche) in a longitudinal study of growth and development.¹⁷ Therefore, we utilised this approach to examine the association of birthweight with only pubic hair development, or only breast development for girls, and only genitalia development for boys. Development of pubic hair, breast or genitalia was determined by Tanner staging, but each facet of puberty was examined independently in determining asynchronous maturation.

Statistical analysis

Binary logistic regression was used to estimate unadjusted and adjusted odds ratios (OR) of being Tanner stage 2+ in contrast with Tanner stage 1 by birthweight categories. Birthweight was categorised as low and high birthweight and in 500 g increments for normal birthweight; in another part of this analysis, birthweight was treated as a continuous variable per 100 g increments. Multinomial logistic regression was used to estimate unadjusted and adjusted ORs of being Tanner Stage 2+ for asynchronous maturation vs. stage 1 for the pubertal pathway. In this analysis, birthweight was categorised in 500 g increments to look at the association between birthweight and pubic hair development, or breast development, or genitalia development. The variables for age, BMI, height, maternal smoking exposure, maternal diabetes status, poverty index and race/ethnicity were considered as covariates. Backward stepping was initially used to determine which variables to include in the model.

Next, beginning with the least significant variable, variables were dropped from the model if they did not result in a 10% or more change in the regression coefficient. The final variables included in the model were age (as a continuous variable in years), race/ethnicity, height (as a continuous variable in inches) and BMI (as a continuous variable). To examine possible effect modification, interaction terms between birthweight and covariates were included in the modelling, with the independent variables for each interaction term entered in the model as well. However, none was significant and therefore they were excluded from our analyses.

All analyses were weighted by the NHANES sample weights and the stratification and multistage cluster design used in the complex sampling was accounted for in the computation of standard errors, confidence interval (CI) and *P*-values. Briefly, the sample weight for each surveyed individual is the inverse of the probability of being sampled multiplied by adjustments for non-response and post-stratification, which make, the weighted distributions by age, race and gender for the NHANES III sample match the US Census.³² Thus, the sample weights were used in our analysis to account for differential sampling by race and ethnicity i.e. Whites, Blacks and Mexican Americans, and by other subgroups (e.g. age, gender and geographical region), and to reduce bias from potential characteristics of non-responders that may differ from responders. The sample weight for a surveyed individual can be interpreted as the number of people in the population that the surveyed individual represents. The sample weights were incorporated in the analyses by multiplying each observation value by the weight. Therefore, our weighted analyses are (approximately) unbiased and generalisable to the US population. It has been shown that not using weighted analyses of survey data can result in biased estimates of associations in epidemiological studies.³³ Because the NHANES III has a complex sample design involving stratified cluster sampling and the clustering of the sample can inflate the standard errors due to intra-cluster correlations, the Taylor Linearization method for estimating standard errors from complex survey samples was used in our analyses.³³ All analyses were carried out using procedures in STATA for analysing complex survey data,³⁴ and all *P*-values are two-sided.

Results

There were approximately equal percentages of participants in each age group (Table 1). Approximately 26% of the girls and 19% of the boys sampled lived in households that were below the poverty level. The highest proportion of participants lived in the southern portion of the United States, followed by the West, the Midwest and Northeast.

The crude ORs of being Tanner Stage 1 (prepubertal) or 2+ was examined by demographic characteristics. In this analysis, any child who was classified as stage 2 or more for pubic hair or breast development in girls, and for pubic hair or genitalia development in boys was considered pubertal. Not surprisingly, age was directly in a monotonic pattern associated with being 2+ among girls and boys with the oldest age group having the highest odds of being 2+. Girls who were at risk for being overweight had a higher crude OR (OR = 1.54, 95% CI 1.04, 2.27) of being stage 2+, although this was not true for the boys. Compared with non-Hispanic whites, African American and Mexican American girls had a higher odds of being stage 2+ (OR = 1.97, 95% CI 1.33, 2.90 and OR = 1.56, 95% CI 1.02, 2.38,

respectively), while African American boys, had a higher odds of being 2+ (OR =1.91, 95% CI 1.22, 3.00). However, poverty level, region of the US, mothers who reported smoking during pregnancy, or ever had a diagnosis of diabetes did not appreciably influence the odds of their children being Tanner stage 2+ at the time of the MEC.

We first examined the association between birthweight and the OR of being Tanner stage 2+ (i.e. greater than PH1/B1 in girls and greater than PH1/G1 in boys) vs. Tanner stage 1. No association was observed between birthweight and the OR of Tanner stage 2+ in girls (Table 2). There was a higher odds of being Tanner Stage 2+ in boys who were born of low birthweight (<2500 g) and among boys weighing 3500–3999 g compared with boys who were born weighing between 3000 and 3499 g (OR = 3.00, 95% CI 1.66, 6.07 and OR = 1.50, 95% CI 1.07, 2.72, respectively) (Table 2).

Using the endpoint of asynchronous puberty, we examined the association between birthweight as a continuous variable in increments of 100 g and breast development in girls (Table 3). Girls who were classified as stages 3 (B3), 4 (B4) or 5 (B5) were combined because of the small numbers in each age group. Increasing birthweight was associated with an increased odds of being B3–5. Also, breast development covaried with age and height (in inches), i.e. the mean (SD) ages of girls were 8.9 (0.9), 9.7 (1.0) and 10.5 (0.8) for B1, B2 and B3–5, respectively, while the mean (SD) heights of girls were 52.8 (2.8), 55.8 (3.2) and 59.4 (2.9) for each breast category, respectively. Next, to examine the association between breast development and birthweight more fully, we analysed the effect of the previous categories of birthweight on breast development (Table 4). Girls who were in the highest category of birthweight (≥ 4000 g) were significantly more likely to be B3+ than girls who were born between 3000 and 3499 g, with an OR of 3.18 [95% CI = 1.39, 8.25].

An inverse association was observed between birthweight and pubic hair development among girls. Birthweight in 100 g increments had a decreased OR of being in PH3 or PH4/PH5 among girls. However, no association between birthweight and pubic hair development was observed among boys (Table 5). Yet again, age and height were directly associated with pubic hair development in girls and boys. For example, the mean (SD) ages of girls were 9.0 (1.0), 9.8 (1.0), 10.4 (0.9) and 10.7 (0.7) for PH1, PH2, PH3 and PH4 & PH5, respectively. The mean (SD) heights of boys were 9.5 (1.2), 10.7 (1.1) and 11.4 (0.9) for PH1, PH2 and PH3–5, respectively. We then examined the association between birthweight and genitalia development for boys (Table 5). Like pubic hair development, no association was observed between genitalia development and birthweight among boys. However, similar to pubic hair development, age and height were directly associated with genitalia development among boys.

Discussion

Among children aged 8–12 years who participated in NHANES III, we examined whether birthweight was associated with being Tanner stage 2+ or asynchronous pubertal development, i.e. the Biro approach. We found that compared with boys weighing 3000–3499 g at birth, boys born of low birthweight (<2500 g) and those weighing 3500–3999 g at

birth were more likely to be Tanner stage 2+. No association between birthweight and being Tanner stage 2+ appeared in girls.

Since early age at menarche is a recognised risk factor for breast cancer, we wished to explore whether birthweight was associated with synchronous or asynchronous pubertal development which has also been associated with breast cancer risk.^{18,20,35} We observed that girls of high birthweight (> 4000 g) were more likely to be at a higher stage of breast development than girls with a birthweight between 3000 and 3499 g. Biro described a paradigm in which the majority of girls undergo puberty in an asynchronous manner,¹⁷ with breast development (thelarche) appearing before pubic hair development (adrenarche). In accordance with Biro, we reported that many girls had asynchronous pubertal status and were more likely to have thelarche than adrenarche.¹⁷ This finding has implications for breast cancer risk, as it has been previously described that women who were of high birthweight were at increased breast cancer risk.² Our data show that high birthweight was associated with breast development of girls. Therefore, high birthweight, or factors associated with high birthweight, may lead to a growth trajectory in childhood that results in earlier pubertal breast maturation. It is interesting to note that Biro also observed that girls who developed through thelarche first, had earlier menarche and greater BMI.^{17,36} An earlier study comparing this NHANES data with earlier data from the National Health Examination Survey cycles II and III from 1963–70 also illustrated that higher weight was associated with an increased likelihood of having reached menarche.³⁷ Since earlier menarche is a risk factor for breast cancer and higher BMI is a risk factor for postmenopausal breast cancer, follow-up of girls who experience breast development (thelarche) first may provide insights in the underlying pathway from breast development to early menarche, and in turn to breast cancer risk.

Similar to the research of others, we reported an association between age, race/ethnicity and BMI with pubertal onset.^{14,17,36,38-40} As expected, age was directly associated with a higher odds of being 2+, after adjustment for other covariates. Also, girls who had a higher BMI had higher odds of being pubertal. Finally/racial differences were observed that confirm previous findings.^{14,39} Specifically, Black girls and boys, and Mexican American girls had higher odds of being Tanner Stage 2+ than their non-Hispanic white peers, after adjustment for other covariates and the complex sampling design for NHANES III.

As a secondary analysis, we investigated the association of birthweight with being Tanner Stage 2+ in boys. Remarkably, little is known about the role of birthweight and Tanner Stage in regards to cancer risk in men. However, a recent meta-analysis reported a U-shaped relationship between birthweight and testicular cancer in men.²¹ We report for the first time that boys born of a low birthweight (<2500 g) had higher odds of being Tanner stage 2+. Low birthweight has been associated with chronic diseases such as coronary heart disease, hypertension and diabetes in men.¹⁻³ Birthweight has also been recognised as an indicator for *in utero* events that may programme an individual for risk of chronic diseases such as cancer.^{2,41-43} Therefore, although it appears that low birthweight conveys risk of certain chronic diseases, little is known regarding the role of all three factors, notably birthweight, puberty and cancer risk in men, in the same study. Earlier pubertal onset may increase hormonal exposure throughout the life course leading to an increase in hormonally regulated

cancers, yet no published reports have appeared. Similar to the effect of low birthweight on the odds of Tanner Stage 2+ among boys, we observed that boys born of a higher than average birthweight (3500–3999 g) also had higher odds of being 2+. Thus our findings are similar to the U-shaped association between birthweight and testicular cancer.²¹

We observed no effect of exposure to maternal smoke *in utero* on puberty onset. It is well recognised that women who smoke during pregnancy have lower birthweight babies.^{44–47} We have corroborative data from our NHANES analysis that illustrate a lower mean birthweight (SD) of children born to mothers who smoked during the index pregnancy [3164.9 (607.3)] compared with children of non-smokers [3332.3 (554.9), $P = 0.0009$, data not shown]. Furthermore, we did not find an association of maternal diabetes with pubertal onset, but we did not have information about gestational diabetes. Thus, this analysis only evaluated women who reported a diagnosis of diabetes at any point during their life.

There are several limitations and strengths of our data analysis. No data on gestational age were collected in NHANES, so we could not determine whether low birthweight was preterm or full-term or due to an underlying co-morbidity in pregnancy such as preeclampsia. Second, birthweight was based on maternal recall which may have introduced misclassification bias. However, many studies have demonstrated a high correlation (~0.90) between maternal recall and actual birthweight.^{48–50} Another limitation is the absence of information on interval growth from birth until the examination to assess evidence of early catch-up weight, especially among the study participants who were of low birthweight. In addition, over 35% of girls and 30% of boys were not included in the analysis because they were missing data on birthweight or pubertal status. Some did refuse the physical exam for Tanner staging, therefore it is possible that selection bias exists if these participants are different than those included. Furthermore, we were unable to assess and adjust for parental anthropometric factors or parental age at entering puberty, both of which may be potential confounders. Finally, a cross-sectional survey with only a single assessment of pubertal development such as NHANES III does not offer accurate determination of the age of initiation of the developmental stage; rather we could only analyse pubertal status at the age/time of the MEC exam. Strengths of this study include that Tanner staging was assessed by trained physicians under standardised conditions limiting the possibility of misclassification. An additional strength is data on three major ethnic groups in the United States because NHANES oversampled minorities.

Based on an analysis of NHANES III, there were no significant associations between birthweight and the odds of having entered puberty by age 11 among girls in the United States; however, boys born of low birthweight were more likely to have begun puberty by age 12 than those born at an average birthweight. Girls who were born with a high birthweight had higher odds of breast development, which may have implications for breast cancer risk. Previous research has documented associations between high birthweight and increased risk of breast cancer as well as early puberty onset and increased breast cancer risk.^{2,18,19} Longitudinal research needs to be done in the future to investigate *in utero* and early life exposures, puberty onset and breast cancer risk and to identify the mechanisms underlying early life exposures, age at pubertal onset and their relation to cancer risk.

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Table 1

Weighted demographic and maternal characteristics by gender: NHANES III, 1988–94

	Total <i>n</i> (%)	Prepubertal <i>n</i> (%)	Pubertal or more mature <i>n</i> (%)	OR [95% CI]
Girls ^a				
Total	956 (100)	365 (42.3)	591 (57.7)	
Age (years)				
8	227 (20.5)	165 (39.5)	62 (6.6)	1.00 Reference
9	248 (29.8)	124 (41.3)	124 (21.4)	3.08 [1.72,5.54]
10	230 (22.5)	62 (16.8)	168 (26.7)	9.45 [5.44,16.41]
11	251 (27.1)	14 (2.4)	237 (45.3)	1.11 [46,269]
Race/ethnicity				
White	254 (66.0)	124 (72.1)	130 (61.6)	1.00 Reference
Black	324 (15.7)	97 (11.3)	227 (19.0)	1.97 [1.33,2.90]
Mexican American	339 (8.4)	126 (7.1)	213 (9.4)	1.56 [1.02,2.38]
Other	39 (9.8)	18 (9.6)	21 (10.0)	1.22 [0.38,3.91]
Poverty index ^b				
Below poverty	378 (26.2)	142 (28.3)	236 (24.8)	1.00 Reference
At or above poverty	509 (70.3)	197 (67.7)	312 (72.2)	1.22 [0.72,2.06]
Region				
Northeast	100 (21.3)	43 (21.0)	57 (21.4)	1.00 Reference
Midwest	166 (19.1)	70 (23.0)	96 (16.1)	0.69 [0.29,1.64]
South	432 (37.6)	150 (29.3)	282 (43.7)	1.47 [0.60,3.58]
West	258 (22.1)	102 (26.7)	156 (18.8)	0.69 [0.26,1.82]
Body mass index				
Underweight (<5%)	39 (5.4)	21 (8.5)	18 (3.1)	0.37 [0.13,1.01]
Normal weight	642 (70.0)	260 (70.6)	382 (69.5)	1.00 Reference
At risk for overweight (85%)	153 (15.2)	47 (11.9)	106 (17.6)	1.54 [1.04,2.74]
Overweight (95%)	117 (9.5)	35 (8.9)	82 (9.8)	1.62 [0.99,2.43]
Exposure to maternal smoke				
No	763 (80.7)	291 (81.6)	472 (80.0)	1.00 Reference
Yes	176 (19.3)	69 (18.4)	107 (20.0)	1.11 [0.75,1.64]

	Total n (%)	Prepubertal n (%)	Pubertal or more mature n (%)	OR [95% CI]
Exposure to maternal diabetes				
No	913 (97.1)	346 (97.8)	567 (96.6)	1.00 Reference
Yes	27 (2.9)	9 (2.2)	18 (3.4)	1.54 [0.37,6.34]
Boys ^c				
Total	1199 (100)	464 (40.8)	735 (59.2)	
Age (years)				
8	240 (19.8)	158 (34.1)	82 (10.0)	1.00 Reference
9	269 (20.5)	126 (28.6)	143 (14.9)	1.77 [1.08,2.90]
10	257 (20.6)	102 (21.5)	155 (20.0)	3.16 [1.92,5.22]
11	256 (19.9)	60 (13.0)	196 (24.7)	6.42 [2.80,14.73]
12	177 (19.1)	18 (2.8)	159 (30.4)	36.5 [13.2,101]
Race/ethnicity				
White	300 (67.1)	121 (71.6)	179 (64.0)	1.00 Reference
Black	428 (16.0)	139 (11.2)	289 (19.2)	1.91 [1.22,3.00]
Mexican American	423 (8.9)	188 (10.0)	235 (8.2)	0.91 [0.49,1.69]
Other	48 (8.0)	16 (7.1)	32 (8.6)	1.36 [0.58,3.21]
Poverty index ^d				
Below poverty	434 (18.9)	153 (16.6)	281 (20.5)	1.00 Reference
At or above poverty	667 (76.5)	264 (77.5)	403 (75.9)	0.79 [0.47,1.32]
Region				
Northeast	135 (19.9)	42 (13.5)	93 (24.3)	1.00 Reference
Midwest	225 (21.8)	75 (24.3)	150 (20.1)	0.46 [0.19,1.09]
South	500 (32.2)	204 (30.5)	296 (33.4)	0.61 [0.26,1.40]
West	339 (26.1)	143 (31.7)	196 (22.3)	0.39 [0.15,1.04]
Body mass index				
Underweight (<5%)	40 (4.2)	16 (3.9)	24 (4.4)	1.03 [0.33,3.19]
Normal weight	789 (66.3)	280 (62.2)	509 (69.2)	1.00 Reference
At risk for overweight (85%)	174 (16.8)	75 (18.0)	99 (15.9)	0.80 [0.50,1.26]
Overweight (95%)	195 (12.7)	88 (16.0)	97 (10.4)	0.59 [0.34,1.00]
Exposure to maternal smoke				

	Total n (%)	Prepubertal n (%)	Pubertal or more mature n (%)	OR [95% CI]
No	806 (73.6)	346 (72.4)	460 (74.7)	1.00 Reference
Yes	197 (26.5)	92 (27.7)	105 (25.3)	0.89 [0.50,1.56]
Exposure to maternal diabetes				
No	1124 (97.7)	435 (98.2)	689 (97.3)	1.00 Reference
Yes	45 (2.3)	20 (1.8)	25 (2.7)	1.46 [0.60,3.57]

^a n = 200 and 320 girls were missing birthweight or Tanner stage, respectively, and therefore were excluded from the analysis.

^b n = 69 girls were missing data for the poverty index.

^c n = 134 and 372 boys were missing birthweight or Tanner stage, respectively, and therefore were excluded from the analysis.

^d n = 98 boys were missing data for the poverty index.

Table 2

Unadjusted and adjusted OR [95% CI] of Tanner stage 2+ by birthweight: NHANES III 1988–94

Birthweight (g)	Prepubertal (PH1/B1 or PH1/G1) n (%)	Tanner Stage 2+ (>PH1/B1 or >PH1/G1) n (%)	Unadjusted OR [95% CI]	Adjusted ^{a,b} OR [95% CI]
Girls				
<2500	26 (2.9)	39 (2.6)	0.68 [0.23,1.96]	0.62 [0.17,2.34]
2500–2999	59 (5.3)	101 (9.9)	1.43 [0.71,2.87]	1.67 [0.70,3.94]
3000–3499	128 (17.1)	209 (22.5)	1.00 Reference	1.00 Reference
3500–3999	82 (12.5)	133 (19.0)	0.73 [0.24, 2.19]	0.80 [0.36,1.77]
4000	26 (4.3)	50 (4.1)	1.16 [0.58,2.30]	1.52 [0.85,1.76]
Boys				
<2500	20 (2.1)	52 (3.2)	1.91 [1.68,5.33]	3.00 [1.66,6.07]
2500–2999	82 (6.0)	85 (7.6)	1.05 [0.68,3.53]	1.03 [0.70,4.80]
3000–3499	151 (18.2)	159 (14.9)	1.00 Reference	1.00 Reference
3500–3999	105 (14.5)	155 (15.3)	1.49 [1.01,2.94]	1.50 [1.07,2.72]
4000	88 (8.2)	125 (10.0)	1.29 [0.66,2.53]	1.68 [0.79,3.57]

^a Adjusted for age, race/ethnicity, height and body mass index.^b Odds ratios were weighted by the NHANES sample weights and the stratification and primary sampling units were accounted for.

Table 3

Adjusted odds ratios for asynchronous breast development by birthweight (per 100 g) among girls: NHANES III Study, 1988–94

	<i>n</i> (%)	Adjusted OR ^{a,b} [95% CI]
Birthweight per 100 g in B1	437 (51.8)	1.00 Reference
Birthweight per 100 g in B2	284 (27.4)	1.01 [0.96,1.07]
Birthweight per 100 g in B3–5	235 (20.9)	1.09 [1.02,1.27]

^a Adjusted for age, race/ethnicity, height and body mass index.

^b All analyses were weighted by the NHANES sample weights and took into account the stratification and primary sampling units.

Adjusted odds ratios for the association of asynchronous breast development among girls: NHANES III Study, 1988–94

Table 4

Birthweight (g)	n (%)	Adjusted OR ^{a,b} [95% CI]	n (%)	Adjusted OR ^{a,b} [95% CI]
Breast development B2				
<2500	16 (1.1)	0.87 [0.27,2.79]	Breast development B3, B4, & B5	
2500–2999	41 (3.1)	0.88 [0.41,1.89]	17 (1.2)	2.26 [0.22,13.13]
3000–3499	104 (10.9)	1.00 Reference	40 (4.2)	3.28 [0.99,7.32]
3500–3999	64 (9.5)	1.11 [0.36,3.40]	77 (6.9)	1.00 Reference
4000	24 (2.0)	1.25 [0.62,2.55]	53 (7.2)	1.53 [0.49,4.80]
			25 (2.0)	3.18 [1.39,8.25]

No breast development (B1) is the referent group.

^a Adjusted for age, race/ethnicity, height and body mass index.

^b Odds ratios were weighted by the NHANES sample weights and the stratification and primary sampling units were accounted for.

Table 5

Adjusted odds ratios for pubic hair development in girls and boys, and genitalia development in boys by birthweight in 100 g increments from NHANES III Study, 1988–94

	<i>n</i> (%)	Adjusted OR ^{a,b} [95% CI]
Pubic hair development		
Girls		
Birthweight per 100 g in PH1	508 (54.8)	1.00 Reference
Birthweight per 100 g in PH2	216 (22.6)	0.99 [0.93,1.05]
Birthweight per 100 g in PH3	154 (16.8)	0.92 [0.86,0.99]
Birthweight per 100 g in PH4&PH5	78 (5.8)	0.87 [0.79,0.95]
Boys		
Birthweight per 100 g in PH1	899 (74.0)	1.00 Reference
Birthweight per 100 g in PH2	175 (12.8)	0.99 [0.95,1.04]
Birthweight per 100 g in PH3–5	125 (13.3)	0.98 [0.93,1.05]
Genitalia development		
Boys		
Birthweight per 100 g in G1	480 (41.8)	1.00 Reference
Birthweight per 100 g in G2	485 (36.5)	1.01 [0.97,1.05]
Birthweight per 100 g in G3–5	234 (21.7)	0.98 [0.94,1.02]

^a Adjusted for age, race/ethnicity, height and body mass index.

^b Odds ratios were weighted by the NHANES sample weights, stratification and primary sampling units were accounted for.