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Secondary Sexual Characteristics in Boys: Data From the Pediatric Research in Office Settings Network

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## Secondary Sexual Characteristics in Boys: Data From the Pediatric Research in Office Settings Network

**WHAT'S KNOWN ON THIS SUBJECT:** Recent investigations of pubertal onset in US girls suggest earlier maturation. The situation for US boys is unknown, and existing investigations are outdated and lack information on a key physical marker of male puberty: testicular enlargement.

**WHAT THIS STUDY ADDS:** US boys appear to be developing secondary sexual characteristics and achieving testicular enlargement 6 months to 2 years earlier than commonly used norms, with African American boys entering Tanner stages 2 to 4 earlier than white or Hispanic boys.

### abstract

**BACKGROUND:** Data from racially and ethnically diverse US boys are needed to determine ages of onset of secondary sexual characteristics and examine secular trends. Current international studies suggest earlier puberty in boys than previous studies, following recent trend in girls.

**METHODS:** Two hundred and twelve practitioners collected Tanner stage and testicular volume data on 4131 boys seen for well-child care in 144 pediatric offices across the United States. Data were analyzed for prevalence and mean ages of onset of sexual maturity markers.

**RESULTS:** Mean ages for onset of Tanner 2 genital development for non-Hispanic white, African American, and Hispanic boys were 10.14, 9.14, and 10.04 years and for stage 2 pubic hair, 11.47, 10.25, and 11.43 years respectively. Mean years for achieving testicular volumes of  $\geq$ 3 mL were 9.95 for white, 9.71 for African American, and 9.63 for Hispanic boys; and for  $\geq$ 4 mL were 11.46, 11.75, and 11.29 respectively. African American boys showed earlier (*P* < .0001) mean ages for stage 2 to 4 genital development and stage 2 to 4 pubic hair than white and Hispanic boys. No statistical differences were observed between white and Hispanic boys.

**CONCLUSIONS:** Observed mean ages of beginning genital and pubic hair growth and early testicular volumes were 6 months to 2 years earlier than in past studies, depending on the characteristic and race/ ethnicity. The causes and public health implications of this apparent shift in US boys to a lower age of onset for the development of secondary sexual characteristics in US boys needs further exploration. *Pediatrics* 2012;130:e1058–e1068

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#### **KEY WORDS**

REE

secondary sexual characteristics, growth and development, Tanner staging, testicular volume, PROS, secular changes, puberty

#### **ABBREVIATIONS**

AAP—American Academy of Pediatrics Cl—confidence interval HHANES—Hispanic Health and Examination Survey NHANES—National Health and Nutrition Examination Survey PROS—Pediatric Research in Office Settings SSCIB—Secondary Sexual Characteristics in Boys

Dr Herman-Giddens is the principal investigator and primary author; Dr Reiter is the co-principal investigator; Dr Reiter, Ms Steffes, Ms Harris, Dr Slora, and Dr Wasserman have made substantial contributions to the conception and design of this study, the acquisition of data, participated in drafting and critically revising this article for intellectual content, and given final approval of the version to be published; Mr Hussey, Dr Serwint, and Dr Smitherman have made substantial contributions to the analysis and interpretation of data, participated in drafting and critically revising this article for intellectual content, and given final approval of the version to be published; and Dr Dowshen has made substantial contributions to the conception and design of this study, interpretation of data, participated in drafting and critically revising this article for intellectual content, and given final approval of the version to be published.

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The secular trend toward a younger age of onset of puberty in girls in many countries is now generally accepted.<sup>1–3</sup> An expert panel convened in 2003 by Serono Symposia International, Inc, concluded that US girls were entering puberty at an earlier age than 40 years ago.<sup>1</sup> One of the key studies leading to this conclusion, conducted by the American Academy of Pediatrics (AAP), found girls were typically developing about a year earlier than previously assumed.<sup>4</sup> For boys, the panel concluded secular evidence was insufficient and further studies were needed. The most recent data on US boys comes from several analyses of the National Health and Nutrition Examination Survey (NHANES) III 1988-1994<sup>1,5-7</sup>; however, the data are 20 years old, the accuracy of the genital staging has been questioned, and testicular volumes were not obtained.<sup>5,8,9</sup> No recent studies representative of US boys or with large numbers in varied locales have been published. Data on male puberty are more difficult to obtain than female data because of the absence of an easily determined marker, such as menarche. Male pubertal stages are harder to assess visually than girls' stages, and orchidometry, an intrusive procedure, is not part of well-child exams.

Consequently, the AAP's Pediatric Research in Office Settings (PROS) practice-based research network undertook this cross-sectional study to determine the current ages of onset of sexual maturity stages 2 to 5 and early testicular volumes in US boys seen for well-child care and to assess whether there has been a shift in what is seen in office practice as compared with older studies. Puberty is complex, including many dynamic components. This study was designed to report only physical changes, and not hormonal or other changes.

#### METHODS

#### Characteristics of Practice Participants

Clinicians were recruited from PROS practices, the National Medical Association Pediatric Research Network, and the Academic Pediatric Association's Continuity Research Network. Participating clinicians comprised 196 (93%) pediatricians, 1 family medicine physician, and 15 (7%) nurse practitioners. Practices from 41 states and 1 Canadian province enrolled subjects between July 2005 and February 2010. Seventeen percent of practices were located in the Midwest, 24% in the Northeast, 31% in the South, and 28% in the West. Approval was obtained from the AAP's Institutional Review Board and 54 local institutional review boards affiliated with participating practices.

#### **Data Collection Process**

Before the main study, Secondary Sexual Characteristics in Boys (SSCIB), we established trained clinicians' interrater reliability for Tanner staging and orchidometry.<sup>10</sup> Tanner staging is a 5stage visual method for assessing development of secondary sexual characteristics (genital and pubic hair growth for males) from prepubertal (stage 1) to fully mature (stage 5).11 Using the study training manual,<sup>12</sup> participating clinicians learned Tanner staging and how to use a Prader orchidometer modified to contain only the 1-mL to 4-mL beads. Clinicians demonstrated competency by passing a question-and-photograph qualifying examination. Intraclass correlations in the clinical setting, where 2 practitioners in 8 practices rated a total of 79 boys, ranged from 0.61 for left testis size to 0.94 for pubic hair stage (all significant at P < .001), which indicate moderate to substantial agreement depending on the variable being measured.<sup>10</sup> For the main study, SSCIB, 212 qualifying clinicians screened boys 6 through 16 years of age presenting for well-child care for eligibility; each enrolled up to 30 consecutive boys (15 from 6-12 years of age and 15 from 13-16) from English- or Spanish-speaking families. Informed consent was obtained from parents/guardians and assent from boys 7 and older before examination. Data for each subject were collected on a form with numbered drawings and verbal anchors to maximize accuracy. The physical examination included height and weight, using each clinician's office equipment, Tanner staging, testicular volume measurement from 1 through 4 mL, and breast palpation for gynecomastia. Testicular volume was collected for each testis as a categorical variable:  $\leq$ 1, 2, 3, or  $\geq$ 4 mL. Examiners graded down the Tanner stage or testis volume if either appeared to fall between categories. Additional demographic data were ascertained by observation, questioning, and medical chart review.

#### **Data Analysis**

We defined continuous age (years) as the number of days between the month of birth, (assuming the subject was born on the first of the month), and the examination date divided by 365.25. When necessary, continuous age was categorized as age rounded to the nearest year. We classified subjects as African American if African American was indicated on the study form (regardless of any other race/ethnicity indication), Hispanic if Hispanic ethnicity was indicated (regardless of any other indication other than African American), and white if only white was indicated.

We calculated descriptive statistics, with exact binomial 95% confidence intervals (Cls) for prevalence of Tanner stage 2 or greater pubic hair and genital development within each age category. We used stratified Mantel-Haenszel row mean score statistics to assess homogeneity of prevalences by race/ ethnicity adjusted for age group.

Median ages and SDs for transition into Tanner stages 2 to 5 were estimated by using probit regression, which links a linear combination of covariates to the cumulative normal probability of having achieved a stage. In probit analysis, the median age is assumed to equal the mean. For testicular volume analysis, we used the larger of the testes if there was a right-left difference.<sup>8</sup> For each outcome, the probit model adjusted for continuous age, categorical race/ethnicity (reference group: whites), and their interaction. Model coefficients were used to jointly test ( $\alpha = 0.05$ ) for equality of the mean ages of transition across the 3 race/ethnicity groups. Pairwise comparisons of race/ethnicity groups were conducted with Bonferroni correction for multiple testing (ie, significance level  $\alpha = 0.05/3 = 0.017$ ). We calculated 95% Cls for the mean ages of transition using Fieller's Theorem.13 All analyses used SAS 9.2 (SAS Institute, Inc, Cary, NC).

#### RESULTS

We enrolled 5355 participants from 144 sites between 2005 and 2010. After exclusion for chronic conditions or medications that could affect puberty, missing data, or "other racial" category, 4131 boys remained for analysis (Fig 1). Of these, 2070 (50%) were classified as white, 1062 (26%) African American, and 999 (24%) Hispanic. Demographic and clinical characteristics of the study population are presented in Table 1.

Fig 2 shows the proportion of boys (95% Cls) entering Tanner stage 2 or greater genital development and pubic hair growth by race/ethnicity and age. Adjusted for age, the proportion for both genital and pubic hair development was found to be statistically different among the 3 race/ethnicity groups (P < .001). African American



#### FIGURE 1

Derivation of the SSCIB study population.

TABLE 1 Demographic and Clinical Characteristics of Study Subjects by Race/Ethnicity

Characteristic	White	African American	Hispanic
	n (%)	n (%)	n (%)
Payment status			
Medicaid	349 (17.5)	673 (65.9)	607 (63.0)
Insurance	1618 (80.9)	340 (33.3)	333 (34.6)
Self-pay	32 (1.6)	9 (0.8)	23 (2.4)
Total	1999	1022	963
Chronic disease			
None	1691 (81.8)	775 (73.3)	806 (80.7)
Asthma only	137 (6.6)	149 (14.1)	82 (8.2)
Other only	217 (10.5)	115 (10.9)	101 (10.1)
Asthma and other	22 (1.1)	18 (1.7)	10 (1.0)
Total	2067	1057	999
Chronic disease and medications			
None	1647 (79.8)	756 (71.7)	796 (79.9)
Disease, no chronic medications	43 (2.1)	16 (1.5)	9 (0.9)
Medication, no chronic diseases	196 (9.5)	151 (14.2)	119 (11.9)
Chronic diseases and chronic medications	179 (8.6)	134 (12.6)	73 (7.3)
Total	2065	1060	997
History of genital abnormalities			
None	1961 (95.9)	1011 (96.8)	957 (97.9)
Undescended testes	28 (1.4)	13 (1.3)	8 (0.8)
Hypospadias	12 (0.6)	3 (0.3)	2 (0.2)
Varicocele	16 (0.8)	3 (0.3)	4 (0.4)
Undescended testes+hypospadias	3 (0.2)	1 (0.1)	0 (0)
Other	26 (1.1)	12 (1.2)	7 (0.7)
Total	2046	1043	978

There were 147 missing values for payment status, 8 missing for chronic disease, and 64 missing for history of genital abnormalities.

boys had higher proportions at a given age for both genital and pubic hair development than white (both P <.001) and Hispanic boys (both P <.001), but white and Hispanic boys showed no difference (P = .54 and P =.16, respectively). Table 2 presents estimates of the mean age of transition to stages 2 to 5 for genital development and pubic hair growth. Entry into stage 2 genital development occurred at 10.14 years for white boys, 9.14 for African American boys, and 10.04 for Hispanic boys.





#### **FIGURE 2**

Percentages (95% confidence intervals) of white non-Hispanic, African American non-Hispanic, and Hispanic boys with secondary sexual characteristics at sexual maturity Stage 2 or greater.

Overall, these were statistically different (P < .0001). Pairwise differences were found between African American and white boys (P < .0001), African American and Hispanic boys (P < .001), but not between white and Hispanic boys (P = .48). For pubic hair, mean ages of entry into stage 2 were 11.47, 10.25, and 11.43 years respectively; overall, these were statistically different (P < .0001). Pairwise differences were found between African American and white boys (P < .001), and African American and Hispanic boys (P < .001), but not between white and Hispanic boys (P = .69). Because earlier pubertal studies assessing testicular volume have used volumes of 3 mL,  $\geq$ 3 mL,  $\geq$ 3 mL, and  $\geq$ 4 mL<sup>8,14-17</sup> as indicative of central pubertal take-off, we present mean ages of transition for both  $\geq$ 3 mL and  $\geq$ 4 mL (Table 2). Data on Cincinnati boys<sup>15</sup> and Swedish boys<sup>16</sup> show that the transition from 2 to 3 mL indicates pubertal take-off. White boys in this study reached a mean age of transition to 3 mL at 9.95 years, African American boys at 9.71, and Hispanic boys at 9.63, with no significant difference (P = .11). Mean ages for reaching volumes of  $\geq 4$ mL were 11.46, 11.75, and 11.29 years, respectively. Overall, these were found to be statistically different (P = .008), with pairwise significance only between African American and Hispanic boys (P = .002).

Data on progression to full sexual maturity present a slightly different pattern. For stages 3 and 4, statistical differences by race/ethnicity were observed, but not for stage 5. Pairwise differences between white and Hispanic boys were found for stages 3 and 4 pubic hair and stage 4 genital development. Estimated ages for entry into stage 5 (sexual maturity) for genital development were 15.57, 15.51, and 15.58 years, and 15.83, 15.72, and 15.89 for pubic hair for white, African American, and Hispanic boys, respectively. 
 TABLE 2
 Median (Mean) Ages of Transition for Secondary Sexual Characteristics and Testicular

 Volume Among White Non-Hispanic, African American Non-Hispanic, and Hispanic Boys

	Median, y	SD	95% CI	<i>P</i> value of Overall Race/Ethnicity Differences
Genital development.				
Stage 2				<.0001
White	10.14	2.18	(9.97-10.31)	
African American	9.14	2.10	(8.88–9.39)	
Hispanic	10.04	1.83	(9.81-10.26)	
Stage 3				<.0001
White	12.49	1.44	(12.36-12.61)	
African American	11.58	1.65	(11.38–11.77)	
Hispanic	12.31	1.18	(12.14-12.47)	
Stage 4				<.0001
White	13.72	1.23	(13.61–13.83)	
African American	13.04	1.72	(12.85-13.23)	
Hispanic	13.45	1.37	(13.28 - 13.61)	
Stage 5	10.10		(10.20 10.01)	.9368
White	15 57	1 53	(15 42-15 73)	
African American	15.51	2.33	(15.21 - 15.87)	
Hispanic	15.58	1.64	(15.34 - 15.86)	
Pubic hair	10.00		(10.01 10.00)	
Stage 2				< 0001
White	11.47	1 62	(11.33-11.61)	
African American	10.25	1 79	(10.03 - 10.46)	
Hispanic	11.43	1.53	(11 23-11 62)	
Stage 3	11.10	1.00	(11.20 11.02)	< 0001
White	12.89	1 18	(1277-1299)	
African American	11.79	1.56	(11.60 - 11.97)	
Hispanic	12.57	1 15	(1241 - 1273)	
Stade 4	12.01	1.10	(12.11 12.10)	< 0001
White	13.76	1 23	(13 65-13 87)	<.0001
African American	13.06	1.20	(12.87 - 13.24)	
Hispanic	13.38	1.07	(13.22 - 13.54)	
Stade 5	10.00	1.22	(10.22 10.01)	6772
White	15.83	1 49	(15.68 - 16.01)	.0172
African American	15.72	1.40	(15.44 - 16.05)	
Hispanic	15.89	1.57	(15.64 - 16.00)	
Testicular volume	10.00	1.00	(10.04 10.22)	
>3 ml				1109
White	9 95	211	(9.76_10.13)	.1105
African Amorican	0.71	2.44	(0.43_0.06)	
Hispanio	9.71	2.40	(9.40-9.90)	
	0.00	2.00	(3.00-3.03)	0070
White	11.46	1 07	(11 30-11 69)	.0073
African Amorican	11.40	1.97 1.97	(11.00-11.02)	
Airican American	11.70	1.00	(11.04-11.00)	
пізрапіс	11.29	1.89	(11.07-11.00)	

Table 3 shows the ages of onset of secondary sexual characteristics from the Marshall and Tanner study, earlier US studies, and our own. In particular, SSCIB white and Hispanic boys entered stage 2 genitalia 1.5 years earlier than the boys studied by Marshall and Tanner. African American boys are more than 2 years earlier.

Because data are conflicting on the effect of obesity on boys' puberty,<sup>9,18–20</sup> we examined relationships between

BMI and ages of onset of sexual maturity stages. Pooling race/ethnicity (because of small sample size) and controlling for age, boys with BMI <15th percentile had later mean ages of transition to stages 2 to 4 for genital and pubic hair growth than boys with BMI >85th percentile (data not shown). No other comparisons for stages or BMI categories were significantly different. It must be noted that because pubertal development itself is associated with an increase in BMI, and that existing BMI standards for youth are based on chronologic age, our cross-sectional data limit the assessment of causeand-effect relationships between BMI and pubertal timing.

#### **DISCUSSION**

We observed that onset of secondary sexual characteristics in US boys as seen in office practice appears to occur earlier than in previous US studies and the 1969 British study commonly used for pubertal norms.<sup>1,11</sup> In addition, we found significant differences in the age of onset of stage 2 genital and pubic hair growth between African American boys as compared with white and Hispanic boys and transition to testicular volumes  $\geq$ 4 mL (but not 3 mL). The meaning of this finding is unclear, as no existing studies inform differences in mean testicular size at given ages, by race/ethnicity, and sexual maturity stage; or in racial/ethnic differences in the rate of advancement through the Tanner stages over time.

Of consequence are the differences we found comparing our results with the 40-year-old data from Marshall and Tanner's landmark study on 228 white institutionalized boys in London.11 White boys in our study entered stage 2 genital growth 1.5 years earlier than the British boys (10.14 vs 11.60 years of age). Comparing ages of onset of stage 2 pubic hair growth from the British study (estimated at 13.4 years of age) is not possible because, as the authors stated, the age "was not accurately determined," because assessments were from photographs.<sup>11</sup> Their observation for entry into stage 3 pubic hair, 13.9 years, is likely more reliable, as stage 3 hair would be visible in photographs. White SSCIB study subjects entered stage 3 pubic hair development at a mean of 12.89 years, a full year earlier. For stage 2 pubic hair, US studies from 1948 to 1995

Chudu/	Data	Tvna	Country	Subjects	Λάρ					neall	100 V				
Authors	Collected, Year Span	of of Study	6		Range, y	$TV \ge 3 \text{ mL}$	TV ≥4 mL	G2	G <sub>3</sub>	G4	G5	$PH_2$	$PH_3$	$PH_4$	$PH_5$
Marshall and Tanner <sup>11</sup>	1950s- 1970s	Mixed	England	228 White	8 /l			11.6 White	12.9 White	13.8 White	14.9 White		13.9	14.4 White	15.2 White
Fels Institute <sup>21</sup>	1930s 1940s	_	United States	59 White	9–21	ł		11.5 White	12.7 White	13.4 White	17.3 White	12.2 White	13.3	13.9 White	16.1 White
NHES II/III <sup>22</sup>	1963 1970	C-S	United States	3047 White	12–17	ł	I	"similar to M Ai	1arshall & Tanr frican America	ner, white and n"		"similar to N A	larshall & Tann frican Americal	ier, white and n"	
Lee Study <sup>38</sup>	1969— 1974	_	United States	36 Not clearly snecified	9-17		I	11.9 White	13.2 White	14.3 White	15.1 White	12.3 White	13.9	14.7 White	15.3 White
Bogalusa Heart Study <sup>23</sup>	1973– 1974	C-S	United States	1153 White; 676 African American	5-14	I	I	11.8 White; 11.2 African American	I	I	I	12.5 White; 11.7 African American			
HHANES <sup>24</sup>	1982– 1984	C-S	United States	704 Mexican American	10-17			12.4 Mexican American	13.5 Mexican American	14.6 Mexican American	16.3 Mexican American	12.8 Mexican American	13.6 Mexican American	14.6 Mexican American	16.1 Mexican American
NHANES III <sup>5</sup>	1988– 1994		United States	536 White; 797 African American; 781 Mexican American	8-19	I	I	10.1 White; 9.5 African American; 10.4 Mexican American	12.4 White: 11.8 African 12.5 Mexican American	13.5 White; 13.4 African American; 13.7 Mexican American	15.9 White; 14.9 African American; 15.7 Mexican	12.0 White; 11.2 African American; 12.3 Mexican American	12.6 White; 12.5 African 13.1 Mexican American	13.5 White; 13.7 African American; 14.1 Mexican American	15.7 White; 15.4 African American; 15.8 Mexican American
Biro Study <sup>15</sup>	1984– 1987	_	United States	278 White; 237 African American	10-18	12.18 White; 12.18 Affrican	I	I	I	I	I	12.8 White/ African American	13.7 White/ African American	14.6 White/ African American	15.2 White/ African American
Susman Study <sup>25</sup>	2000- 2006	_	United States	364 White; 63 African American	9.5– 15.5		I	10.4 White; 9.6 African American	12.4 White; 11.6 African American	13.6 White; 12.8 African American	14.9 White; 14.3 African American	11.5 White; 10.5 African	12.8 White; 11.9 African American	13.7 White; 13.0 African American	15.1 White; 14.5 African American
SSCIB	2005– 2010	C-S	United States	2070 White; 1062 African American; 999 Hispanic	6-16	9.95 White; 9.71 African American; 9.63 Hispanic	11.46 White; 11.75 African American; 11.29 Histanic	10.14 White; 9.14 African American; 10.04 Hispanic	12.49 White; 11.58 African American; 12.31 Hispanic	13.72 White; 13.04 African American; 13.45 Hispanic	15.57 White; 15.51 African American; 15.58 Hispanic	11.47 White; 10.25 African American; 11.43 Hispanic	12.89 White; 11.79 African 12.57 Hispanic	13.76 White; 13.06 African American; 13.38 Hispanic	15.83 White; 15.72 African American; 15.89 Hispanic
C-S, cross-sect	ional; G, genit	al; L, Iong	gitudinal; NHE	ES, National Health	h Examinati	ion Survey; PH, pr	ubic hair; TV, test	ticular volume.							

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found a mean age of onset from 12.0 to 12.8 years of  $age^{5-7,15,21-23}$  for white boys. Results from SSCIB boys demonstrate this is occurring 6 months to a year earlier than previously reported.

Although comparison of our results with those of earlier studies is limited because of lack of early data on minorities and differences in methodologies, socioeconomic status, age at enrollment, and small numbers of subjects in most studies.<sup>1,4,18</sup> the 6-month to 2-year earlier development of secondary sexual characteristics or testicular enlargement as documented in our study is notable. Few older studies on African American or Hispanic boys exist. Results from the 40-year-old nationally representative US Health Examination Survey, Cycle III, on African American boys were stated to be "comparable to the mean ages in Marshall and Tanner's data on white boys."22 Foster et al,23 in a study 35 years ago, found African American boys in Louisiana began genital and pubic hair development at 11.2 and 11.7 years as compared with our ages of 9.14 and 10.25.

The only previous US studies on Hispanic boys involved Mexican American boys: the Hispanic Health and Examination Survey (HHANES), 1982 to 1984, and NHANES III, 1988 to 1992.5-7,24 Because we enrolled Hispanic boys without regard to country of origin, direct comparison may not be valid. HHANES and NHANES III found attainment of genital stage 2 declined from 12.4 to 10.4 years of age over a 10-year period, although the accuracy of the latter's genital data has been questioned as discussed in the following paragraph.5-7,24 SSCIB Hispanic boys entered stage 2 genital development at 10.04 years.

Findings for genital data between the PROS study and NHANES III are similar; however, it should be noted that several authors have questioned the accuracy of the NHANES III results, <sup>5,8,9,18</sup> which

found very early onset of genital stage 2 for all groups and noted that the 2year span between genital stage 2 and pubic hair stage 2 was longer than that found in any other puberty study. Thus, genital Tanner stage misclassification may have occurred and the genital data may be unreliable. Stage 2 pubic hair onset for Mexican American boys between HHANES and NHANES III declined from 12.8 to 12.3 years. SSCIB Hispanic boys reached stage 2 pubic hair at a mean of 11.43 years of age. Non-Hispanic white and African American boys in SSCIB reached stage 2 pubic hair 0.53 and 0.95 years earlier than the NHANES III boys. Comparisons of pubic hair stages should be more reliable, as assessment of pubic hair is not as subjective as that of genital development. Our findings are also similar to a recent longitudinal puberty study that included 364 white and 63 African American boys (Table 3).25

Very few European or US studies have included testicular volumes. Largo and Prader's landmark 1983<sup>14</sup> longitudinal study on white Swiss boys proposed testicular volume of 3 mL as the most accurate sign of central pubertal takeoff based on their earlier work, later confirmed by the Cincinnati<sup>15</sup> and Swedish studies.<sup>16</sup> Boys in the Swiss study were a mean age of 11.2 at genital stage 2 and 11.8 at a testicular volume of 3 mL. The study by Biro et al<sup>15</sup> is the only US puberty study that reported testicular volumes. Their subjects, studied from 1984 to 1987 (Frank M. Biro, MD, personal communication, 2010), had a mean age of 12.18 years when reaching a volume of 3 mL, with no differences between the white and African American boys. SSCIB white and African American boys were 2.23 and 2.47 years younger, respectively. Recent data from Denmark also report a decline in age for achieving a testicular volume >3 mL.<sup>8</sup> Because our study is the first US study

to measure testicular volumes on widely distributed boys, it can serve as a baseline for future studies.

We also note the pattern presented by our data on progression to stage 5 genital development and pubic hair growth indicating sexual maturity. Our subjects reached stage 5 at ages 15.7 to 15.8 for all racial/ethnic groups, similar to the NHANES III data<sup>5</sup>; however, our stage 5 probit model estimates (including comparisons of race/ethnicity) should be interpreted with caution because they are artificially bounded by SSCIB's maximum enrollment age of 16 years. It is interesting that the 2010 US longitudinal study found boys' age for genital maturity to be 14.9 and 14.3 for white and African American boys, respectively.25

The strengths of the PROS study include its large sample size and broad geographical and minority patient representation. In addition, observations were made only on well boys in primary care sites by trained pediatricians and other clinicians. Testicular volumes were measured through 4 mL.

The study has several limitations. Our convenience sample of US boys seen in pediatric offices for well-child care is not a statistically representative sample of the US population. The study results could be guestioned if the boys in our study were biologically different from boys in the US population; however, there is no plausible reason that would support this contention. Because these data are cross-sectional, statistical methods allow for only the estimation of mean ages of transition into the sexual maturity stages. Longitudinal data are required to assess duration, peak height velocity, and relationships between duration and timing of pubertal stages. Populationbased longitudinal studies in the United States have not been conducted because of methodological challenges and expense. Our age calculations may

lack precision because, to protect privacy, we could not collect the day of birth. This, however, is unlikely to have introduced meaningful differences. Our training in sexual maturity staging and orchidometer use was designed with the input of several pediatric endocrinologists and accomplished through an instruction manual with photographs and explanatory and instructive text. As previously described, testing ensured staging proficiency among qualifying clinicians. We are aware of no large US study that has so carefully documented its training methods with a manual and testing, and shown interrater reliability among a sample of those trained. Although it would have been ideal to have assessments completed by pediatric endocrinologists with extensive experience in sexual maturity staging, this was not feasible in a study of thousands of nonreferred children across 41 states. Testicular volumes were assessed as  $\leq$ 1, 2, 3, or  $\geq$ 4 mL; therefore, data from studies that used >3 mL but <4mL rather than  $\geq 3$  mL or  $\geq 4$  mL as their criteria for central pubertal takeoff are not strictly comparable. Ultrasound, regarded as a more precise method for measuring testes,<sup>26,27</sup> is not practical for large-scale studies and is not part of the usual pediatric examination.<sup>28</sup> Volume comparisons with the Prader orchidometer have been shown to be reasonably accurate.27

In conclusion, our data suggest that US boys are beginning genital and pubic hair growth earlier than several decades ago in concordance with recent reports on girls.<sup>1</sup> These data are consistent with recent trends from other countries, such as Denmark, Sweden, Great Britain, Italy, and China.<sup>2,8,29–33</sup> For example, urban Han Chinese boys achieve a testicular volume of  $\geq$ 4 mL (13% by age 9) and spermarche earlier than studies conducted several decades ago; Danish boys achieve a testic

ular volume >3 mL more than 3 months earlier now than 15 years ago. Our findings are somewhat surprising. given that factors associated with earlier physical development in girls, such as overweight and certain endocrine disrupters,34 are not known to be associated with earlier development in boys and could even be theorized to have a delaying effect.<sup>2,35</sup> Our data do not allow for an analysis of the possible underlying mechanisms of these observed decreases in the apparent age of onset of secondary sexual characteristics as assessed by physical examination. They do, however, demonstrate the importance in the physical examination of boys of observing the ontogeny of changes in testicular volumes along with the stage of pubic hair growth. For example, in a 7-year-old, the presence of pubic hair with concomitant testicular volume increase needs close scrutiny and endocrinologic evaluation to be sure that true sexual precocity is not occurring. In the absence of increased testicular volume or systemic changes of androgenization, the more likely process in this example would be that of "benign" premature adrenarche.

Current environmental factors, including exposure to chemicals, changes in diet, less physical activity, and other modern lifestyle changes and exposures may be related to this apparent rapid decrease in the age of onset of secondary sexual characteristics and may not reflect healthy conditions.<sup>36,37</sup> Psychological, emotional, and behavioral affects of earlier sexual maturity may be pivotal, given the current phenomena of social and emotional delay in achieving adulthood.<sup>4,33</sup> Longitudinal tracking is needed to clarify any impact of overweight/obesity on boys' sexual development. The secular decrease we observed in ages of onset of secondary sexual characteristics in US boys requires further study.

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#### Secondary Sexual Characteristics in Boys: Data From the Pediatric Research in Office Settings Network

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