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Original Contribution

Associations Between Childhood Obesity and Pubertal Timing Stratified by Sex and Race/Ethnicity

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Earlier puberty has been associated with numerous adverse mental, emotional, and physical health outcomes. Obesity is a known risk factor for earlier puberty in girls, but research with boys has yielded inconsistent findings. We examined sex- and race/ethnicity-specific associations between childhood obesity and puberty in a multiethnic cohort of 129,824 adolescents born at a Kaiser Permanente Northern California medical facility between 2003 and 2011. We used Weibull regression models to explore associations between childhood obesity and breast development onset (thelarche) in girls, testicular enlargement onset (gonadarche) in boys, and pubic hair development onset (pubarche) in both sexes, adjusting for important confounders. Clear dose-response relationships were observed. Boys with severe obesity had the greatest risk for earlier gonadarche (hazard ratio = 1.23, 95% confidence limit: 1.15, 1.32) and pubarche (hazard ratio = 1.44, 95% confidence limit: 1.34, 1.55), while underweight boys had delayed puberty compared with peers with normal body mass index. A similar dose-response relationship was observed in girls. There were significant interactions between childhood body mass index and race/ethnicity. Childhood obesity is associated with earlier puberty in both boys and girls, and the magnitude of the associations may vary by race/ethnicity. Prevention of childhood obesity may delay pubertal timing and mitigate health risks associated with both conditions.

adolescent health; health disparities; longitudinal study; obesity; puberty; race/ethnicity

Abbreviations: API, Asian/Pacific Islander; BMI, body mass index; CL, confidence limit; HR, hazard ratio; KPNC, Kaiser Permanente Northern California; OR, odds ratio; OWOB, overweight and obese; SMR, sexual maturity rating; TR, time ratio.

Earlier puberty is associated with numerous adverse outcomes throughout the life course. Girls who develop earlier are at higher risk for anxiety, depression, body dissatisfaction, and early sexual initiation during adolescence (1–5), as well as cardiac problems, all-cause mortality, and breast and reproductive cancers later in life (2, 6–9). Growing evidence also suggests that early-maturing boys experience negative consequences such as behavioral misconduct, substance use (1, 5), and psychological problems during adolescence (10, 11), as well as higher risks of testicular and prostate cancer later in life (2, 12).

Childhood obesity is a known risk factor of earlier pubertal development in girls. However, few studies have explored the associations between childhood obesity and pubertal timing among boys, with inconsistent results. Most studies of boys have been conducted outside the United States, where the rate of childhood obesity is substantially lower (13–20). Additionally, US studies have been limited by predominantly White cohorts and/or have failed to include large racial/ethnic minority populations such as Asians and Pacific Islanders (21–23) despite evidence of racial/ethnic differences in pubertal timing (24, 25). Further, most studies include varying or later measures of obesity and therefore cannot establish temporality between exposure and outcome (14–17, 19–23). This is especially important given that adolescents experience natural increases in weight at puberty (fat mass in girls and fat-free mass in boys) (26). We conducted a longitudinal study using a large and diverse cohort of boys and girls from Northern California to examine sex- and race/ethnicity-specific associations between childhood

(ages 5–6 years) body mass index (BMI) and timing of pubertal onset, using clinician-assessed sexual maturity ratings (SMRs).

METHODS

Participants

This study included 68,571 boys and 61,253 girls born at a Kaiser Permanente Northern California (KPNC) medical facility between 2003 and 2011. KPNC is a large integrated health-care system that serves a diverse population of approximately 4.5 million members in Northern California. Study eligibility included being born full-term (≥37 weeks' gestation) and singleton, and having at least 1 documented SMR and childhood BMI calculation (using documented childhood height and weight measurements). The follow-up period for assessing pubertal development extended through September 30, 2021.

Children with medical conditions that might influence pubertal development (e.g., congenital adrenal hyperplasia) were excluded (n = 3,598). Of the 133,208 eligible children, 3,384 (2.5%) were missing information on ≥1 clinically important covariate (parity, 248; maternal education, 3,344; maternal age, 1). Observed characteristics of those with complete versus incomplete data were comparable (Web Table 1, available at https://doi.org/10.1093/aje/kwac148). Due to the low rate of missingness we concluded that a complete-case analysis would not bias our results and excluded individuals with incomplete data. The final analytical cohort included 129,824 boys and girls. All data were obtained from KPNC clinical and administrative databases. The KPNC Institutional Review Board approved the study.

Measurements

Exposure. Child weight and height measurements were obtained from clinic visits at the ages of 5–6 years. BMI percentiles were calculated using age- and sex-specific Centers for Disease Control and Prevention (year 2000) standard population distributions (27). BMI was classified into categories: underweight (<5th percentile), normal weight (above the 5th and below the 85th percentile), overweight (at least 85th and below the 95th percentile), and obese (95th percentile and above). Children with BMIs of ≥120% of the 95th percentile were categorized as severely obese (28).

Puberty outcomes. Documentation of SMRs in the electronic health record became a routine part of KPNC pediatric appointments for children aged ≥6 years beginning in 2010. SMR is a 5-point ranking system used to measure pubertal development from prepuberty (SMR 1) to full maturation (SMR 5) (29, 30).

At KPNC, boys are evaluated for testicular size. Clinicians palpate and measure the length of the testicle using a measuring tape or estimate testicular volume using an orchidometer. Girls are rated for breast development using palpation and visual inspection. Pubic hair is measured in both sexes using visual inspection. Additionally, girls and their caregivers are routinely asked if they have begun their menses starting at approximately age 10 years. Girls who reported starting menses before age 12 were categorized as having earlier menarche.

The accuracy of the KPNC SMR was validated in a previous study (31), in which research staff were trained by a Kaiser pediatric endocrinologist (L.C.G.) to rate over 400 girls. L.C.G. assessed ratings conducted by research staff to ensure the accuracy of assessments. We compared the results of these assessments with SMRs conducted by KPNC clinicians within 6 months of research appointments (n = 217) and found weighted κ of >0.60 for breast and pubic hair SMRs (unpublished data). We also checked for interobserver reliability among clinicians by measuring SMR agreement for individuals who were assessed by 2 different clinicians within 6 months of each other. Weighted κ were >0.70 for breast and pubic hair in girls and testicular size and pubic hair in boys. κ values were similar among overweight and obese (OWOB) girls and boys.

In this study, our primary outcomes of interest were age at transition from SMR 1 (prepubertal) to SMR 2+ (pubertal) for onset of testicular enlargement onset (gonadarche) in boys, breast development (thelarche) in girls, and pubic hair development (pubarche) in both sexes. We also explored timing of menarche as a secondary outcome in girls.

Covariates. All models adjusted for potential confounding by including covariates associated with both childhood BMI and pubertal onset: child's race/ethnicity (White, Black, Hispanic, Asian/Pacific Islander (API), or other/unknown) (25), birth weight (grams) (32, 33) and maternal education as a proxy for socioeconomic status (high school or less, some college (<2 years), 4-year college, or graduate school) (34, 35), parity (0, 1, or ≥2) (36, 37), and age at delivery (years) (38, 39).

Statistical analyses

The association between childhood BMI and pubertal onset was determined using Weibull regression models, which are both accelerated failure time and proportional hazards regression models, with accommodation for left, right, and interval censoring. Weibull regression, an alternative to the semiparametric Cox proportional hazards regression, is a flexible, parametric, widely used survival analysis technique. We chose the Weibull approach given the computational complexity in fitting Cox regression with interval-censored data and, more importantly, it has been noted that parametric regression models are robust and generally more informative than corresponding nonparametric models in the presence of heavy interval censoring (40, 41).

Children were considered left-censored if they had already transitioned to SMR 2+ at the time of the first SMR exam. They were right-censored at the time of their last exam if they had not transitioned to SMR 2+ or had only 1 assessment at SMR 1. Children who had an exam with an assessment of SMR 1 and a later assessment of SMR 2+ were considered interval-censored, as the exact age at transition between SMR 1 and 2+ is unknown. Two effect size measurements were calculated: the time ratio (TR) and the hazard ratio (HR). TR estimates represent the ratio of the median time to event for a given level of the exposure

variable in relation to its reference level (e.g., obese vs. normal weight). Associations between childhood BMI and earlier menarche (<12 years) were examined using binary logistic regression models.

We examined race/ethnicity as a potential effect modifier by using a cross-product term of race/ethnicity and BMI category. Baseline characteristics were compared between exposure groups using χ^2 tests for categorical variables and analysis of variance for continuous variables. All analyses were conducted using SAS, version 9.4 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Participant characteristics

The study cohort included 68,571 boys and 61,253 girls. Among boys aged 5–6 years, 3.9% were underweight, 14.3% overweight, 10.6% obese, and 3.2% severely obese. Among girls, approximately 3.6% were underweight, 14.9% overweight, 9.3% obese, and 2.6% severely obese (Tables 1 and 2). In gonadarche models, about 15.4% of boys were left-censored and 47.1% were right-censored. In pubarche models, 12.5% and 52.1% of boys were left- and right-censored, respectively. In thelarche models, approximately 23.9% of girls were left-censored, and 36.6% were right-censored. In pubarche models, 19.0% and 44.8% of the girls were left- and right-censored, respectively.

Associations between childhood BMI and puberty in boys

Gonadarche. OWOB boys had greater risk of experiencing earlier gonadarche compared with normal-weight counterparts, with a clear dose-response association ($P < 0.001$, Web Table 2). After accounting for maternal age, education, parity, birth weight, and race/ethnicity, and compared with normal-weight boys, risk of earlier gonadarche was increased by approximately 23% (HR = 1.23, 95% (confidence limit (CL): 1.15, 1.32) among severely obese boys, 22% (HR = 1.22, 95% CL: 1.17, 1.27) among obese boys, and 15% (HR = 1.15, 95% CL: 1.11, 1.19) among overweight boys. In contrast, underweight boys had reduced risk of earlier gonadarche (HR = 0.83, 95% CL: 0.77, 0.88). In severely obese boys, the time ratios for this association corresponds to an approximately 3-months earlier gonadarche compared with boys with normal BMI (Table 3).

Pubarche. A dose-response relationship was also observed between childhood BMI and timing of pubarche among boys. Severely obese boys had the strongest association, with a 44% higher risk of earlier pubarche (HR = 1.44, 95% CL: 1.34, 1.55) compared with peers of normal weight (Table 3).

Associations between childhood BMI and puberty in girls

Thelarche. A clear dose-response relationship between childhood BMI and pubertal onset was also observed in girls (Web Table 3). After adjusting for covariates, severely obese girls had the highest risk of experiencing earlier thelarche (HR = 1.63, 95% CL: 1.50, 1.77), followed by girls with obesity (HR = 1.48, 95% CL: 1.41, 1.54) and overweight (HR = 1.35, 95% CL: 1.30, 1.39). Underweight girls were more likely to experience a delayed thelarche compared with girls of normal weight (HR = 0.79, 95% CL: 0.74, 0.84) (Table 4).

Pubarche. Severely obese girls also had the highest risk of experiencing earlier pubarche (HR = 1.88, 95% CL: 1.73, 2.04) compared with normal-weight girls. Associations were weaker but remained significant among girls of other BMI categories (Table 4).

Menarche. Severely obese girls were 2.6 times more likely (odds ratio (OR) = 2.59, 95% CL: 2.25, 2.99) and obese girls were 2.2 times more likely (OR = 2.25, 95% CL: 2.08, 2.43) to experience earlier menarche (<12 years) compared with counterparts with normal weight. Overweight girls were also at higher risk of earlier menarche (OR = 1.70, 95% CL: 1.59, 1.82), while underweight girls were less likely to experience it (OR = 0.59, 95% CL: 0.50, 0.69) (Table 4).

Effect modification by race/ethnicity

There were significant interactions by race/ethnicity in the association between childhood BMI and pubarche ($P = 0.03$), but not gonadarche ($P = 0.16$), among boys. The strongest associations were observed among severely obese White boys (HR = 1.68, 95% CL: 1.43, 1.97) and obese Black boys (HR = 1.64, 95% CL: 1.41, 1.92). These associations correspond with approximately 7- and 6-months earlier pubarche than their normal-weight counterparts, respectively (Table 5).

Interactions by race/ethnicity were highly significant in girls ($P < 0.001$). The strongest associations between childhood BMI and earlier thelarche were observed among Black and API girls: Those who were severely obese were more than twice as likely to have earlier thelarche (HR = 2.12, 95% CL: 1.65, 2.72; HR = 2.02, 95% CL: 1.59, 2.56, respectively) compared with those with normal BMI. These associations corresponded to approximately 9-months earlier thelarche. A similar association was observed for severely obese White girls (HR = 1.87, 95% CL: 1.57, 2.23). The associations were significant but weaker among Hispanic girls (Table 6).

Similar to thelarche models, severely obese White (HR = 1.90, 95% CL: 1.60, 2.27), Black (HR = 2.77, 95% CL: 2.11, 3.64), and API (HR = 2.37, 95% CL: 1.89, 2.98) girls were at greatest risk of earlier pubarche, corresponding to approximately 8-, 12-, and 11-months earlier pubarche, respectively (Table 6).

Severely obese White (OR = 3.30, 95% CL: 2.43, 4.49) and API (OR = 3.44, 95% CL: 2.36, 5.01) girls were over 3 times more likely to experience earlier menarche (earlier than age 12 years). Black girls had the weakest association between childhood BMI and age at menarche of all girls (Table 6).

Table 1. Distribution of Boys' Characteristics According to Childhood Body Mass Index Category (n = 68,571), KPNC Puberty Study, Kaiser Permanente Northern California, 2008–2021

Characteristic	Total (n = 68,571)		Childhood BMI Category[a,b]										P Value
			Severe Obesity (n = 2,199)		Obesity (n = 7,245)		Overweight (n = 9,815)		Normal Weight (n = 46,627)		Underweight (n = 2,685)		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Maternal age at delivery, years[c]	30.2 (5.6)		29.5 (5.9)		29.6 (5.8)		29.8 (5.8)		30.3 (5.5)		30.6 (5.3)		<0.001
Parity													<0.001
0	29,753	43.4	847	38.5	2,978	41.1	4,225	43.0	20,436	43.8	1,267	47.2	
1	23,983	35.0	716	32.6	2,460	34.0	3,316	33.8	16,541	35.5	950	35.4	
≥2	14,835	21.6	636	28.9	1,807	24.9	2,274	23.2	9,650	20.7	468	17.4	
Education													<0.001
High school or less	19,574	28.5	1,040	47.3	2,707	37.4	3,220	32.8	12,021	25.8	586	21.8	
Some college	20,405	29.8	713	32.4	2,444	33.7	3,002	30.6	13,515	29.0	731	27.2	
College graduate	17,587	25.6	319	14.5	1,364	18.8	2,261	23.0	12,832	27.5	811	30.2	
Postgraduate	11,005	16.0	127	5.8	730	10.1	1,332	13.6	8,259	17.7	557	20.7	
Race/ethnicity													<0.001
White	24,676	36.0	455	20.7	1,995	27.5	3,372	34.4	17,985	38.6	869	32.4	
Black	4,832	7.0	192	8.7	596	8.2	816	8.3	3,083	6.6	145	5.4	
Hispanic	17,226	25.1	966	43.9	2,619	36.1	2,882	29.4	10,319	22.1	440	16.4	
Asian/Pacific Islander	15,456	22.5	393	17.9	1,397	19.3	1,817	18.5	10,904	23.4	945	35.2	
Other/unknown	6,381	9.3	193	8.8	638	8.8	928	9.5	4,336	9.3	286	10.7	
Birth weight, g[c]	3,520.0 (475.2)		3,669.1 (523.4)		3,641.0 (497.9)		3,622.0 (482.0)		3,487.6 (458.6)		3,261.3 (437.0)		<0.001

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention.

[a] Ages 5–6 years.

[b] Weight (kg)/height $(m)^2$. BMI was classified into categories using age- and sex-specific BMI percentiles. BMI percentiles were calculated using CDC standard population distributions.

[c] Values are expressed as mean (standard deviation).

Table 2. Distribution of Girls' Characteristics According to Childhood Body Mass Index Category (n = 61,253), KPNC Puberty Study, Kaiser Permanente Northern California, 2008–2021

Characteristic	Total (n = 61,253)		Childhood BMI Category[a,b]										*P* Value
			Severe Obesity (n = 1,573)		Obesity (n = 5,683)		Overweight (n = 9,109)		Normal Weight (n = 42,677)		Underweight (n = 2,211)		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Maternal age at delivery, years[c]	30.2 (5.6)		29.3 (6.1)		29.5 (5.9)		29.9 (5.7)		30.4 (5.6)		30.6 (5.3)		<0.001
Parity													<0.001
0	27,257	44.5	600	38.1	2,350	41.4	4,037	44.3	19,238	45.1	1,032	46.7	
1	21,265	34.7	503	32.0	1,931	34.0	3,100	34.0	14,933	35.0	798	36.1	
≥2	12,731	20.8	470	29.9	1,402	24.7	1,972	21.6	8,506	19.9	381	17.2	
Education													<0.001
High school or less	17,417	28.4	747	47.5	2,189	38.5	2,972	32.6	11,025	25.8	484	21.9	
Some college	17,899	29.2	564	35.9	1,919	33.8	2,762	30.3	12,046	28.2	608	27.5	
College graduate	15,812	25.8	180	11.4	1,054	18.5	2,100	23.1	11,815	27.7	663	30.0	
Postgraduate	10,125	16.5	82	5.2	521	9.2	1,275	14.0	7,791	18.3	456	20.6	
Race/ethnicity													<0.001
White	21,777	35.6	356	22.6	1,600	28.2	3,208	35.2	15,968	37.4	645	29.2	
Black	4,234	6.9	183	11.6	557	9.8	773	8.5	2,592	6.1	129	5.8	
Hispanic	15,307	25.0	675	42.9	2,082	36.6	2,695	29.6	9,497	22.3	358	16.2	
Asian/Pacific Islander	13,919	22.7	204	13.0	900	15.8	1,600	17.6	10,379	24.3	836	37.8	
Other/unknown	6,016	9.8	155	9.9	544	9.6	833	9.1	4,241	9.9	243	11.0	
Birth weight, g[c]	3,399.6 (452.9)		3,583.2 (506.1)		3,521.5 (464.7)		3,503.1 (455.1)		3,367.9 (439.0)		3,140.8 (425.0)		<0.001

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention.
[a] Ages 5–6 years.
[b] Weight (kg)/height (m)^2. BMI was classified into categories using age- and sex-specific BMI percentiles. BMI percentiles were calculated using CDC standard population distributions.
[c] Values are expressed as mean (standard deviation).

Table 3. Association Between Childhood Body Mass Index Category and Timing of Puberty in Boys, KPNC Puberty Study, Kaiser Permanente Northern California, 2008–2021

Childhood BMI[a,b]	Gonadarche[c]					Pubarche[c]				
	No.	TR	95% CL	HR	95% CL	No.	TR	95% CL	HR	95% CI
Severe obesity	2,171	0.98	0.97, 0.98	1.23	1.15, 1.32	2,194	0.96	0.96, 0.97	1.44	1.34, 1.55
Obesity	7,177	0.98	0.97, 0.98	1.22	1.17, 1.27	7,232	0.97	0.97, 0.97	1.34	1.29, 1.40
Overweight	9,730	0.98	0.98, 0.99	1.15	1.11, 1.19	9,799	0.98	0.98, 0.98	1.24	1.19, 1.28
Normal weight	46,226	1.00	Referent	1.00	Referent	46,540	1.00	Referent	1.00	Referent
Underweight	2,654	1.02	1.01, 1.03	0.83	0.77, 0.88	2,680	1.02	1.01, 1.02	0.85	0.79, 0.90

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention; CL, confidence limit; HR, hazard ratio; TR, time ratio.
[a] Ages 5–6 years.
[b] Weight (kg)/height (m)^2. BMI was classified into categories using age- and sex-specific BMI percentiles. BMI percentiles were calculated using CDC standard population distributions.
[c] Adjusted for maternal age at delivery, education, parity, birth weight, and race/ethnicity.

DISCUSSION

To our knowledge, this is the largest longitudinal study to examine sex-specific associations between childhood obesity and pubertal timing. We found that childhood obesity was associated with a higher risk of earlier puberty among boys and girls, with clear dose-response associations and significant racial/ethnic variability. The findings from the present study corroborate findings from previous studies on obesity and girls' puberty, where most reported clear associations between obesity and earlier pubertal timing (42). Our study also demonstrated clear dose-response associations between obesity and boys' pubertal timing. Since these results have been inconsistent in previous studies, this discussion focuses on boys' findings and potential mechanisms.

Previous studies have investigated the role of childhood BMI on boys' pubertal timing with mixed results. For instance, a recent mixed cross-sectional and longitudinal study of 730 Danish boys aged 5–21 years found that BMI z scores (zBMI) were inversely associated with age at various pubertal milestones, including age at pubarche, genital development, testicular growth (≥4 mL), and higher testosterone levels (14). A related study found that obese boys (zBMI $>$ +2 standard deviations) experienced earlier testicular growth (≥4 mL) than controls (−2 standard deviations $<$ zBMI $\leq$ +2 standard deviations) but no significant differences in overall genital development or pubarche (15). In contrast, data from over 8,000 Chinese boys aged 6–12 years found significant associations between obesity and genital development (16).

There are few US-based studies examining associations between obesity and puberty in boys. A recent study found no associations between BMI at age 5 years and pubertal onset in a sample that included 136 low-income Mexican-American boys (43). A cross-sectional study of approximately 4,000 boys aged 6–16 years reported that OWOB White and Black boys transitioned to stage 2 for genital development earlier than normal-weight boys, while OWOB Hispanic boys transitioned later. When comparing median age at stages 3–5, OWOB boys were observed to transition at the same time or later than their normal-weight counterparts, with the exception of overweight Black boys for stages 3–4 and overweight White and Hispanic boys for stage 5, who were observed to transition earlier. In addition, OWOB boys had reached testicular volumes of ≥3 mL and ≥4 mL earlier than their normal-weight counterparts. It should be noted that most of these differences were not statistically significant ($P > 0.05$). This study was also limited by its cross-sectional design, where obesity was measured at the same time as the pubertal assessment, such that temporality could not be established (23). In a prospective cohort study of approximately 400 boys, higher BMI trajectories in childhood were associated with later pubertal development (21). Similarly, a population-based cohort of 346 boys found that boys with greater adiposity reached all maturation stages at older ages (22, 44). However, both studies used obesity measures later in adolescence (mean zBMI at age 11.5 years and BMI in ages 10–15 years, respectively). In the present study, we used BMI measured at age 5–6 years as an estimate of BMI prior and proximal to pubertal onset. Overall, the use of different pubertal outcomes, including definitions of what constitutes pubertal onset (e.g., testicular volume ≥3 mL vs. ≥4 mL) and differences in study designs may contribute to the disparities in the directions of observed associations.

The association between childhood obesity and puberty may be partially attributed to differences in the hormonal profiles of OWOB vs. normal-weight boys prior to and throughout puberty. As boys approach puberty, the hypothalamus releases gonadotropin-releasing hormones, signaling the pituitary gland to release follicle-stimulating hormones (FSH) and luteinizing hormones (LH). FSH and LH are responsible for the growth of sperm-producing cells and the synthesis of gonadal testosterone, both of which directly cause the testicles to enlarge. A recent study of 1,148 Chinese boys aged 6–14 years found that prepubertal OWOB boys had significantly higher levels of adrenal testosterone compared with normal-weight boys (45). It

Table 4. Association Between Childhood Body Mass Index Category and Timing of Puberty in Girls, KPNC Puberty Study, Kaiser Permanente Northern California, 2008–2021

Childhood BMI[a,b]	Thelarche[c]					Pubarche[c]				Menarche[c,d]		
	No.	TR	95% CL	HR	95% CL	No.	TR	95% CL	HR	95% CL	No.	OR	95% CL
Severe obesity	1,553	0.94	0.94, 0.95	1.63	1.50, 1.77	1,535	0.93	0.92, 0.94	1.88	1.73, 2.04	855	2.59	2.25, 2.99
Obesity	5,606	0.96	0.95, 0.96	1.48	1.41, 1.54	5,551	0.95	0.95, 0.96	1.55	1.48, 1.62	3,241	2.25	2.08, 2.43
Overweight	9,003	0.97	0.96, 0.97	1.35	1.30, 1.39	8,918	0.97	0.97, 0.97	1.30	1.26, 1.35	5,312	1.70	1.59, 1.82
Normal weight	42,214	1.00	Referent	1.00	Referent	41,778	1.00	Referent	1.00	Referent	25,114	1.00	Referent
Underweight	2,189	1.03	1.02, 1.04	0.79	0.74, 0.84	2,172	1.02	1.01, 1.03	0.83	0.77, 0.89	1,251	0.59	0.50, 0.69

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention; CL, confidence limit; HR, hazard ratio; OR, odds ratio; TR, time ratio.

[a] Ages 5–6 years.

[b] Weight (kg)/height (m)^2. BMI was classified into categories using age- and sex-specific BMI percentiles. BMI percentiles were calculated using CDC standard population distributions.

[c] Adjusted for maternal age at delivery, education, parity, birth weight, and race/ethnicity.

[d] Probability modeled is menarche <12 years.

is possible that higher prepubertal levels of testosterone may initiate testicular growth earlier in OWOB boys. In fact, a case study demonstrated that testicular growth can be initiated with testosterone treatment in patients with LH gene mutations (46). Additionally, primate studies have found that administration of testosterone can induce premature testicular growth in multiple species (47–49). OWOB children are also more likely to be taller and have advanced bone structure compared with normal-weight peers, suggesting increased bioavailability of insulin-like growth factor 1 (IGF-1), a hormone involved in linear growth (50). A small UK-based study found that IGF-1 was positively correlated with testosterone levels and SMR progression, suggesting that IGF-1 concentrations may play a role in the timing and tempo of pubertal development (51). Finally, interactions between leptin (a hormone found in adipocytes) and leptin receptors on the hypothalamus and pituitary may also trigger earlier pubertal onset in OWOB boys. Studies using animal models found correlations between increases in leptin and more frequent release of gonadotropin-releasing hormones (52, 53). Conversely, it has also been postulated that higher aromatase concentrations in fat tissue may convert testosterone to estrogen, thereby stunting pubertal development in boys with greater fat mass (23). A more robust understanding of boys' hormonal profiles from prepuberty to full maturation is needed to understand how body fat affects various endocrinological systems.

In our study, we also found significant effect modification by race/ethnicity. Racial/ethnic variations in the association between BMI and puberty have been documented in prior studies (23), although underlying mechanisms remain elusive. Given that race/ethnicity is largely a social construct, it is unlikely that racial/ethnic variations in these and similar associations can be explained by biology alone. Instead, there is likely a complex interplay of biological, sociocultural, and environmental factors that make individuals of different racial/ethnic backgrounds more or less susceptible to the observed associations. Identifying these factors is an important area of current and future research.

Strengths and limitations

It is important to note that our study is based on data collected routinely through pediatric visits and not collected for research purposes. As a result, we did not have detailed data on diet, exercise, and other exposures that may influence pubertal development and obesity but are not documented clinically. Some studies suggest that consumption of animal proteins, including dairy, or high fat and carbohydrate intake during childhood can predict earlier pubertal onset, although BMI is a likely mediator in most of these associations (54, 55). Another limitation of the present study was that we did not have direct measures of body fat composition or sex hormone levels. Third, puberty was assessed primarily by pediatricians rather than more highly trained endocrinologists, and thus may be less accurate. However, this large a cohort would not be possible in studies that require specialized research training for SMR assessments or more expensive methods of assessing pubertal growth, such as hormone measurements or skeletal age assessments.

Table 5. Association Between Childhood Body Mass Index and Timing of Puberty in Boys, Stratified by Race/Ethnicity, KPNC Puberty Study, Kaiser Permanente Northern California, 2008–2021

Stage and BMI[a,b]	White			Black			Hispanic			Asian/Pacific Islander			Other/Unknown		
	No.	HR	95% CL	No.	HR	95% CL	No.	HR	95% CL	No.	HR	95% CL	No.	HR	95% CL
Gonadarche[c]															
Severe obesity	450	1.34	1.14, 1.56	188	1.20	0.92, 1.57	956	1.29	1.15, 1.44	386	1.13	0.96, 1.33	191	1.08	0.85, 1.37
Obesity	1,974	1.23	1.14, 1.32	592	1.33	1.14, 1.54	2,592	1.16	1.08, 1.25	1,390	1.30	1.19, 1.42	629	1.27	1.10, 1.46
Overweight	3,349	1.13	1.07, 1.20	815	1.22	1.07, 1.39	2,855	1.11	1.03, 1.19	1,791	1.29	1.19, 1.40	920	1.06	0.94, 1.20
Normal weight	17,876	1.00	Referent	3,063	1.00	Referent	10,211	1.00	Referent	10,772	1.00	Referent	4,304	1.00	Referent
Underweight	863	0.84	0.75, 0.95	143	0.77	0.56, 1.05	434	0.82	0.69, 0.97	929	0.82	0.73, 0.92	285	0.79	0.64, 0.98
Pubarche[c]															
Severe obesity	455	1.68	1.43, 1.97	192	1.43	1.08, 1.90	963	1.43	1.28, 1.60	392	1.33	1.13, 1.56	192	1.32	1.03, 1.70
Obesity	1,991	1.38	1.28, 1.49	595	1.64	1.41, 1.92	2,613	1.21	1.13, 1.30	1,395	1.40	1.27, 1.53	638	1.41	1.22, 1.63
Overweight	3,365	1.23	1.16, 1.31	815	1.43	1.25, 1.65	2,876	1.17	1.09, 1.26	1,817	1.32	1.22, 1.43	926	1.16	1.02, 1.31
Normal weight	17,952	1.00	Referent	3,077	1.00	Referent	10,293	1.00	Referent	10,890	1.00	Referent	4,328	1.00	Referent
Underweight	868	0.84	0.75, 0.95	145	0.91	0.66, 1.25	439	0.79	0.66, 0.93	943	0.85	0.76, 0.96	285	0.83	0.67, 1.04

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention; CL, confidence limit; HR, hazard ratio.

[a] Ages 5–6 years.

[b] Weight (kg)/height $(m)^2$. BMI was classified into categories using age- and sex-specific BMI percentiles. BMI percentiles were calculated using CDC standard population distributions.

[c] Adjusted for maternal age at delivery, education, parity, and birth weight.

Table 6. Association Between Childhood Body Mass Index Category and Timing of Puberty in Girls, Stratified by Race/Ethnicity, KPNC Puberty Study, Kaiser Permanente Northern California, 2008–2021

Stage and BMI[a,b]	White			Black			Hispanic			Asian/Pacific Islander			Other/Unknown		
	No.	HR	95% CL	No.	HR	95% CL	No.	HR	95% CL	No.	HR	95% CL	No.	HR	95% CL
Thelarche[c]															
Severe obesity	350	1.87	1.57, 2.23	181	2.12	1.65, 2.72	667	1.40	1.24, 1.59	201	2.02	1.59, 2.56	154	1.35	1.05, 1.74
Obesity	1,580	1.63	1.50, 1.76	545	1.70	1.45, 1.99	2,054	1.35	1.26, 1.46	889	1.49	1.33, 1.66	538	1.37	1.19, 1.58
Overweight	3,177	1.36	1.28, 1.44	765	1.57	1.37, 1.80	2,661	1.19	1.12, 1.27	1,576	1.53	1.41, 1.67	824	1.37	1.22, 1.54
Normal weight	15,800	1.00	Referent	2,571	1.00	Referent	9,380	1.00	Referent	10,263	1.00	Referent	4,200	1.00	Referent
Underweight	640	0.74	0.65, 0.83	128	0.64	0.48, 0.86	353	0.84	0.71, 0.99	826	0.83	0.74, 0.93	242	0.79	0.64, 0.96
Pubarche[c]															
Severe obesity	341	1.90	1.60, 2.27	181	2.77	2.11, 3.64	661	1.64	1.45, 1.85	201	2.37	1.89, 2.98	151	1.58	1.23, 2.02
Obesity	1,553	1.64	1.51, 1.78	546	1.60	1.36, 1.90	2,036	1.42	1.31, 1.53	886	1.69	1.52, 1.88	530	1.53	1.32, 1.76
Overweight	3,132	1.26	1.18, 1.34	760	1.55	1.34, 1.80	2,636	1.22	1.14, 1.30	1,573	1.43	1.32, 1.56	817	1.29	1.15, 1.45
Normal weight	15,598	1.00	Referent	2,541	1.00	Referent	9,268	1.00	Referent	10,209	1.00	Referent	4,162	1.00	Referent
Underweight	636	0.72	0.63, 0.82	128	0.67	0.49, 0.93	345	0.83	0.70, 0.99	824	0.94	0.84, 1.05	239	0.89	0.72, 1.10
	No.	**OR**	**95% CL**	**No.**	**OR**	**95% CL**	**No.**	**OR**	**95% CL**	**No.**	**OR**	**95% CL**	**No.**	**OR**	**95% CL**
Menarche[c,d]															
Severe obesity	187	3.30	2.43, 4.49	105	1.91	1.27, 2.88	354	2.25	1.81, 2.80	115	3.44	2.36, 5.01	94	2.45	1.59, 3.77
Obesity	916	2.64	2.26, 3.08	318	1.58	1.23, 2.04	1,164	1.92	1.68, 2.19	532	2.85	2.37, 3.42	311	2.39	1.85, 3.08
Overweight	1,900	1.71	1.51, 1.94	420	1.47	1.17, 1.85	1,522	1.80	1.60, 2.03	982	1.73	1.50, 2.00	488	1.44	1.15, 1.80
Normal weight	9,646	1.00	Referent	1,433	1.00	Referent	5,241	1.00	Referent	6,305	1.00	Referent	2,489	1.00	Referent
Underweight	398	0.64	0.46, 0.89	61	0.68	0.37, 1.26	189	0.72	0.51, 1.03	465	0.48	0.36, 0.62	138	0.69	0.43, 1.09

Abbreviations: BMI, body mass index; CDC, Centers for Disease Control and Prevention; CL, confidence limit; HR, hazard ratio; OR, odds ratio.

[a] Ages 5–6 years.

[b] Weight (kg)/height $(m)^2$. BMI was classified into categories using age- and sex-specific BMI percentiles. BMI percentiles were calculated using CDC standard population distributions.

[c] Adjusted for maternal age at delivery, education, parity, and birth weight.

[d] Probability modeled is menarche <12 years.

The strengths of the present study outweigh its limitations. Using a large and diverse cohort of boys and girls, prospective study design, and objective measures from electronic health records enabled us to demonstrate a clear dose-response association, in which boys and girls with extreme obesity may be at highest risk of earlier pubertal development, and to demonstrate significant effect modification by race/ethnicity.

Conclusions

Obesity at ages 5–6 years is associated with earlier gonadarche and pubarche in boys and earlier thelarche, pubarche, and menarche in girls. The strengths of these associations may vary by race/ethnicity. These results highlight the importance of childhood obesity prevention interventions that start early in life.

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The data sets generated and/or analyzed during the present study are not publicly available due to our institutional policy. Individuals who are interested in accessing the data may contact the corresponding author regarding (or to discuss or set up) a data use agreement.

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