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Original Contribution

Associations of Maternal Gestational Weight Gain and Obesity With the Timing of Pubertal Onset in Daughters

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Early puberty is associated with adverse health outcomes, but little is known regarding early-life determinants influencing pubertal timing. We examined the associations between maternal gestational weight gain (GWG) and the timing of the onset of breast development (thelarche) and pubic hair development (pubarche) in a cohort of 2,070 girls born in a Kaiser Permanente Northern California facility between 2005 and 2006. Using Weibull regression models accommodating interval censoring and adjusting for important confounders, we found that excess GWG was associated with increased risk of early thelarche (hazard ratio (HR) = 1.50, 95% confidence interval (CI): 1.26, 1.78) and early pubarche (HR = 1.35, 95% CI: 1.10, 1.66). Inadequate GWG was associated with early thelarche (HR = 1.36, 95% CI: 1.08, 1.71). The associations between excess or inadequate GWG and risk of earlier thelarche were stronger if mothers were obese before or at the beginning of pregnancy (body mass index ≥30 kg body weight per m height squared) (HR = 2.01, 95% CI: 1.53, 2.63; HR = 2.08, 95% CI: 1.45, 2.98, respectively). Similar associations were found for pubarche outcome. Inclusion of girls' prepubertal body mass index slightly attenuated these associations, but they remained significant. Monitoring of maternal weight before and throughout pregnancy might help prevent early pubertal onset and subsequent negative health outcomes.

developmental origin of health and disease; gestational weight gain; obesity; puberty

Abbreviations: BMI, body mass index; CI, confidence interval; EHR, electronic health record; GWG, gestational weight gain; HR, hazard ratio; IOM, Institute of Medicine; KPNC, Kaiser Permanente Northern California.

The average age of girls' pubertal onset has declined significantly in the United States (1). Girls who experience early puberty are at higher risk for emotional and behavioral conditions such as depression, anxiety, substance abuse, and early sexual debut (2, 3). Beyond immediate health outcomes, early puberty has been associated with numerous adverse health outcomes later in life, including heart disease and cancers (2, 4–7). There are also significant racial/ethnic differences in the timing of pubertal onset. Our recent study demonstrated that the median age at onset of breast development was 8.8 years for black girls and 9.3 years for Hispanic girls, compared with 9.7 years for white girls, despite the fact that less than a century ago menarche in black girls occurred later than in white girls (1, 8, 9). Childhood obesity has been linked to early puberty and disproportionately affects black and Hispanic children (1). However, obesity alone does not explain the trend toward earlier onset of puberty; girls with normal body mass index (BMI) of all racial/ethnic backgrounds are also experiencing earlier development compared with previous years (1).

Emerging studies have begun to examine the relationship between early-life factors and timing of puberty. We have recently reported that maternal obesity is associated with timing of pubertal onset in girls (10, 11). In addition, a few recent studies reported that maternal excess gestational weight gain (GWG) might be associated with earlier timing of pubertal outcomes in daughters (12–14). To our knowledge, no US-based studies have examined whether maternal GWG is associated with timing of pubertal onset in girls, despite the recent evidence that timing of onset (i.e., initiation of development of breasts or pubic hair) also has important implications for short- and long-term mental health and disease risk (2, 3). Thus, we assessed this association using a population-based cohort of mother-daughter pairs in Northern California.

METHODS

Participants

The study was conducted within Kaiser Permanente Northern California (KPNC), a large integrated health-care delivery system that serves over 4 million members in Northern California. Using the KPNC electronic health record (EHR) system, we created a retrospective cohort of 2,070 mother-daughter pairs. We included girls who were born at a KPNC facility between 2005 and 2006 and who had at least 1 measured prepubertal BMI and 1 Tanner Stage assessment documented starting at age 6. All girls had continuous KPNC membership coverage with no gaps of >90 days. Girls with diagnoses of conditions that affect pubertal development (such as congenital adrenal hyperplasia or gonadal, adrenal, or germ cell tumors) were excluded from the study ($n = 26$). Additionally, girls who were born prematurely (<37 weeks) ($n = 204$) or from pregnancies with multiple births ($n = 92$) were also excluded. Mothers with extreme pregravid BMIs (<15 or >60) were not included. All the mothers had prenatal checkups at KPNC. All the data were drawn from the KPNC EHR, and the study was approved by the KPNC Institutional Review Board.

Measurements

Exposure variables (maternal GWG). When possible, we used pregravid weight measured within a year prior to conception ($n = 312$). If pregravid weight was not available, we used the first weight measured, starting at conception and no later than the time of α-fetoprotein testing, which is usually performed near gestational age 16–18 weeks ($n = 1,758$). Maternal BMI was calculated by dividing weight (kilograms) by height (meters) squared and was categorized using the World Health Organization categories (15). Last weight before delivery was measured within 45 days prior to the day of delivery, and the GWG was estimated by subtracting the initial weight from the last weight before delivery. GWG categories (exceeded, met, below) were assigned in line with Institute of Medicine (IOM) guidelines (16) according to the maternal BMI described above. According to these recommendations, pregnant women with a pregravid BMI of <18.5, 18.5–24.9, 25.0–29.9, and ≥30 are expected to gain 28–40 pounds, 25–35 pounds, 15–25 pounds, and 11–20 pounds, respectively.

In order to assess the combined effects of maternal pregravid BMI and GWG, we created a 9-category composite measure of GWG (exceeded, met, below) and BMI (<25.0, 25.0–29.9, ≥30.0).

Outcomes. Documentation of Tanner stage, the 5-stage scale developed by Marshall and Tanner (17), in the EHR was adopted as a routine part of pediatric checkups at KPNC starting in 2010. KPNC pediatricians assess breast development in girls using palpation and/or visual inspection and pubic hair development using visual inspection. In this study, we measured the transition from Tanner Stage 1 (prepubertal, or no onset) to Tanner Stage 2 and above, which captures the onset of pubertal development.

To assure that these Tanner data are of high quality, we conducted a validation study. Among the girls who participated in a recently conducted prospective study of adolescent girls (the Cohort Study of Young Girls' Nutrition, Environment, and Transitions (CYGNET Study)) (11, 18, 19), we compared the pediatrician-assessed Tanner stages obtained from the EHR with the Tanner stages obtained for research purposes. In the CYGNET Study, we rigorously trained staff in Tanner stage assessment, followed by observation of assessment by a board-certified pediatric endocrinologist (L.C.G.), ensuring that the Tanner data collected from this study were of the highest quality. Comparing CYGNET Study clinical assessments with KPNC pediatrician assessments (selecting those done within 6 months of study visits, $n = 217$), the weighted κ was 0.66 (95% confidence interval (CI): 0.61, 0.72) for breast development and 0.65 (95% CI: 0.59, 0.71) for pubic hair development (L.H.K., unpublished data, 2015). Because the KPNC pediatrician and CYGNET Study Tanner assessments did not occur at the same time, this level of agreement is notable, strongly suggesting acceptable levels of agreement and reasonable validity of use of routine pediatric assessments in research. Pediatrician-assessed Tanner stage is more reliable than self-reported or parent-reported assessments, methods commonly used in previous studies (20).

Covariates. We used girls' BMI measured at the last known Tanner Stage 1 assessment or within 60 days prior to or after the assessment. Percentiles and z scores were calculated using age- and sex-specific Centers for Disease Control and Prevention (2000) standard population distributions (21). We categorized a girl's BMI as <85th versus ≥85th percentile. We also obtained birth weight (grams), gestational age at birth (weeks), and age at Tanner stage assessment (years).

Maternal race/ethnicity was coded as black, Hispanic, Asian, or non-Hispanic white. Education was categorized as high school or less, some college (<2 years), 4-year college, or graduate school. Mothers who indicated any tobacco use at prenatal checkups were categorized as being exposed to tobacco ("yes"). In addition, age at delivery, gestational diabetes mellitus status, pregnancy hyperglycemia (≥140 mg/dl), and parity (0, 1, or ≥2) were also included.

Statistical analyses

We analyzed associations between GWG, or GWG according to maternal BMI, and pubertal onset using Weibull regression, an accelerated failure time and proportional hazards regression model that accommodates left, right, and interval censoring. Girls were considered left-censored if they had already transitioned to Tanner Stage 2+ at the time of their first exam (baseline) and right-censored if they had not transitioned from Tanner Stage 1 to Stage 2+ by the time of their last exam (end of follow-up). Weibull regression analyses provided two estimates of the association (and 95% CI) between a covariate and the outcome of time to puberty onset: the time ratio and the hazard ratio. Time ratio estimates represent the ratio of the median time to event for a given level of a covariate in relation to its reference level. Pubarche and thelarche were analyzed as 2 separate outcomes, with adjustments for maternal age, race/ethnicity, education, parity, and smoking during pregnancy. We also examined hyperglycemia as a potential confounder but omitted it from the model because its inclusion did not change the effect estimate substantially (>10%) (22).

We assessed the mediating role of the girl's prepubertal BMI and birth weight by comparing the results of both models before and after including each variable, respectively. Effect

modification by mother's race/ethnicity was examined by including a cross-product term of maternal race/ethnicity and GWG categories. Because the *P* values of the cross-product terms were not significant, we have not presented the stratified data. All analyses were conducted using SAS, version 9.3 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Participant characteristics

A total of 2,070 mother-daughter pairs were included in this analysis. Approximately 49% of the mothers exceeded GWG recommendations, and 17% gained below the recommendations (Table 1). Women who were overweight or obese before or at the beginning of the pregnancy, white, or nulliparous were more likely to exceed the recommended GWG. Daughters of mothers who had excess GWG had higher birth weights and more often had BMI over the 85th percentile compared with their counterparts. Approximately 13% of girls were left-censored for the breast development analyses and 11% for pubic-hair development analyses. Approximately 63% of the girls were right-censored for breast and 72% for pubic hair analyses.

Primary analyses

Association between GWG and timing of thelarche. Daughters of mothers who gained less than or more than IOM

Table 1. Maternal and Daughter Characteristics According to Gestational Weight Gain, Kaiser Permanente Northern California Puberty Study, 2011–2017

	Compliance With GWG Recommendations						*P* Value
	Below (*n* = 346)		Met (*n* = 704)		Exceeded (*n* = 1,020)		
	No.	%	No.	%	No.	%	
Maternal Characteristics							
Age at delivery, years[a]	31.0 (5.3)		30.5 (5.1)		29.5 (5.4)		<0.001
Pregnancy hyperglycemia (≥140 mg/dl)	86	25.7	145	21.0	172	17.3	0.003
BMI category[b]							
Underweight	11	3.2	13	1.9	7	0.7	<0.001
Normal	145	41.9	436	61.9	384	37.7	
Overweight	68	19.7	141	20.0	358	35.1	
Obese	122	35.3	114	16.2	271	26.6	
Race/Ethnicity							
Non-Hispanic white	120	34.7	252	35.8	440	43.1	<0.001
Asian	89	25.7	217	30.8	201	19.7	
Hispanic	105	30.4	189	26.9	299	29.3	
Black	32	9.3	46	6.5	80	7.8	
Parity							
0	110	31.8	275	39.1	481	47.2	<0.001
1	124	35.8	288	40.9	340	33.3	
≥2	112	32.4	141	20.0	199	19.5	
Education							
High school or less	105	30.4	190	27.0	326	32.0	0.05
Some college	121	35.0	219	31.1	342	33.5	
College/university	80	23.1	192	27.3	244	23.9	
Postgraduate	40	11.6	103	14.6	108	10.6	
Tobacco use during pregnancy							
Yes	2	0.6	3	0.4	13	1.3	0.18
Daughter Characteristics							
Prepubertal BMI							
≥85th percentile	102	29.5	164	23.3	354	34.7	<0.001
Birth weight (g)[a]	3,249.2 (427.2)		3,317.9 (410.5)		3,488.7 (446.0)		<0.001

Abbreviations: BMI, body mass index; GWG, gestational weight gain.
[a] Values are expressed as mean (standard deviation).
[b] Weight (kg)/height $(m)^2$ and categorized according to the World Health Organization categories.

Table 2. Associations Between Gestational Weight Gain and Timing of Breast Development in Daughters, (n = 2,043), Kaiser Permanente Northern California Puberty Study, 2011–2017

Maternal GWG	No.	Timing of Breast Development							
		Model 1[a]				Model 2[b]			
		TR	95% CI	HR	95% CI	TR	95% CI	HR	95% CI
Below	345	0.97	0.96, 0.99	1.36	1.08, 1.71	0.98	0.96, 1.00	1.32	1.05, 1.66
Met	692	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Exceeded	1,006	0.97	0.95, 0.98	1.50	1.26, 1.78	0.97	0.96, 0.99	1.38	1.16, 1.65

Abbreviations: CI, confidence interval; GWG, gestational weight gain; HR, hazard ratio; TR, time ratio.
[a] Adjusted for mother's race/ethnicity, maternal age, education, parity, and smoking during pregnancy.
[b] Also adjusted for daughter's body mass index.

recommendations were more likely to experience earlier breast onset than daughters of mothers who met IOM guidelines (respectively, unadjusted hazard ratio (HR) = 1.30, 95% CI: 1.04, 1.63; HR = 1.50, 95% CI: 1.26, 1.78) (data not shown). Associations remained strong after adjusting for maternal age, race/ethnicity, education, smoking during pregnancy, and parity (below IOM guidelines: HR = 1.36, 95% CI: 1.08, 1.71; exceeded IOM guidelines: HR = 1.50, 95% CI: 1.26, 1.78) (Table 2). The estimated time ratio corresponds to approximately 3 and 3.5 months' earlier onset (for below and exceeded GWG, respectively) than the referent.

Including the daughter's prepubertal BMI slightly attenuated the results, but they remained significant. Associations between GWG and breast development remained significant in mothers with inadequate (HR = 1.32, 95% CI: 1.05, 1.66) and excess GWG (HR = 1.38, 95% CI: 1.16, 1.65) (Table 2). Attenuation by girl's birth weight was negligible (data not shown).

Association between GWG and timing of pubarche. Daughters of mothers who exceeded IOM guidelines were more likely to experience earlier pubertal onset (unadjusted HR = 1.41, 95% CI: 1.15,1.72); however, associations were insignificant in daughters whose mothers gained below the recommended GWG (unadjusted HR = 1.19, 95% CI: 0.92,1.55) (data not shown). In models adjusting for maternal factors, daughters of mothers who exceeded the IOM recommendation were >30% more likely to experience earlier pubic hair development compared with daughters of mothers who met the recommendations (HR = 1.35, 95% CI: 1.10, 1.66). Associations assessing pubertal onset of daughters of mothers with inadequate GWG were not statistically significant (Table 3). The estimated time ratio corresponds to approximately 3 months' earlier onset for daughters of mothers with excess GWG. The result for excess GWG and pubic hair onset was attenuated but remained significant (HR = 1.28, 95% CI: 1.04, 1.58) when daughter's prepubertal BMI was included in the model. Inclusion of girl's birth weight did not substantially attenuate the associations (data not shown).

Secondary analyses

Composite effects of maternal GWG and BMI on timing of thelarche in daughters. Adjusting for the covariates, girls whose mothers had a BMI of ≥30 were at higher risk of experiencing earlier breast onset regardless of GWG, although when mothers exceeded or did not reach the IOM recommendation, the associations were stronger (Table 4). For example, daughters of mothers with BMI ≥30 and excess or inadequate GWG were over 2 times more likely to experience earlier breast development (respectively, HR = 2.01, 95% CI: 1.53, 2.63; HR = 2.08, 95% CI: 1.45, 2.98) than daughters in the referent group (BMI <25 and GWG within the recommendation). The estimated time ratio corresponds to approximately 6 and 6.5 months' earlier onset for these girls (exceeded and below GWG, respectively), compared with those whose mother had a BMI of <25 and met the GWG recommendation (data not shown). Both

Table 3. Associations Between Gestational Weight Gain and Timing of Pubic Hair Development in Daughters (n = 1,897), Kaiser Permanente Northern California Puberty Study, 2011–2017

Maternal GWG	No.	Timing of Pubic Hair Development							
		Model 1[a]				Model 2[b]			
		TR	95% CI	HR	95% CI	TR	95% CI	HR	95% CI
Below	321	0.98	0.96, 1.01	1.19	0.92, 1.56	0.99	0.96, 1.01	1.17	0.90, 1.54
Met	653	1.00	Referent	1.00	Referent	1.00	Referent	1.00	Referent
Exceeded	923	0.97	0.96, 0.99	1.35	1.10, 1.66	0.98	0.96, 1.00	1.28	1.04, 1.58

Abbreviations: CI, confidence interval; GWG, gestational weight gain; HR, hazard ratio; TR, time ratio.
[a] Adjusted for mother's race/ethnicity, maternal age, education, parity, and smoking during pregnancy.
[b] Also adjusted for daughter's body mass index.

Table 4. Associations Between Gestational Weight Gain According to Maternal Body Mass Index and the Timing of Breast Development in Daughters (n = 2,043), Kaiser Permanente Northern California Puberty Study, 2011–2017

Maternal GWG[a]	Maternal Body Mass Index[b]								
	<25.0			25.0–29.9			≥30.0		
	No.	HR[c]	95% CI	No.	HR[c]	95% CI	No.	HR[c]	95% CI
Below	156	1.26	0.90, 1.75	68	1.62	1.05, 2.51	121	2.08	1.45, 2.98
Met	443	1.00	Referent	138	1.29	0.92, 1.81	111	1.64	1.12, 2.38
Exceeded	386	1.49	1.16, 1.92	354	1.76	1.36, 2.27	266	2.01	1.53, 2.63

Abbreviations: CI, confidence interval; GWG, gestational weight gain; HR, hazard ratio.
[a] Maternal GWG compared with Institute of Medicine recommendations.
[b] Weight (kg)/height (m)^2.
[c] Adjusted for mother's race/ethnicity, maternal age, education, parity, and smoking during pregnancy.

girls whose mothers were overweight (BMI of 25.0–29.9) and gained more than recommended and girls whose mothers had BMI <25 and gained more than recommended were at higher risk of earlier breast onset than those in the referent group (Table 4).

Adding prepubertal BMI attenuated the associations, although they remained strong and significant. For example, girls whose mothers had a BMI of ≥30 and excess or inadequate GWG were still at higher risk of experiencing earlier thelarche than girls in the referent group, after adjusting for prepubertal BMI (HR = 1.60, 95% CI: 1.20, 2.13, and HR = 1.80, 95% CI: 1.24, 2.60, respectively) (Web Table 1, available at https://academic.oup.com/aje). Adding birth weight to the model did not substantially change the effect estimate (data not shown).

Composite effects of maternal GWG and BMI on timing of pubarche in daughters. Similar to the thelarche analyses, daughters of mothers who had a BMI of ≥30 were at significantly higher risk of experiencing earlier pubarche when their mothers exceeded or did not reach the IOM recommendation (Table 5). The estimated time ratios correspond to pubarche approximately 6 months earlier for daughters of mothers with a BMI of ≥30 and excess GWG and 6.5 months earlier for daughters of mothers with a BMI of ≥30 and inadequate GWG (data not shown). Adding the prepubertal BMI variable, but not birth weight, to these models slightly attenuated the associations, but they remained significant (Web Table 2). Daughters of mothers with a BMI of 25.0–29.9 who exceeded IOM recommendations were also at higher risk for earlier pubarche; however, associations were not statistically significant when maternal BMI was less than 25, regardless of the GWG (Table 5).

DISCUSSION

In this population-based cohort study, we found that maternal GWG is an important factor associated with pubertal timing in daughters. Our data suggest that both excess and inadequate GWG are associated with earlier timing of thelarche and pubarche, and the associations were stronger when mothers were overweight or obese. Neither prepubertal BMI nor birth weight fully mediated the observed associations, and hyperglycemia did not confound the associations, suggesting that maternal GWG might independently affect the timing of sexual development in girls.

Our findings extend the previous knowledge regarding early-life risk factors of pubertal timing in girls. In a recent study, Lawn et al. (13) found that GWG was inversely associated with the timing of thelarche and pubarche in a cohort of primarily white girls born in Avon, United Kingdom. Studies that investigated the associations between GWG and age at menarche have also reported inversely linear relationships (13), with greater GWG increasing the risk of earlier age at menarche (12–14). While age at menarche has remained

Table 5. Associations Between Gestational Weight Gain According to Maternal Body Mass Index and the Timing of Pubic Hair Development in Daughters (n = 1,897), Kaiser Permanente Northern California Puberty Study, 2011–2017

Maternal GWG[a]	Maternal Body Mass Index[b]								
	<25.0			25.0–29.9			≥30.0		
	No.	HR[c]	95% CI	No.	HR[c]	95% CI	No.	HR[c]	95% CI
Below	143	1.04	0.69, 1.55	65	1.30	0.78, 2.17	113	2.00	1.32, 3.02
Met	415	1.00	Referent	131	1.41	0.96, 2.08	107	1.29	0.83, 2.00
Exceeded	351	1.27	0.94, 1.71	325	1.55	1.14, 2.11	247	1.95	1.43, 2.67

Abbreviations: CI, confidence interval; GWG, gestational weight gain; HR, hazard ratio.
[a] Maternal GWG compared with Institute of Medicine recommendations.
[b] Weight (kg)/height (m)^2.
[c] Adjusted for mother's race/ethnicity, maternal age, education, parity, and smoking during pregnancy.

fairly constant at 12–13 years for the past 60 years (23–24), American girls are experiencing earlier pubertal onset, making it important to understand factors influencing this trend. Our findings are consistent with the U-shaped associations found in participants of the Nurses' Health Study II, the largest study to examine relationships between GWG and puberty thus far (14). In this cohort, compared with daughters of mothers who gained 20–29 pounds, daughters of mothers who self-reported GWG of <10 pounds or >40 pounds had a 30% increased risk of experiencing early menarche, adjusting for various maternal and child health and social factors, including child body size at age 5 years and maternal and child physical activity (14).

Our findings might be explained by some biological mechanisms. Children of obese mothers are at higher risk of childhood obesity due to similarity in genetic and/or lifestyle factors (25, 26). We hypothesized that there would be associations between maternal excess GWG and earlier onset of puberty and that the associations would be at least partially explained by childhood obesity. However, we found that most associations remained significant even after accounting for daughters' prepubertal BMI, suggesting that there are other pathways through which maternal GWG and obesity might play a role in girls' pubertal timing. In utero exposure to maternal leptin, a hormone associated with obesity, might influence the onset of daughters' reproductive development in later years (27). Moreover, increases in maternal fat levels reduce adiponectin, a plasma protein involved in glucose regulation, subsequently inducing the production of placental growth hormone and human chorionic somatomammotropin, a placental lactogen that can prompt fetal hyperinsulinemia by means of β-cell replication (28). Increased levels of insulin might in turn boost androgen production from the adrenal glands by binding to insulin receptors on the adrenal cortex, triggering adrenarche and earlier puberty (29–32). With regard to the association between inadequate GWG (i.e., gaining below the recommended range) and early onset of breast development, it is possible that undernutrition leads to lower birth weight or subsequent catch-up growth and greater fat distribution later in childhood, as seen in children born with intrauterine growth retardation or very low birth weight (33–35). We additionally adjusted for both birth weight and prepubertal BMI, but the associations remained significant. However, it must be noted that the presence of unmeasured confounders might be potentially biasing results. Likewise, a better understanding of the relationship between prepubertal BMI, birth weight, GWG, and pubertal outcomes is needed to conclusively determine the potentially mediating role of prepubertal BMI and birth weight on the association between GWG and pubertal onset. The presence of unmeasured mediator-outcome confounding and possible interactions between exposure and mediator might be a potential source of bias that is not captured in traditional mediation analyses, which we have employed for the present study. Future studies should examine whether biologically relevant factors such as early-life catch-up growth, body composition, or biomarkers might explain some of these associations.

Our results from the combined analyses of maternal BMI and GWG suggest that BMI and GWG might have a synergistic effect when influencing timing of pubertal onset; the associations between GWG and timing of thelarche or pubarche were significant and increased with greater BMI even when women gained below IOM recommendations, and within IOM recommendations in thelarche models. These results corroborate the findings of past research on pregravid BMI and puberty, including ours, in which maternal obesity was independently associated with the risk of earlier pubertal onset as well as age at menarche (12, 13, 25, 36, 37). However, our findings also show that women with a BMI of <25 who also had excess GWG had daughters who were 49% more likely to experience earlier breast onset, highlighting the important independent association between GWG and pubertal onset. Additionally, for a woman who is already overweight or obese at the beginning of pregnancy, our results suggest that staying within the recommended range is still beneficial in lowering risk of earlier pubertal onset in daughters.

The present study has several notable strengths. To our knowledge, it is among the first to investigate the relationship between maternal GWG and pubertal onset using pediatrician-assessed Tanner stages. The majority of studies examining the association between GWG and puberty have depended solely on retrospective self-reports of menarcheal age (12, 14, 25). In some cases, daughters' menarcheal age was reported by their guardians or assumed based on school grade (12, 13, 25). Emerging studies demonstrate that other hallmarks of pubertal development in girls aside from menarche, such as onset of breast or pubic hair development or the tempo (the rate at which adolescents progress through puberty), might be more important indicators of negative health outcomes later in life (38–41). Second, all weights and heights were measured by health professionals, eliminating the risk of recall or reporting bias. Last, the availability of comprehensive KPNC electronic databases allowed us to link maternal and child health records to efficiently build a birth cohort that would normally take many years.

The downsides of using EHR, however, should also be noted as potential limitations of this study. We did not have participant-reported data on diet, physical activity, and other social, psychosocial, environmental, and behavioral variables that might play roles in child development and maturation. Although we have extracted as many potential confounders that are known to influence pubertal development from the EHR as possible—such as birth weight, prepubertal BMI, maternal race/ethnicity, education, smoking during pregnancy, and parity—it is possible that we could not capture other potential confounders. Another limitation was the lack of available pregravid data from all the women. Not all the participants were born after the launch of the KPNC EHR system in 2006; therefore, pregravid weight could not be captured for some mothers. As the best proxy, we used the earliest weight measured between conception and the α-fetoprotein test. However, our validation study that was limited only to those with pregravid BMI ($n = 312$) showed that the results were similar to the results using the entire cohort (data not shown), suggesting that bias from differential misclassification is unlikely. Last, Tanner stage data assessed by KPNC pediatricians might not be as accurate as the assessment conducted by pediatric endocrinologists. However, it is unlikely that the misclassifications are differential by maternal GWG or BMI. Nondifferential misclassification biases the results towards the null, so the data reported here might underestimate the true associations. Many of the existing studies use self-reported or parent-reported Tanner assessments, and pediatrician-assessed Tanner stage is found to be more reliable than those recalled data (20). The strengths of

this study, using a large and diverse population, longitudinal follow-up, and use of objective measures, overcome these limitations.

Our findings suggest that there are significant associations between maternal GWG and daughters' breast and pubic hair onset, especially when mothers were overweight before or at the beginning of the pregnancy. Our results underscore the importance of raising awareness among women of childbearing age to maintain healthy weight and among pregnant women to gain weight within the recommended range given their BMI. Taking these precautionary steps will likely improve not only pregnancy outcomes but also the health of offspring, including reducing the risks of childhood obesity and early puberty.

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