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## Interrelationships among age at adiposity rebound, BMI during childhood, and BMI after age 14 years in an electronic health record database

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### Abstract

**Objective:** This study compared the importance of age at adiposity rebound versus childhood BMI to subsequent BMI levels in a longitudinal analysis.

**Methods:** From the electronic health records of 4.35 million children, a total of 12,228 children were selected who were examined at least once each year between ages 2 and 7 years and reexamined after age 14 years. The minimum number of examinations per child was six. Each child's rebound age was estimated using locally weighted regression (lowess), a smoothing technique.

**Results:** Children who had a rebound age < 3 years were, on average, 7 kg/m<sup>2</sup> heavier after age 14 years than were children with a rebound age ≥ 7 years. However, BMI after age 14 years was more strongly associated with BMI at the rebound than with rebound age ( $r = 0.57$  vs.  $-0.44$ ). Furthermore, a child's BMI at age 3 years provided more information on BMI after age 14 years than did rebound age. In addition, rebound age provided no information on subsequent BMI if a child's BMI at age 6 years was known.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

**Conclusions:** Although rebound age is related to BMI after age 14 years, a child's BMI at age 3 years provides more information and is easier to obtain.

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## INTRODUCTION

Levels of BMI increase from birth to about 1 year of age, decrease to a minimum between 2 and 8 years of age, and increase again during later childhood and adolescence. Based on serial data from about 155 individuals, Rolland-Cachera et al. reported that the earlier the nadir of BMI occurs, the higher the BMI at age 16 years and early adulthood (1,2). This U-shaped pattern of BMI change between ages 2 and 8 years was termed "adiposity rebound."

Numerous investigators have since confirmed the inverse relationship between age at rebound and subsequent BMI levels, body fatness, and obesity in adolescence and adulthood (3–9). Various authors have considered the adiposity rebound to be either a critical period for developing obesity, a statistical effect, or a developmental marker (10–13).

However, it is uncertain whether age at rebound provides additional information on adolescent or adult obesity beyond that conveyed by BMI levels at various ages in childhood. For example, Williams et al. (6) suggested that BMI at age 7 years could provide similar information concerning subsequent obesity that would be easier to obtain. Determining the age at rebound requires at least three measurements that include the BMI nadir, but several additional BMI values would likely be needed for most children. We have previously shown that the inverse relationship of age at rebound to BMI among young adults was not independent of BMI at age 6 years (7,14).

Our objectives are to examine the longitudinal relationship of rebound age to subsequent BMI among 12,228 children from an electronic health record (EHR) database and quantify the amount of information provided by BMI at various ages between 2 and <8 years. All children had at least one BMI value each year between the ages of 2 and <8 years, along with a subsequent BMI between ages 14 and <20 years.

## METHODS

### Study sample

PEDSnet (15) is a multi-institutional clinical research network that aggregates EHR data from several of the nation's largest children's health systems (16). PEDSnet standardizes EHR data across institutional data marts to the PEDSnet common data model, an expanded version of the Observational Medical Outcomes Partnership (OMOP) common data model (16,17). Since 2009, PEDSnet has accrued data for more than 6.5 million children from all inpatient and outpatient clinical settings (16,18). The states with the greatest concentration of PEDSnet patients are Colorado, Delaware, Florida, Illinois, Indiana, Kentucky, Missouri, New Jersey, Ohio, Pennsylvania, and Washington.

The longitudinal data in the current study are from four of the hospitals in PEDSnet: the Children's Hospital of Philadelphia; the Children's Hospital of Colorado; the Nationwide Children's Hospital in Ohio; and the Nemours Children's Health System (a Delaware and

Florida health system). Because this is a secondary analysis of children in this database, no sample size calculations were performed.

The Children's Hospital of Philadelphia Institutional Review Board (IRB) determined this project does not meet human subjects research criteria. The Centers for Disease Control and Prevention (CDC) determined that this secondary data analysis is not human subjects research, and, therefore, CDC IRB review/approval is not required. The analyses used a deidentified data set; participant identifiers were replaced, and temporal information was limited to the year of birth and age in days.

## Data management

The use of EHR data from clinical care for research purposes requires assessing the data's quality (19,20). PEDSnet implements a data quality assessment workflow that includes >1,000 checks to determine completeness, plausibility, value conformance, and relational conformance of the data (21,22). When this process identifies issues, they are remediated by member institutions.

There were 33.0 million patient weights and 20.3 million heights from 4.35 million 2- to 19-year-old individuals at an in-person clinical encounter at PEDSnet member institutions between 1999 and 2019. These in-person encounters included inpatient hospital stays, outpatient specialty and primary care visits with a physician or non-physician, emergency department visits, and observation stays. We refer to these encounters as "visits" throughout the text.

We identified weights and heights that were likely to be errors using Daymont's algorithm for the longitudinal detection of outliers (23,24). This method identifies 22 categories of possible mistakes, many of which are based on the distance of the weight or height from its weighted moving average of a child's *z* score (25). Other categories of potential errors include unexpected height changes and values that appear to be carried forward from a previous visit. Of the weights in this data set, 9% were same-day multiples, 7% were carried forwards, and <1% were other types of potential errors. Of the heights, 4.5% were same-day multiples, 5.5% were carried forwards, and 1% decreased by >3 cm between consecutive visits.

We excluded all weights and heights identified as carried forwards or as other types of errors, resulting in a data set of 28 million weights and 18 million heights. Because of the large number of weights without a same-day height, we allowed heights to match with weights obtained within 30 days. This matching resulted in 19.3 million records, with both weight and height from 3.5 million children. We calculated BMI as kilograms per meters squared, and extreme values (52,348; 0.24%) of weight, height, and BMI were further identified and excluded based on their modified *z* score (25). For these analyses, we required that a child have at least one visit per year of age between 2 and 7 years, along with an additional visit after 14 years. In addition, we used the BMI at the last visit for children who had two or more visits after age 14 years. These restrictions resulted in a sample of 12,228 children examined in four hospitals (the Children's Hospital of Colorado, the Children's Hospital of Philadelphia, the Nationwide Children's Hospital, and the Nemours Children's

Health System). The initial examination among these children occurred between 1999 and 2008, and the final examination occurred between 2011 and 2019.

### Statistical methods

BMI  $z$  scores (BMI $z$ ) were based on the CDC growth charts (26,27), and obesity was defined as a BMI  $\geq$  95th sex- and age-specific percentile of the growth charts.

We performed data management and analyses using R (version 4.05) (R Core Team). Inspection of BMI plots for individual children indicated that most children had several BMI values between ages 2 and  $<8$  years that were very close to the BMI nadir. Furthermore, these low BMI values frequently occurred at nonconsecutive visits. Therefore, most analyses are based on using locally weighted regression (lowess) (28) to smooth each child's BMI values and identify the minimum, smoothed BMI. Age at rebound was the age at which the minimum, smoothed BMI occurred. The minimum number of BMI values between ages 2 and  $<8$  years was six, whereas the median was fifteen.

We performed sensitivity analyses in which age at rebound was based on the following: 1) minimum observed BMI; 2) the minimum BMI after smoothing with Friedman's super-smoother (29); or 3) the minimum of the median BMI values calculated for each year of age. Intercorrelations between the rebound age determined by these four methods ranged from  $r = 0.76$  to  $0.86$ . We did not include race/ethnicity as a covariate in most regression models, as 8% of the children had a value coded as "other," "multiple," or "unknown." However, we present analyses stratified by race/ethnicity.

We examined mean levels of various characteristics by categories of age at the rebound. We then assessed whether the relationship of rebound age to adolescent BMI and obesity was independent of BMI levels between ages 2 and  $<8$  years by comparing the multiple  $R^2$ s of several regression models that predicted BMI after age 14 years. Predictor variables in these models included rebound age, sex, height-for-age  $z$  score at rebound age, and age at the last visit. Various models also included a child's BMI at each year between ages 2 and 7 years. We used the mean value for children with multiple BMI values at these ages, but we also conducted additional analyses in which one BMI per year of age was selected at random. We modeled continuous variables using natural cubic splines (30,31) to allow for nonlinearity.

We constructed a nomogram using the *rms* package in R (32) that summarized the probability of obesity after age 14 years based on logistic regression. This plot assigns points to each predictor's value, which can be summed over all variables to derive the child's total points and the predicted probability of obesity at the last visit. We included race/ethnicity as an additional predictor for this analysis and excluded 3% of the children whose race was coded as "unknown," "refused," or "no information."

Logistic regression models were also used to examine the relationship of BMI at rebound ages of 2, 4, 5, and 7 years to the probability of obesity after age 14 years.

## RESULTS

All children were first examined at age 2 years, the mean age at the last visit was 15.5 (1.2) years, and the prevalence of obesity after age 14 years was 19%. Girls comprised 48% of the sample; 54% were White, 31% were Black, 8% were Hispanic, and 2% were Asian.

Table 1 shows the relationship of rebound age to various characteristics at both the age at BMI rebound (top) and after age 14 years (bottom). On average, children who had a rebound < 3 years were 7 kg/m<sup>2</sup> heavier at their last visit than were those with a rebound at age 7 years (27.4 vs. 20.2 kg/m<sup>2</sup>). Furthermore, the prevalence of obesity at the last visit was 36% (rebound < 3 years) and 2.5% (rebound = 7 years). However, as shown by the longitudinal correlations in the final columns, BMI and BMIz at the last visit were more strongly associated with the BMI at rebound than with age at rebound ( $r = 0.57$  vs.  $-0.44$  to  $-0.45$ ).

As shown in Table 1, the mean BMIz at the final visit was 1.4 standard deviations higher (1.2 vs.  $-0.2$ ) for children who had a rebound age < 3 years than those with a rebound age = 7 years. This difference was similar to those based on determining age at rebound using super-smoother (1.3), the observed minimum BMI (1.5), and by the minimum of the median BMI values at each year of age (1.3).

Table 2 shows the sex- and race-specific correlations between BMIz at the last visit and both rebound age and the BMI at the rebound. Except for the 149 children whose race was coded as “Other,” BMIz at the last visit was more strongly associated with the BMI at the rebound than with rebound age within each subgroup. For example, the two correlation coefficients were  $r = 0.58$  (BMI at rebound) and  $r = -0.44$  (rebound age) among boys and were  $r = 0.57$  (BMI at rebound) and  $r = -0.48$  (rebound age) among Black children. Among children with a race of “Other,” the absolute values of the two correlations were identical ( $r = 0.50$ ).

Figure 1 shows a nomogram, based on logistic regression, for predicting obesity at the last visit from a child’s sex, race/ethnicity, rebound age, and BMI at age 3 years. In order to calculate the probability of obesity at the last visit after age 14 years for a child, the number of points (top row) for each predictor is first calculated. These points are then summed and converted to a probability (bottom row). For example, a Hispanic boy (7 + 0 points) with a rebound age of 7 years (1 point) and a BMI at age 3 years of 24 (47 points) would have a total of 55 points (penultimate line) and a predicted probability of obesity of about 0.67. In contrast, a White girl (4 + 2 points) with a rebound age of 2.5 years (17 points) and a BMI at age 3 years of 14 (12 points) would have 35 points and a predicted probability of obesity of about 0.07. This regression model also indicated that, compared with White children, the adjusted odds for obesity at the last visit were twofold higher among Black children, 1.6-fold higher among Hispanic children, and 50% lower among Asian children.

We then constructed a series of regression models to determine whether the relationship of rebound age to BMI in adolescence was independent of a child’s BMI at various ages. A regression model that included the covariates (sex, age at last visit, and height z score at rebound age) and rebound age accounted for 24% of the BMI variability after age 14 years. Table 3 presents the multiple  $R^2$ s for these additional models predicting BMI after age 14

years by either the BMI at ages 2 to 7 years or with the additional information conveyed by rebound age. A model based on the covariates and BMI at age 2 years, but not rebound age, accounted for almost as much (0.23) of the BMI variability after age 14 years as did rebound age. Furthermore, a model containing BMI at age 3 years accounted for more variability (0.32) in BMI after age 14 years than the model containing rebound age. The amount of variability accounted for by BMI (alone) increased with each subsequent age, whereas the additional information supplied by rebound age decreased from 19% (0.42 vs. 0.23) at age 2 years to 7% at age 4 years and to virtually 0 at ages 6 and 7 years.

Figure 2 shows the results of logistic regression models for children who had a rebound age of 2, 4, 5, or 7 years, showing the probability of obesity at the last visit according to the child's BMI at the rebound age. The probabilities of obesity were calculated for an individual with the mean age (15.2 years) at the last visit. Within each group and based on rebound age, the probability of obesity at the final visit increased as the BMI at the rebound age increased. Furthermore, the strength of this association generally increased with age. For example, compared with a child at the 25th percentile of BMI, the adjusted odds ratio for a 2-year-old child at the 75th percentile of BMI was about four. In contrast, the comparable odds ratio for a 7-year-old child (75th vs. 25th percentile) was about 13.

## DISCUSSION

Our results indicate that age at BMI rebound is inversely associated with subsequent levels of BMI and obesity after age 14 years. However, the BMI at age 2 years accounts for a similar amount of the variability in BMI levels among adolescents as does rebound age ( $R^2$  of 0.23 and 0.24), whereas the BMI at age 3 years accounts for more ( $R^2 = 0.32$ ) of the variability. Furthermore, rebound age provides almost no independent information on BMI in adolescence if the BMI at ages 6 or 7 years is known. In addition, among children with a BMI rebound of age 2 years, the BMI value at age 2 years was a strong predictor of obesity after age 14 years.

Williams et al. (6) suggested that although the BMI rebound may be of scientific interest, it could be easier to use the BMI at age 7 years to predict adult BMI. Despite the many studies that have examined rebound age, we know of only two other studies that have assessed whether a child's BMI at various ages provides similar information (7,14). A small ( $n = 105$ ) study from the Bogalusa Heart Study (7) found that children with a relatively early rebound age were 4 to 5 kg/m<sup>2</sup> heavier in early adulthood than children with a rebound age 7 years. However, the rebound age conveyed no information on adult BMI if the BMI at age 7 years was known. A larger study of 17,000 children (14) also found that rebound BMI provided as much information on BMI levels after age 10 years as did rebound age. The mean age at the final examination was 12 years in this 2020 publication, but it was 15 years (range: 14–19 years) in the current study based on children in a different EHR database.

Because the estimation of rebound age requires at least three BMI values throughout childhood, it is uncertain why childhood BMI has received little attention in previous studies of adiposity rebound. Although rebound age was originally defined as the age corresponding to the lowest BMI before the increase in adiposity (1), it can be challenging to determine



the BMI nadir for many children. Rather than having a U-shaped pattern, as shown in several figures in the literature (2,11,33–35), BMI values between ages 2 and <8 years in the current study frequently showed irregular patterns with a plateau or several nonadjacent BMI values close to the minimum. Some of these patterns are evident in a 2017 study of growth trajectories among children (37).

Figure 3 shows BMI values at various ages for 16 randomly selected children in the current study, with 10 to 12 examinations between ages 2 and <8 years. Some children (e.g., 3, 10) exhibited a U-shaped pattern, but others had BMI levels that generally decreased (e.g., 8, 13) or had several BMI values at different ages that were close to the minimum BMI (e.g., 2, 7, 9, 16). Because the BMI values of most children showed a zigzag pattern, with alternating increases and decreases, it may be challenging for a practitioner to determine rebound age.

In order to address the difficulties in determining rebound age, some investigators have used various regression models to identify rebound age (3,6,37), and others (35,37–39) have required all BMI values after the nadir to show increases of more than 0.1 kg/m<sup>2</sup>. However, this latter approach would substantially increase the rebound age for many children in Figure 3 (e.g., 7, 12, 15, 16). Furthermore, some children had a final BMI lower than at the penultimate visit (e.g., 1, 13), complicating this technique's use.

We used lowess to determine rebound age but obtained very similar results with other techniques. However, minor errors in measuring weight and height, particularly if height is recorded in whole inches, can lead to relatively large BMI differences (40) and account for some of the patterns seen in Figure 3. For example, a child with a weight of 39 lb (17.7 kg) and a height of 42 in (106.7 cm) would have a BMI of 15.5 kg/m<sup>2</sup>. However, if this child's weight and height were recorded as 39.5 lb and 41 in, the BMI will be 16.5, a difference of 1 kg/m<sup>2</sup>. Measurement errors such as measuring height with or without shoes and the day-to-day variability in weight would further complicate the determination of the rebound age in clinical practice. In contrast to the difficulty in determining rebound age, we found that a single BMI measurement at age 2 years provided almost as much information, whereas BMI at age 3 years provided more information than did the age at BMI rebound on BMI levels after age 14 years.

Although the prevalence of obesity in PEDSnet data agrees well with National Health and Nutrition Examination Study (NHANES) (41) estimates and the tracking of BMI in studies based on EHR are similar to the tracking in research studies (42), there are several limitations in the secondary use of EHR data. First, the analysis depends on the accuracy of data generated in the context of clinical care. PEDSnet implements a comprehensive data quality assessment workflow to characterize and maximize data quality (21). Although errors in height and weight data will persist, these are mitigated by repeated measurements (41) and the use of the Daymont algorithm (24). Second, as the data are generated in the context of clinical care, they reflect practice patterns. For example, the larger number of weights than heights in the data reflects expected outpatient practice (41). Third, the population of children receiving care at PEDSnet member institutions, including inpatient and specialty care, may result in an overrepresentation of children with illness, injury, and other medical conditions.

Imposing data sufficiency requirements such as follow-up time or the number of measurements could further increase bias (43). We required children to have at least one weight and height measurement for each year of age between ages 2 and 7 years, along with a measurement after age 14 years. This requirement, resulting in at least six BMI values for determining rebound age, substantially reduced the sample size and may limit the generalizability of our results to children from more stable and adherent families. However, the mean BMI values for each year of age among the 12,228 children were very similar to the age-specific BMI values among children in the EHR database from the four hospitals included in the current study, as was the mean BMIz after age 14 years. However, a larger proportion of children in the present analyses were Black (31%) than in the four hospitals (22%). We also conducted additional analyses among 38,600 children examined at least one time at ages 2 to 3 years, 4 to 5 years, and 6 to 7 years (rather than at each year of age). These results confirmed that a single BMI measured at ages 2 or 3 years provided more information on subsequent BMI levels than rebound age. Furthermore, although we used the mean BMI for children with multiple BMI values for a given year of age, we obtained similar results by randomly selecting one of these BMI values. However, it should be noted that we did not have information about the pubertal status of the children at the final examination, nor did we have information about other predictors of obesity, such as breastfeeding.

The PEDSnet data used in the current study reflect a reasonably broad geographic distribution of the United States, but there are gaps, and children in rural areas are underrepresented. In the entire PEDSnet data set, about 4% of the children appear to have received care at multiple institutions and are represented as different individuals from each site.

## CONCLUSION

Our results confirm that an early BMI rebound is associated with higher BMI levels in adolescence. However, as compared with the information provided by rebound age ( $R^2 = 0.24$ ) on BMI levels after age 14 years, a child's BMI at age 2 years provides almost as much information (0.23), whereas the BMI at age 3 years conveys more information (0.32). Because it can be challenging to determine a child's rebound age, particularly from a small number of BMI values, it may be more practical to identify subsequent obesity at a very early age by a child's BMI at ages 2 or 3 years.

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### Study Importance

#### What is already known?

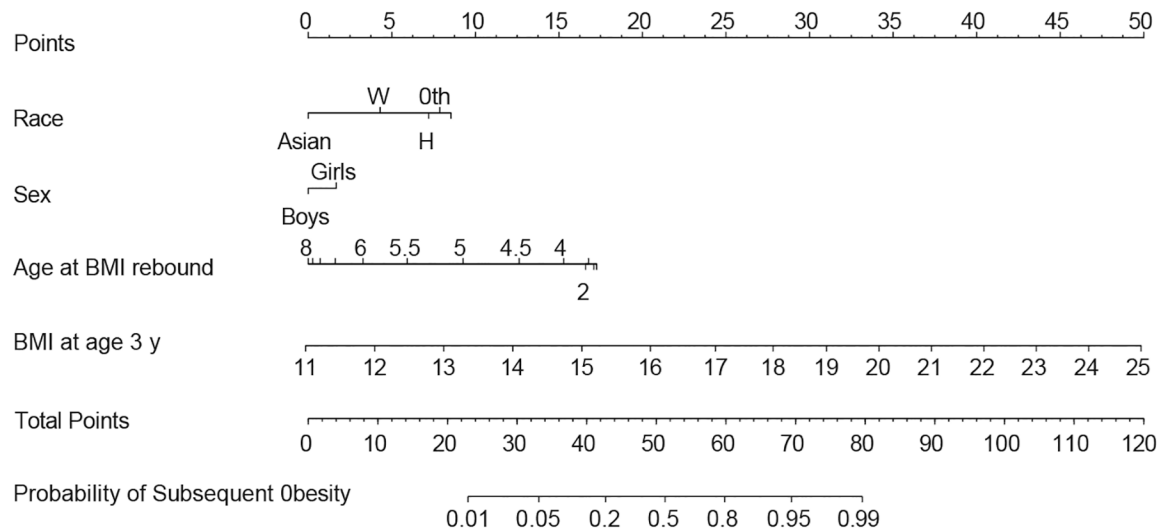
- An early adiposity rebound (e.g., <4 years) increases the risk for obesity in adolescence and adulthood.

#### What does this study add?

- A child's BMI at age 3 years provides more information on BMI after age 14 years than does the child's rebound age (multiple  $R^2$ s of 0.32 vs. 0.24).
- Information on age at adiposity rebound provides no information on BMI levels after age 14 years if the BMI at age 6 years is known.

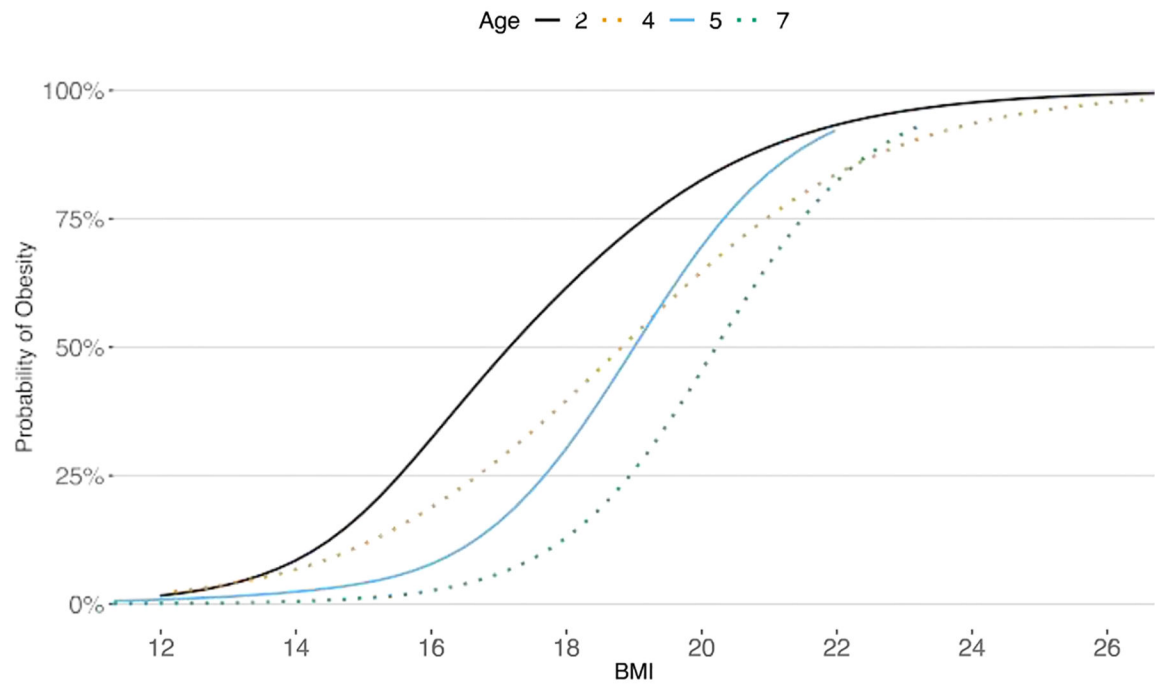
#### How might these results change the direction of research or the focus of clinical practice?

- Because it can be challenging to determine adiposity rebound, it may be best to use the BMI at age 3 years to predict subsequent obesity.



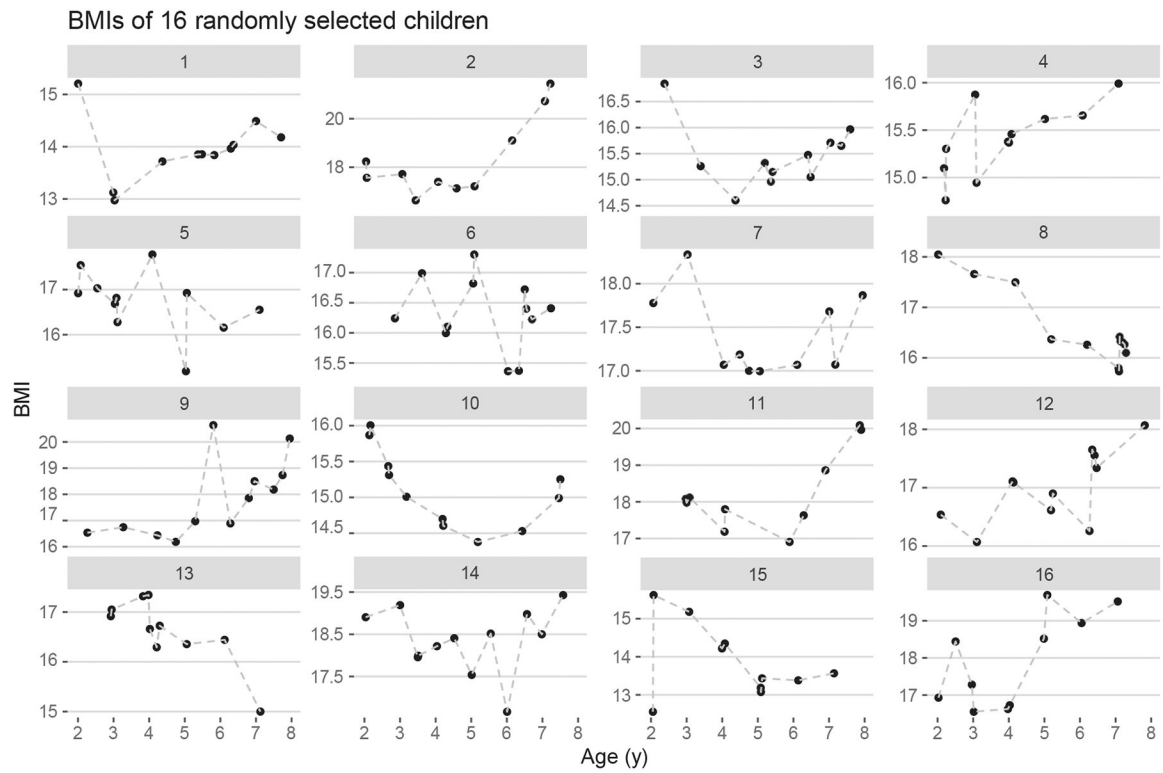
**FIGURE 1.**

Nomogram for predicted probability of obesity after age 14 years (bottom row) based on sex, race/ethnicity, rebound age, and BMI at age 3 years. For each predictor variable, the number of points (top line) would be calculated. These values would then be summed to derive a child's total points and probability of obesity (final two rows). For the race/ethnicity categories, "W" indicates White non-Hispanic children, "H" indicates Hispanic children, and "Oth" indicates a race coded as other. Black children had nine points



**FIGURE 2.**

Predicted probability of obesity after age 14 years by BMI level at a rebound age of 2, 4, 5, or 7 years. Predicted probabilities, based on logistic regression, are for a 15-year-old individual. BMI values represent the BMI or mean BMI at the rebound age

**FIGURE 3.**

BMI values of 16 children who were randomly selected from children who had 10 to 12 visits between ages 2 years and <8 years



**TABLE 1**

Relation of age at rebound to various characteristics at the time of the rebound and to values at the final visit among 12,228 children (PEDSnet)<sup>a</sup>

		Age (y) at BMI rebound				Correlation with rebound age	Correlation with BMI at rebound age
		<3	3–4.9	5–6.9	7		
At BMI rebound	<i>N</i>	3,233	2,764	3,627	2,604		
	Girls (%)	55%	50%	45%	43%		
	Age	2.2 ± 0.3	4.0 ± 0.5	5.7 ± 0.5	7.5 ± 0.3		
	BMI	16.1 ± 1.9	15.8 ± 1.5	15.3 ± 1.3	15.1 ± 1.2	----	----
	BMIz	−0.25 ± 1.3	0.17 ± 1.2	−0.10 ± 1.0	−0.44 ± 0.9	----	----
	Height-for-age <i>z</i> score	0.57 ± 1.17	0.44 ± 1.11	0.16 ± 1.06	−0.23 ± 1.09	---	---
At last visit	Age	15.5 ± 1.2	15.5 ± 1.2	15.5 ± 1.2	15.4 ± 1.2	----	----
	BMI	27.4 ± 7.5	24.9 ± 5.8	21.9 ± 4.1	20.2 ± 3.4	−0.44 (−0.43 to −0.46)	0.57 (0.56 to 0.58)
	BMIz	1.20 ± 1.1	0.84 ± 1.0	0.27 ± 1.0	−0.17 ± 1.0	−0.46 (−0.47 to −0.44)	0.57 (0.56 to 0.59)
	Obesity (%)	36%	23%	6.9%	2.5%	---	---

Values are mean ± SD or correlation coefficient (95% CI).

<sup>a</sup>Mean follow-up time: 13.3 years (range: 11.1–17.9 years).

**TABLE 2**

Stratified analyses of longitudinal correlations between BMIz at last visit and both age at rebound and BMI at age at rebound

		Correlation with BMIz at last visit	
	<i>N</i>	Age at rebound	BMI at rebound
Sex			
Boys	6,348	−0.44	0.58
Girls	5,880	−0.47	0.60
Race/ethnicity			
White	6,562	−0.43	0.57
Black	3,743	−0.48	0.57
Hispanic	964	−0.47	0.59
Asian	293	−0.43	0.55
Multiple	133	−0.30	0.55
Other	149	−0.50	0.50
Unknown	384	−0.45	0.61

Abbreviation: BMIz, BMI z score.

TABLE 3

Multiple  $R^2$ s for various regression models predicting final BMI from covariates<sup>a</sup>, age<sub>rebound</sub>, and BMI value at various ages (PEDSnet)

BMI at specified age (y)	Multiple $R^2$	
	BMI <sup>b</sup>	BMI and rebound age
Age 2	0.23	0.42
Age 3	0.32	0.43
Age 4	0.41	0.48
Age 5	0.50	0.54
Age 6	0.57	0.58
Age 7	0.62	0.62

<sup>a</sup>Linear regression models include sex, childhood height-for-age z score at specified age, and last age as covariates. The  $R^2$  of a model with these three covariates alone was 0.08, whereas the  $R^2$  of a model with the covariates and rebound<sub>age</sub> was 0.24.

<sup>b</sup>For children who had more than one BMI value per year of age, we used the mean BMI in the analyses. Additional models that included one randomly selected BMI for a given age yielded virtually identical results.