Acceleration of BMI in Early Childhood and Risk of Sustained Obesity

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ABSTRACT

BACKGROUND

The dynamics of body-mass index (BMI) in children from birth to adolescence are unclear, and whether susceptibility for the development of sustained obesity occurs at a specific age in children is important to determine.

METHODS

To assess the age at onset of obesity, we performed prospective and retrospective analyses of the course of BMI over time in a population-based sample of 51,505 children for whom sequential anthropometric data were available during childhood (0 to 14 years of age) and adolescence (15 to 18 years of age). In addition, we assessed the dynamics of annual BMI increments, defined as the change in BMI standard-deviation score per year, during childhood in 34,196 children.

RESULTS

In retrospective analyses, we found that most of the adolescents with normal weight had always had a normal weight throughout childhood. Approximately half (53%) of the obese adolescents had been overweight or obese from 5 years of age onward, and the BMI standard-deviation score further increased with age. In prospective analyses, we found that almost 90% of the children who were obese at 3 years of age were overweight or obese in adolescence. Among the adolescents who were obese, the greatest acceleration in annual BMI increments had occurred between 2 and 6 years of age, with a further rise in BMI percentile thereafter. High acceleration in annual BMI increments during the preschool years (but not during the school years) was associated with a risk of overweight or obesity in adolescence that was 1.4 times as high as the risk among children who had had stable BMI. The rate of overweight or obesity in adolescence was higher among children who had been large for gestational age at birth (43.7%) than among those who had been at an appropriate weight for gestational age (28.4%) or small for gestational age (27.2%), which corresponded to a risk of adolescent obesity that was 1.55 times as high among those who had been large for gestational age as among the other groups.

CONCLUSIONS

Among obese adolescents, the most rapid weight gain had occurred between 2 and 6 years of age; most children who were obese at that age were obese in adolescence. (Funded by the German Research Council for the Clinical Research Center "Obesity Mechanisms" and others; ClinicalTrials.gov number, NCT03072537.)

From the Center for Pediatric Research, University Hospital for Children and Adolescents (M.G., T.L., U.S., R.P., W.K., A.K.), Leipzig Research Center for Civilization Diseases (LIFE Child) (M.G., M.V., W.K., A.K.), CrescNet, Medical Faculty (R.G., E.K., R.P.), and Integrated Research and Treatment Center (IFB), Adiposity Diseases, University Medical Center (T.L., U.S., A.K.), University of Leipzig, Leipzig, Germany. Address reprint requests to Dr. Körner at the Center for Pediatric Research, University Hospital for Children and Adolescents, University of Leipzig, Liebigstr. 20a 04103 Leipzig, Germany, or at antje.koerner@medizin .uni-leipzig.de.

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Ascertainment of the age at which obesity develops and determination of whether there are specific critical periods in childhood and adolescence that are characterized by accelerated and sustained weight gain are thus important and may aid in the development of effective preventive strategies.[6] Studies to predict the development of obesity on the basis of childhood BMI have suggested a positive correlation, but most have evaluated outcomes at a young age[8,9] or have had a relatively late baseline evaluation,[10] a short observation period,[11,12] or a small sample size.[13-16] The exact pattern of weight gain during childhood that leads to sustained obesity is unclear and warrants longitudinal data that cover the entire age span from infancy to adolescence in a population of an appropriate sample size. In the current study, we tracked BMI in individual children from infancy to adolescence in a large population to determine the age at which children are most vulnerable to excessive weight gain that ultimately results in obesity in adolescence.

METHODS

STUDY POPULATION

We retrieved data from the CrescNet patient registry, a network for clinical and scientific monitoring of growth data in children.[17] Participating pediatricians regularly transfer anonymized data on the age, sex, height, and weight of children seen for well-child visits or other consultations. The registry was approved by the Federal Saxonian Data Protection Authority and is registered at ClinicalTrials.gov. Details regarding the registry are provided in Section Ia in the Supplementary Appendix, available with the full text of this article at NEJM.org. There were no agreements concerning confidentiality of the data between the sponsors and the authors or the institutions involved in this study.

We included children who had at least one visit with a participating pediatrician between 0 and 14.9 years of age ("childhood") and another visit between 15.0 and 18.9 years of age ("adolescence"); a total of 51,505 children with 336,227 data points met these criteria. Details are provided in Section Ib in the Supplementary Appendix.

STATISTICAL ANALYSIS

To track BMI data, we categorized children according to specific age groups: 0 (0.0 to 0.9) years, 1 (1.0 to 1.9) years, 2 (2.0 to 2.9) years, and continuing to 14 (14.0 to 14.9) years and 15 to 18 (15.0 to 18.9) years. If data from multiple visits were available for a child in a given age group, we chose the visit closest to the approximate middle of the age range of the age group (e.g., 0.5 years, 1.5 years, or 2.5 years); for the age group defined as 15 to 18 years, we chose the visit closest to 15.5 years of age. Hence, children had a minimum of 2 visits and a maximum of 16 visits, with 1 visit per age group.

We converted BMI and height to standard-deviation scores by applying German reference data according to current German national guidelines.[18] Accordingly, we assigned children to groups that included underweight (BMI standard-deviation score of −5 or more to less than −1.28), normal weight (BMI standard-deviation score of −1.28 or more to less than 1.28), overweight (BMI standard-deviation score of 1.28 or more to less than 1.88), and obesity (BMI standard-deviation score of 1.88 or more to less than 5). In retrospective analyses, we determined the percentages of patients included in each of these weight groups during the childhood years according to their weight group in adolescence. In prospective analyses, we calculated, on the basis of the patients' weight category in childhood, the percentages whose weight group in adolescence became underweight, normal weight, overweight, or obese (see Section Ic in the Supplementary Appendix).

To assess the effect of annual changes in BMI standard-deviation score, we analyzed data from children who had at least two visits within a 1-year interval during childhood and had an additional visit between 15 and 18 years of age. We excluded patients who had an increase or decrease in BMI standard-deviation score of more than 2.0. To compare the annual change in BMI standard-deviation score at preschool age (2 to

6 years) with that at school age (8 to 12 years), we stratified the changes according to stable change in BMI standard-deviation score (change of more than −0.2 to less than 0.2) and accelerated change in BMI standard-deviation score (change of 0.2 or more to less than 2.0) and calculated the probability and relative risk for overweight or obesity (defined as a BMI standard-deviation score of 1.28 or more) in adolescence.

We analyzed the dynamics of BMI, the change in BMI standard-deviation score, and the probability of overweight in adolescence on the basis of three birth-weight categories: appropriate for gestational age (birth-weight standard-deviation score of −1.28 or more to less than 1.28), large for gestational age (birth-weight standard-deviation score of 1.28 or more), or small for gestational age (birth-weight standard-deviation score of less than −1.28). The analyses according to birth weight were performed in a subgroup of 3893 adolescents (with 14,876 data points).

In addition, we analyzed data from the Leipzig Research Center for Civilization Diseases (LIFE) Child study[19] to investigate the effect of maternal weight on BMI dynamics in children. Details of the study are provided in Section III in the Supplementary Appendix. All the analyses of the current study were performed with the use of the R statistical package, version 3.4.3.

RESULTS

TRACKING OF BMI FROM CHILDHOOD TO ADOLESCENCE

Anthropometric data from our study population across the age ranges are provided in Section Id in the Supplementary Appendix. A total of 51,505 children with 241,715 data points were included in the assessment of BMI tracking (see Sections Ic and Id in the Supplementary Appendix).

Figure 1 shows the results of the retrospective analysis, in which we assessed the percentage of children who were underweight, had normal weight, were overweight, or were obese at prespecified ages during childhood according to their weight group in adolescence. A majority of the adolescents with normal weight had had a normal weight throughout their childhood (Fig. 1B). A majority of the adolescents who were obese had had a normal weight as infants, but by the time they were 5 years of age, they had already become overweight (22%) or obese
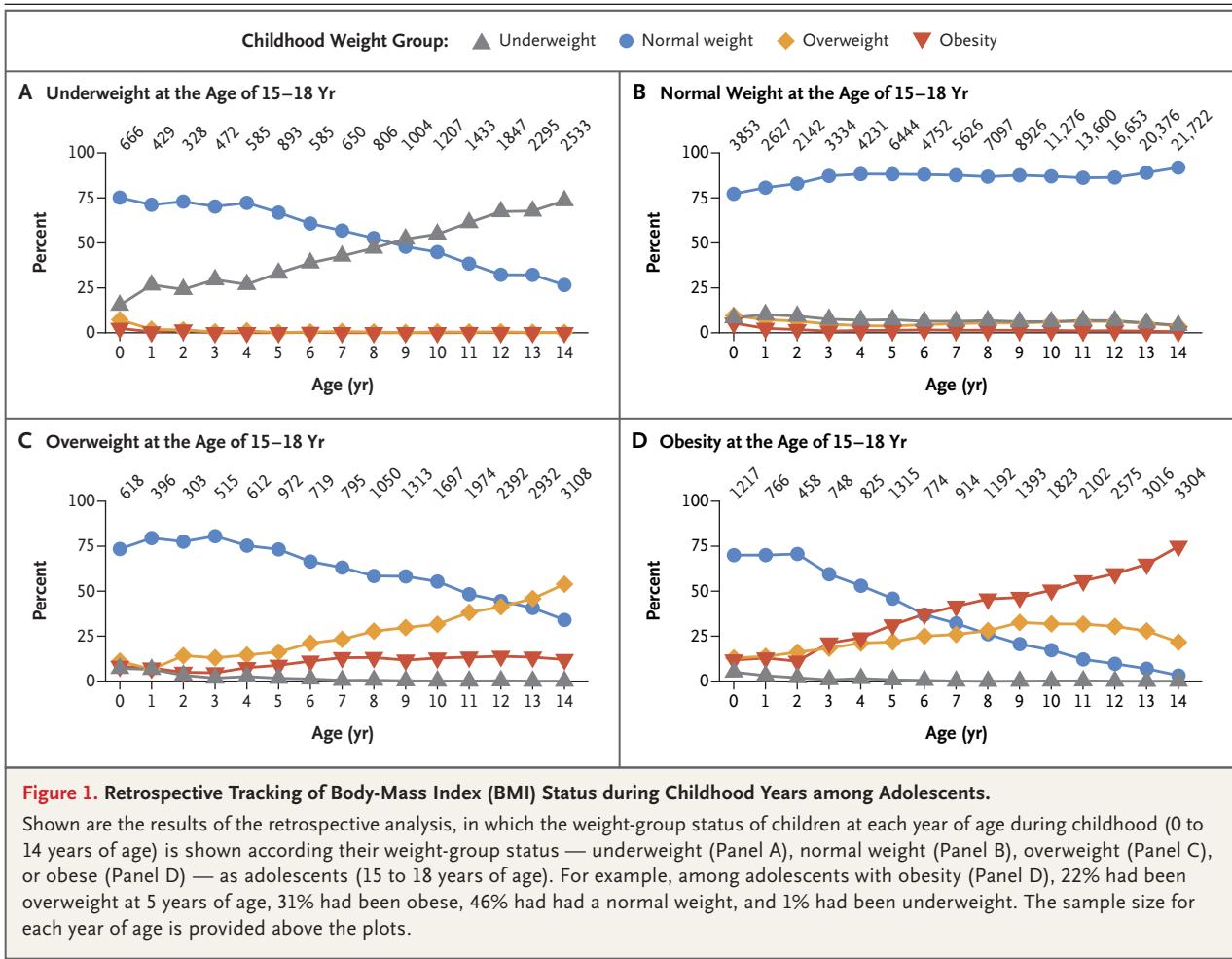
(31%); the percentage of obese children who became obese adolescents increased continuously with age (Fig. 1D). When the normal-weight adolescent group was further stratified according to lower (<0) or higher (≥0) BMI standard-deviation score, we found that most of the adolescents in each subgroup remained in the weight group that they had been in beginning at 5 years of age and that very few children in the lower-weight subgroup became obese in adolescence (Section II in the Supplementary Appendix).

Figure 2 shows the results of the prospective analysis, in which we assessed the percentage of children in each weight category in adolescence relative to the weight group during childhood to estimate the probability that an obese child would be obese as an adolescent. Approximately 50% of the children who were overweight at 2 years of age or younger returned to a normal weight in adolescence (Fig. 2C), whereas among children who were obese at 3 years of age, the probability of being overweight or obese in adolescence was almost 90%, and only a minority of young children with obesity returned to a normal weight (Fig. 2D). Children who were lean (BMI standard-deviation score <0) rarely became overweight or obese in adolescence (Section II in the Supplementary Appendix). These age-related BMI patterns were found to be similar in boys and girls.

ACCELERATION OF BMI IN CHILDHOOD AND DEVELOPMENT OF OBESITY IN ADOLESCENCE

To assess the age at which the most pronounced acceleration of BMI occurred, we examined the annual change in BMI standard-deviation score during childhood in relation to the occurrence of a BMI standard-deviation score of 1.28 or more in adolescence. A total of 34,196 patients with 245,092 visits were assessed. The overall annual mean (±SD) change in BMI standard-deviation score was 0.020±0.001.

The mean BMI standard-deviation score and the annual change in BMI standard-deviation score were stable among children who were underweight or had normal weight, remaining close to the expected mean BMI standard-deviation score of 0 (Fig. 3), whereas children who were overweight or obese already had an elevated BMI standard-deviation score in infancy that increased continuously throughout childhood (Fig. 3A). Hence, the BMI standard-deviation score was

Figure 1. Retrospective Tracking of Body-Mass Index (BMI) Status during Childhood Years among Adolescents.

Shown are the results of the retrospective analysis, in which the weight-group status of children at each year of age during childhood (0 to 14 years of age) is shown according their weight-group status — underweight (Panel A), normal weight (Panel B), overweight (Panel C), or obese (Panel D) — as adolescents (15 to 18 years of age). For example, among adolescents with obesity (Panel D), 22% had been overweight at 5 years of age, 31% had been obese, 46% had had a normal weight, and 1% had been underweight. The sample size for each year of age is provided above the plots.
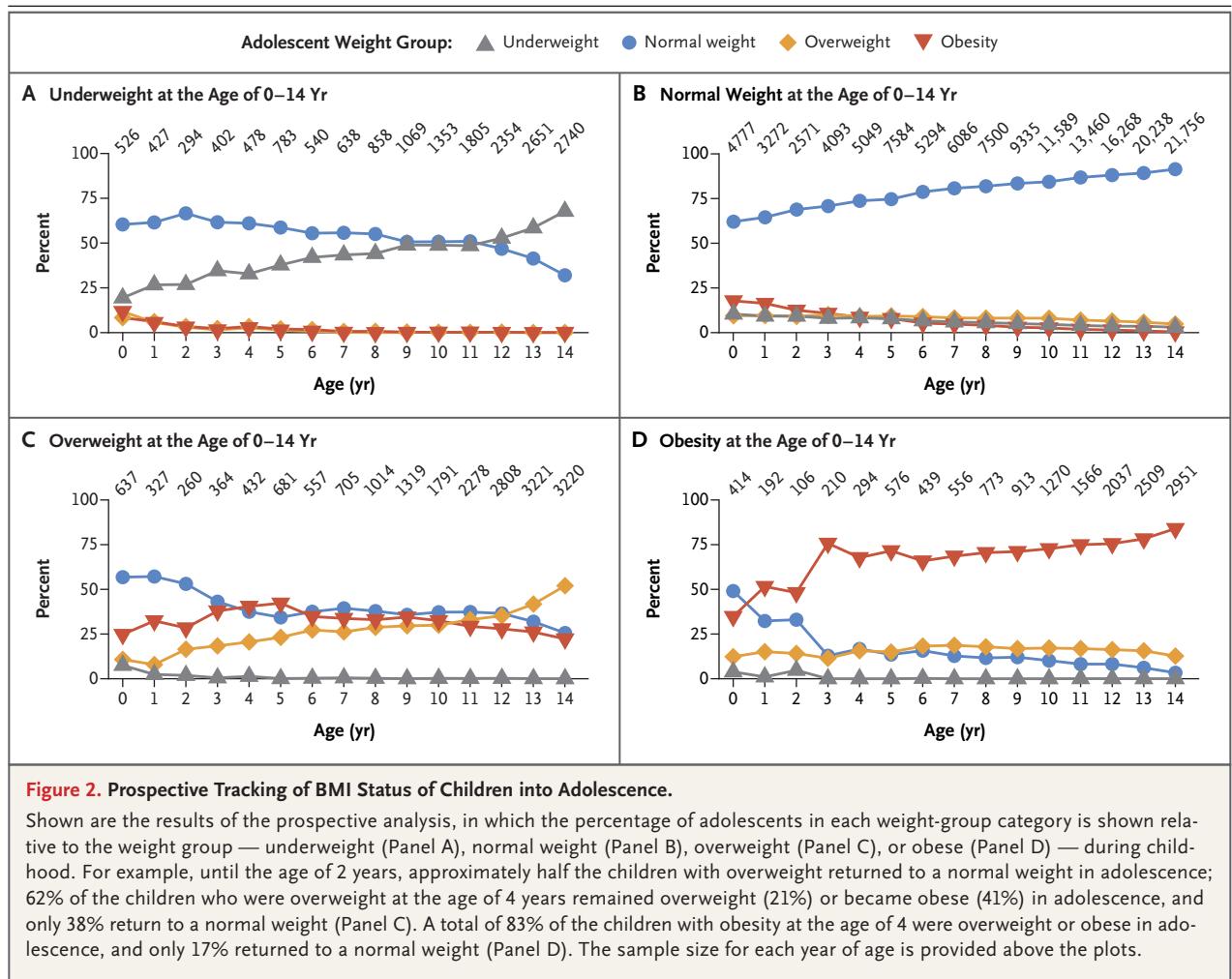
much more stable among adolescents in the normal-weight group than among those in the overweight or obese group. Among overweight and obese adolescents, the greatest acceleration in the BMI standard-deviation score had occurred between 2 and 6 years of age (Fig. 3B), and the annual change in BMI standard-deviation score had remained positive (although at a lower rate) thereafter, which led to a greater degree of obesity. These patterns were found to be similar in boys and girls. Hence, the greatest weight accumulation occurred in early childhood with a further steady increase in BMI standard-deviation score thereafter, which eventually led to overweight or obesity.

The probability of overweight or obesity in adolescence was higher among children who had had an accelerated annual change in the BMI standard-deviation score (change of 0.2 or more to less than 2.0) during the preschool years

(but not among those who had had an accelerated change during the school years) than among those whose BMI had been stable (change of more than −0.2 to less than 0.2) during the preschool years (28.6% vs. 20.0%; relative risk, 1.43; 95% confidence interval [CI], 1.35 to 1.49). Details are provided in Section II in the Supplementary Appendix.

EFFECT OF BIRTH WEIGHT ON BMI DYNAMICS DURING CHILDHOOD AND ADOLESCENCE

Children who were large for gestational age at birth continued to have a consistently higher BMI during childhood and adolescence than children who had an appropriate weight for gestational age or were small for gestational age (Fig. 4A). The annual change in the BMI standard-deviation score remained relatively stable in all three birth-weight groups (Fig. 4B). Almost half (43.7%) of children who were large for gestational

Figure 2. Prospective Tracking of BMI Status of Children into Adolescence.

Shown are the results of the prospective analysis, in which the percentage of adolescents in each weight-group category is shown relative to the weight group — underweight (Panel A), normal weight (Panel B), overweight (Panel C), or obese (Panel D) — during childhood. For example, until the age of 2 years, approximately half the children with overweight returned to a normal weight in adolescence; 62% of the children who were overweight at the age of 4 years remained overweight (21%) or became obese (41%) in adolescence, and only 38% return to a normal weight (Panel C). A total of 83% of the children with obesity at the age of 4 were overweight or obese in adolescence, and only 17% returned to a normal weight (Panel D). The sample size for each year of age is provided above the plots.

age at birth were overweight or obese in adolescence, whereas less than 30% of children who had an appropriate weight for gestational age or were small for gestational age became overweight or obese in adolescence (P<0.001) (Fig. 4C), which implies a relative risk for overweight or obesity of 1.55 (95% CI, 1.38 to 1.74) among adolescents who had been large for gestational age at birth. Conversely, 17.3% of adolescents who were overweight or obese had been large for gestational age at birth, whereas only 9.6% of the adolescents who had a normal weight or were underweight had been large for gestational age (Fig. 4D). Therefore, being large at birth conferred a significant risk of obesity during childhood and adolescence, but the dynamics of BMI patterns (i.e., when obesity first manifested) were similar among the various birth-weight groups.

EFFECT OF MATERNAL WEIGHT ON BMI DYNAMICS DURING CHILDHOOD

We analyzed data from 1618 mother–child pairs from the LIFE Child study[19] to assess the effect of maternal weight on dynamic BMI development in children. We found that children of mothers who were overweight or obese had higher birth weights and, thereafter, increasingly higher BMI than children of mothers who were not overweight or obese. However, within both the group that included children who were underweight or had a normal weight and the group that included children who were overweight or obese, the children of mothers who were underweight or had normal weight did not differ substantially from the children of mothers who were overweight or obese with respect to either the absolute BMI standard-deviation score or the annual change in BMI standard-deviation score (Section
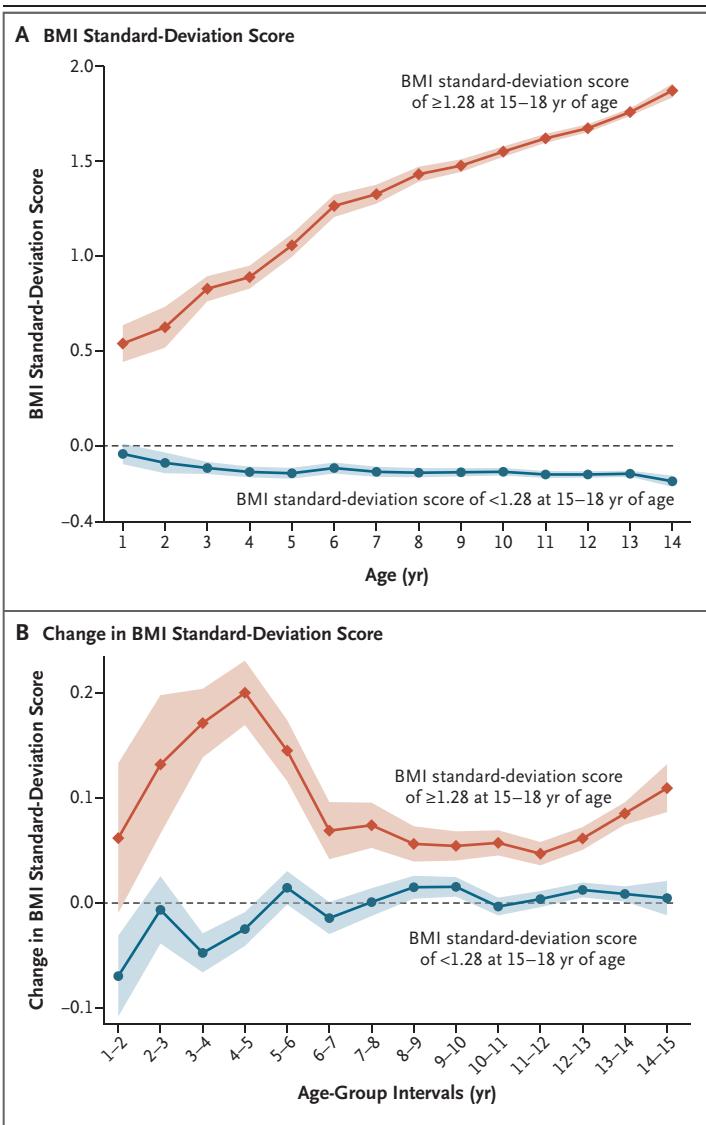
A BMI Standard-Deviation Score

B Change in BMI Standard-Deviation Score

Figure 3. Dynamics of BMI Changes during Childhood.

Shown are the BMI standard-deviation score (Panel A) and the change in BMI standard-deviation score in 1-year age-group intervals (e.g., 1 to 2 represents the change from the 1-year age group to the 2-year age group) (Panel B), according to adolescent weight categories of underweight or normal weight (BMI standard-deviation score of <1.28; 26,883 adolescents) and overweight or obesity (BMI standard-deviation score ≥1.28; 7313 adolescents). Values are shown as means; shaded areas indicate 95% confidence intervals. Beginning at 1 year of age, the mean BMI standard-deviation score of the adolescents who were overweight or obese was already significantly higher than that of the adolescents who were underweight or had a normal weight, and the score continued to increase with increasing age (Panel A). Adolescents with overweight or obesity had the greatest annual increases in the BMI standard-deviation score between 2 and 6 years of age (Panel B).

timing or dynamics of BMI development during childhood.

DISCUSSION

In this population-based longitudinal study, we found that overweight and obesity manifested early in childhood. A majority of children who were obese by 3 years of age remained obese into adolescence. Among adolescents who were overweight or obese, the most excessive weight gain (i.e., the most rapid BMI acceleration) had occurred between 2 and 6 years of age. Even after this period of rapid weight gain, the BMI continued to increase at a lower but still positive rate, which led to a greater degree of obesity in this group, whereas in the group of adolescents with normal weight, the BMI standard-deviation score had been stable throughout childhood. Children who were large for gestational age at birth and children whose mothers were obese had an especially high risk of obesity, although the timing of the development of obesity did not differ from that among children whose mothers were of normal weight.

The mean BMI and the prevalence of obesity in our population were similar to those in recent representative national samples[20,21] but are higher than those reported in earlier studies.[22] A secular trend of increasing prevalence of obesity has been described previously,[23,24] and the secular upward divergence of the 97th BMI percentile also occurs in early childhood,[5] which is consistent with the age at which we observed the most rapid weight gain.
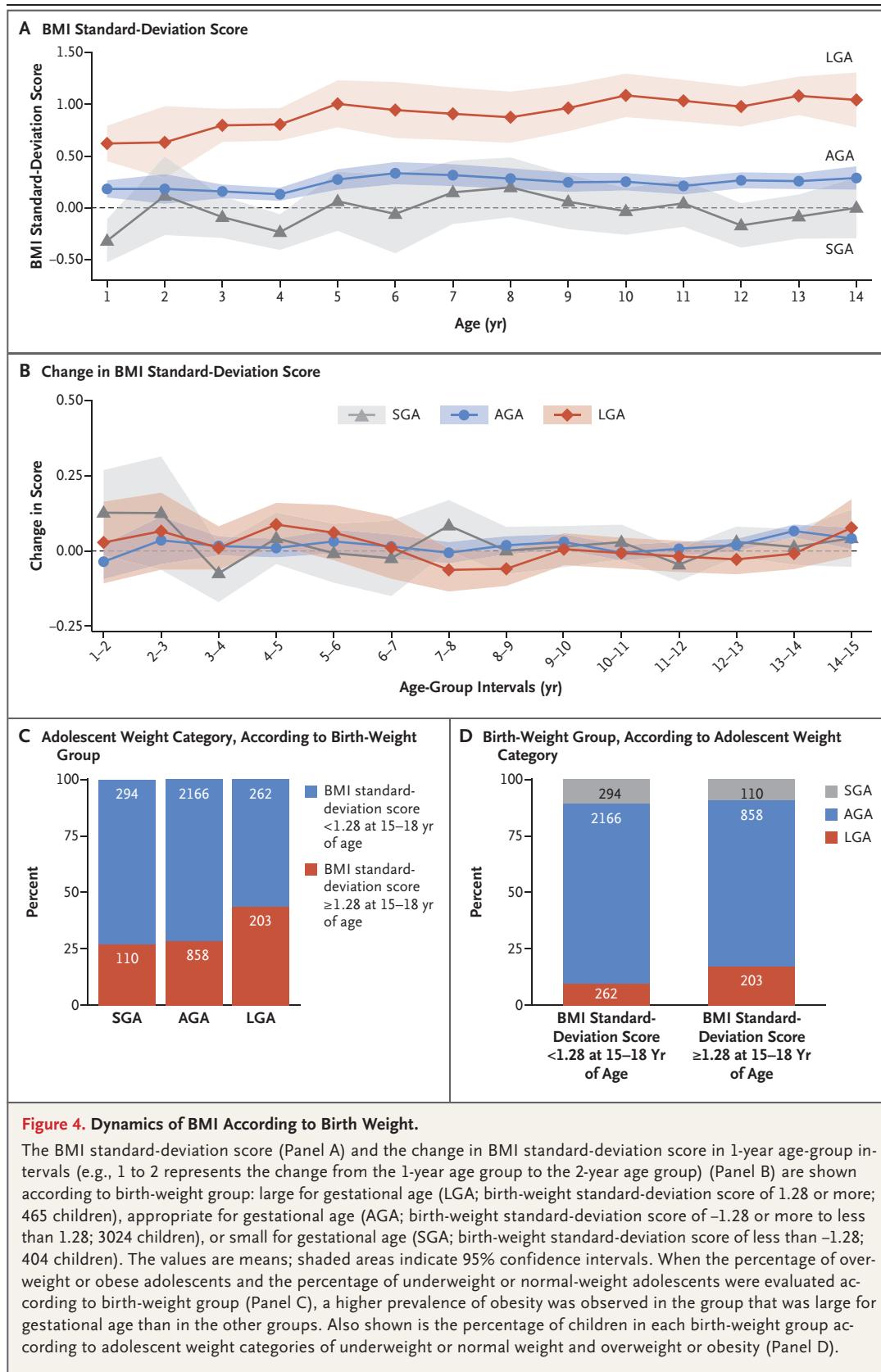
With our large sample size and a longitudinal study design that covered the entire age span from infancy to adolescence, we can discern that early childhood is the critical age for the development of sustained obesity. This period encompasses the "adiposity rebound," the phase in early childhood during which the BMI starts to increase again, after having reached a nadir after infancy.[25] Epidemiologic studies have shown that the risk of childhood obesity is far greater among children with an earlier or pronounced adiposity rebound.[26] An upward deviation in BMI percentile may be an even more direct predictor of later adiposity.[27] Therefore, the specific dynamics and patterns of BMI in this early childhood period, rather than the absolute BMI, appear to be important factors in identifying children at risk for obesity later in life.[28]

III in the Supplementary Appendix). Overall, these data confirm maternal overweight as an independent risk factor for childhood obesity; however, maternal overweight did not affect the

Figure 4. Dynamics of BMI According to Birth Weight.

The BMI standard-deviation score (Panel A) and the change in BMI standard-deviation score in 1-year age-group intervals (e.g., 1 to 2 represents the change from the 1-year age group to the 2-year age group) (Panel B) are shown according to birth-weight group: large for gestational age (LGA; birth-weight standard-deviation score of 1.28 or more; 465 children), appropriate for gestational age (AGA; birth-weight standard-deviation score of −1.28 or more to less than 1.28; 3024 children), or small for gestational age (SGA; birth-weight standard-deviation score of less than −1.28; 404 children). The values are means; shaded areas indicate 95% confidence intervals. When the percentage of overweight or obese adolescents and the percentage of underweight or normal-weight adolescents were evaluated according to birth-weight group (Panel C), a higher prevalence of obesity was observed in the group that was large for gestational age than in the other groups. Also shown is the percentage of children in each birth-weight group according to adolescent weight categories of underweight or normal weight and overweight or obesity (Panel D).

To date, most studies have not assessed an age span as comprehensive as that in our study, have had a limited sample size (fewer than 1000 children),[16] or even if well-powered, have been restricted to an observational period that assessed only the first 2 years of life[12] or that did not begin until 7 years of age and hence began after the most pronounced weight gain had occurred.[10] Nevertheless, a considerable correlation exists between a high BMI during early childhood and prevalence of obesity later in life.[4,9,12,29,30] The probability that young children who are obese will return to a normal weight in adolescence appears to be less than 20% and decreases further with age.

Children with normal weight showed much less variation in BMI standard-deviation score throughout childhood and adolescence than children who were obese. This finding may imply distinct dynamic BMI patterns in children with normal weight as compared with obese children. In studies that evaluated developmental trajectories of BMI, groups of children with "high rising BMI trajectory" diverged from those with fairly stable BMI trajectories beginning at approximately 3 years of age.[31,32]

Our data further showed that children who were large for gestational age at birth retained a higher BMI throughout childhood and adolescence, and almost half these children became overweight or obese in adolescence. This finding may seem to contradict the "Barker hypothesis" of low birth weight being associated with an increased likelihood of diabetes and cardiovascular complications, although not obesity per se, in adulthood.[33] Rather, a rapid weight gain during childhood in children who had been small for gestational age at birth, even with the absolute BMI remaining within normal limits, was associated with later insulin resistance and coronary events.[34] Hence, the association of cardiovascular disease and diabetes with low birth weight and rapid catch-up should be differentiated from the association of obesity with high birth weight.

The dynamic of increasing BMI does not end with adolescence but continues into adulthood.[4] Obesity rates among adults are considerably higher than those among children, and most adults with obesity had had normal weight in childhood.[35] However, if obesity does develop in childhood and continues through adolescence, it tends to persist; most obese adolescents become obese adults.[4]

With regard to prevention, the clinical manifestation of obesity is a late starting point. An excessive weight gain (an annual increase of ≥0.2 in the BMI standard-deviation score) during the preschool years was found to be even more relevant for adolescent overweight than excessive weight gain during late childhood and can be regarded as an early sign of ensuing obesity in adolescence that appears much earlier than the actual clinical manifestation of overweight.[36] This same age interval of 2 to 6 years has been described as an important growth period for the prediction of adult overweight.[16]

A practical clinical implication of our study results would be surveillance for BMI acceleration, which should be recognized before 6 years of age, even in the absence of obesity. The tracking of growth and weight patterns, particularly in children with predisposing factors (e.g., maternal overweight or large-for-gestational-age status at birth), may help to identify children at increased risk and prompt early intervention even before overweight is evident. It is therefore important for health care professionals, educational staff, and parents to become more sensitive to this critical time period.

In addition to the mere expansion of fat mass, alterations in adipose tissue function occur in early childhood in parallel with the clinical increase in BMI.[37] The early exposure to excess and dysfunctional fat triggers the development of preclinical metabolic and cardiovascular changes even in childhood.[38] Epidemiologic evidence suggests that early childhood may be a sensitive period for arteriosclerosis on the basis of a positive association between childhood BMI at 4 years of age and high carotid intima media thickness in men at 60 to 64 years of age.[39]

The major strengths of the current study are the population-based design with a large, unselected cohort encompassing more than 51,000 children and 300,000 measurements across the entire age span from infancy to adolescence; the longitudinal design that allowed for childhood and adolescence data to be available for every child; and the specific evaluation of the rate of weight gain in 1-year intervals. In addition, selection bias was reduced because anthropometric data were obtained directly and uniformly at pediatric offices for all children who were seen by the participating pediatricians, regardless of the reasons for the visit, and were not dependent on active participation rates; hence they were

less biased by socially patterned nonresponse. Finally, the analyses are based on real measurements rather than on the modeling of synthetic BMI trends from prediction models.

There are several limitations of the study. First, the number of visits ranged from 2 to 15, and there was some variation in the length of observation intervals because this was not a prospectively designed study but rather a patient registry study in which data were recorded at regularly planned and unplanned visits. Still, owing to the German system of well-child surveillance at defined ages, early childhood in particular is well represented with sequential data. Second, many of the children whose data were included in the CrescNet patient registry could not be included in our study owing to missing data points beyond 14 years of age; most of the children had simply not yet reached that age, and many were no longer being seen by pediatricians. Third, because we did not have access to the complete medical histories of the children, we cannot entirely exclude the possibility that chronically ill children were included in the data set, although this limitation is probably minimized by the large sample size. Finally, data on parental weight and on perinatal risk factors for obesity (e.g., maternal diabetes, maternal smoking history, and breast-feeding) would be desirable.[20] Nevertheless, our objective was to determine, on the basis of BMI percentiles, the age at which obesity occurs and whether there is a critical period. Preliminary data from the LIFE Child study confirmed maternal BMI as a risk factor for childhood obesity, but the dynamics of BMI development in the children did not differ substantially according to the weight status of the mother. A child with known familial risk factors should be monitored closely for upward trends in BMI.

In our study, we categorized normal weight or obesity on the basis of BMI. Although BMI is not a direct reflection of body fat and may be affected by increasing muscle mass, BMI is the most widely applied criterion, with sex, age, and often ethnic-specific reference ranges available across the entire age span, and it is easily recordable without additional equipment.

In conclusion, in this current population-based longitudinal study, we found that obesity occurred early in life and once present, persisted into adolescence. The most excessive weight gain occurred early — between 2 and 6 years of age — and subsequently continued at a lower but still positive rate, which led to a greater degree of obesity.

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