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Birth Weight and Weight Changes from Infancy to Early Childhood as Predictors of Body Mass Index in Adolescence

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Objective To assess the time point during infancy and early childhood at which greater than expected weight gain is associated with overweight in adolescence.

Study design Current height, weight, and body mass index (BMI) were assessed in 1520 adolescents (mean age of boys, 15.52 ± 0.84 years; mean age of girls, 15.37 ± 0.77 years). Information on weight and height trajectories during infancy and early childhood (birth and 6 other time points) was extracted from mother-child booklets. Conditional relative weights were computed to estimate greater or lower than expected weight gain (ie, soft tissue gain at a specific age independent of linear growth), and their association with BMI in adolescence was investigated using linear regression analysis.

Results The mean BMI in adolescence was 21.77 ± 3.69 in boys and 21.70 ± 3.50 in girls. The proportion of overweight was 14.8% in each group. Overweight adolescents had significantly higher weight z-scores at birth, 1.2 month, 3.3 months, 7.6 months, 1 year, 2 years, and 4 years of age as compared with normal-weight adolescents. There were significant positive associations of weight z-scores and conditional relative weights with adolescent BMI at all ages except birth, which were strongest after the first year of life. In a majority of overweight adolescents, overweight had manifested within the first 4 years of life.

Conclusions Greater than expected weigh gain at any time in the first years of life is associated with an increased BMI in adolescence. The effect is strongest after the first year. *(J Pediatr 2020;222:120-6)*.

In the developed world, cardiovascular disease is a major cause of morbidity and mortality in adulthood.[1] A major risk factor for cardiovascular disease in young adults is overweight or obesity in adolescence.[2] Obesity develops early in life, transfers from childhood into adolescence, and once acquired often persists in adulthood.[3,4] The prevalence of obesity in childhood and adolescence is high.[5] To implement adequate prevention programs, knowledge about the onset of obesity is crucial.

Most studies evaluating the association between obesity in adolescence and weight development in childhood relied on repeated assessments of the body mass index (BMI) as a criterion for obesity.[6-8] For example, obese adolescents were shown to have the most prominent BMI changes between 2 and 6 years of age.[6] However, weight gain in childhood is a result of both linear growth and an increase in body soft tissue (fat mass and fat-free mass), which cannot be discriminated by the assessment of BMI alone.[9] Using conditional relative weight, soft tissue gain and therefore weight change can be distinguished from change in height.[9]

The aim of this study was to assess the critical time point during infancy and early childhood at which greater than expected weight gain (ie, soft tissue gain) represented by positive conditional relative weight gain is associated with a higher BMI in adolescence.

Methods

This study is part of the regional cohort study—Early Vascular Aging (EVA) Tyrol—that was conducted at the Department of Pediatrics, Medical University of Innsbruck, Austria, from May 2015 to July 2018. EVA Tyrol investigated cardiovascular risk profiles in adolescents at 2 study visits over a time span of 2 years. In brief, the baseline examination included an assessment of anthropometric measurements and a thorough questionnaire about medical history,

BMI	body mass index
EVA	Early Vascular Aging

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*List of additional members of the EVA Study Group are listed in **Appendix 1** (www.jpeds.com).

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cardiovascular risk factors, lifestyle habits, and socioeconomic status. A detailed description was published elsewhere.[10]

The study was conducted in Tyrol (Austria), a state with about 745 000 inhabitants and 7600 live births per year, and in the city of Brunico in South Tyrol (Italy) with approximately 16 850 inhabitants and 150 live births per year. Adolescents at local schools and training companies attending tenth grade were invited to participate in the study.

As described elsewhere, information on maternal, perinatal, and infant characteristics was derived either from hospital records or a mother-child booklet.[10] Both the Austrian and the Italian mother-child booklets are official European health records covering pregnancy, birth, and the first 5 years of life, during which all Austrian and Italian children attend regular examinations in pediatric practices. Data on height and weight during the first 5 years of life were taken from the routine clinical measurements documented in the mother-child booklets. The mother-child booklet includes a total of 8 examinations during the first 5 years of life in addition to the examination at birth.

Current weight was assessed using medical precision scales. The current height was determined using a Harpenden stadiometer (Holtain, Crymich, United Kingdom). Weight and height measurements were converted into age and sex specific z-scores according to reference data sets.[11,12] BMI was computed as follows: BMI = kg/m^2. BMI percentiles were calculated according to a reference dataset.[12] Overweight was defined as having a BMI above the age- and sex-specific 90th percentiles.[13]

Socioeconomic status was assessed using the Family Affluence Scale Score II.[14] Physical activity was measured using the Baecke Sport Score.[15] In brief, adolescents were asked if they participate in sports, how many hours a week, and how many months per year they train. Sports were rated according to intensity, and values were inserted in the Baecke Sports Score as published elsewhere.[15]

Alcohol consumption per week was calculated after an in-person interview. Adolescents were asked to disclose the type, amount, and frequency of the consumed alcohol. Subsequently, the alcohol intake per week was calculated using the formula: amount of alcohol beverage in milliliters $\times \frac{\text{Vol\%}}{100} \times 0.8$ = alcohol in grams. Adolescents were categorized as smokers if they stated that they currently smoked at the time of the baseline examination.

We used the 6 most common ages for childhood measurements from mother-child booklets in addition to birth. The median ages considered for present analysis were 1.2 months (IQR, 1.0-1.4 months), 3.3 months (IQR, 3.0-3.9 months), 7.6 months (IQR, 7.0-8.2 months), 1.0 year (IQR, 0.9-1.1 years), 2.0 years (IQR, 1.9-2.1 years), and 4.0 years (IQR, 3.8-4.6 years) in addition to birth. The weight z-scores were presented as means with 95% CIs. Associations between weight z-scores and BMI were examined using linear regression.

To isolate the effect of weight gain from linear growth and to account for repeated measurements in the same study participant we computed sex-specific conditional relative weight measurements as published elsewhere.[9,16,17] In brief, standardized residuals for current weight were obtained by regressing current weight (represented as z-scores) on current height and on all prior weight and height measurements.

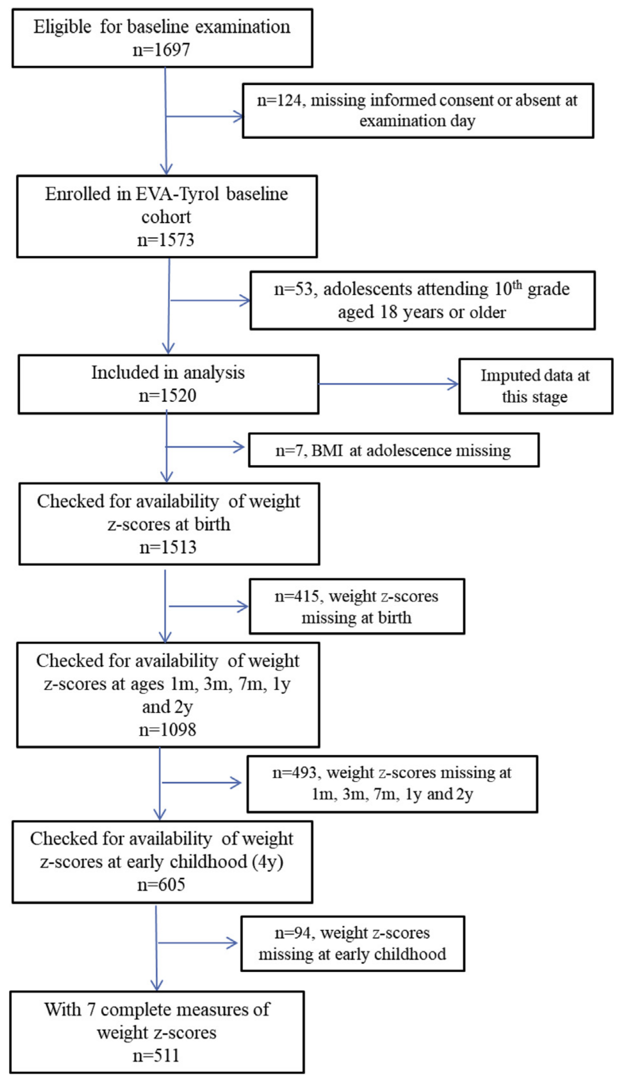

Figure 1. Flow chart for inclusion of study participants.

To illustrate the interpretation of a conditional relative weight, for instance, a study participant with a positive conditional relative weight at 4 years of age is heavier than expected given his growth up to an age of 4 years and his weight at 2 years and thus had an expedited soft tissue gain from age 2 years to 4 years.

Conditional relative weight variables are not correlated to each other and hence they were included together in linear regression models without collinearity concerns.[9,16,17] Regression analyses were adjusted for various adolescent characteristics (age, physical activity, socioeconomic status, and alcohol and tobacco consumption), infant characteristics (gestational age and ever breast fed), and maternal characteristics (mother's age at pregnancy and mother's BMI at first trimester). Because Tyrol and South Tyrol have similar

Table I. Characteristics of study participants

	Boys (n = 667)		Girls (n = 853)		
Characteristics	**No.†**	**% or mean (±SD) or median (IQR)**	**No.†**	**% or mean (±SD) or median (IQR)**	***P* value***
Maternal characteristics					
Age during pregnancy (years)	443	29.6 (±4.8)	532	29.6 (±5.2)	0.896
BMI at first trimester (kg/m^2)	257	22.9 (±3.7)	351	22.8 (±3.5)	0.748
Infancy characteristics					
Gestational age (wk)	458	39.3 (±2.0)	663	39.4 (±2.0)	0.329
Birth length (cm)	451	50.6 (±2.7)	660	50.1 (±2.6)	**0.002**
Birthweight (g)	455	3356 (±544)	665	3185 (±511)	**<0.001**
Ever breastfed					
No	75	11.2	100	11.7	0.556
Yes	245	36.7	333	39.0	
Characteristics in adolescence					
Age (y)	667	15.5 (±0.8)	853	15.4 (±0.8)	**<0.001**
School type					
High school	101	15.1	275	32.2	**<0.001**
Vocational school	459	68.8	498	58.4	
Apprenticeship	107	16.04	80	9.38	
Study region					
Tyrol	560	84.0	653	76.6	**<0.001**
Brunico	107	16.0	200	23.5	
FAS score					
Low	7	1.1	7	0.8	0.100
Medium	203	30.4	311	36.5	
High	444	66.6	518	60.7	
Baecke score	355	2.8 (±1.7)	456	2.0 (±1.7)	**<0.001**
Alcohol consumption per week (g)‡	648	5.0 (0-36.8)	817	4.8 (0-25.0)	0.098
Smoking status					
No	557	83.5	662	77.6	**0.015**
Yes	104	15.6	183	21.5	
BMI (kg/m^2)	664	21.8 (±3.7)	849	21.7 (±3.5)	0.706
BMI >90 percentile	99	14.8	126	14.8	0.998

FAS, Family Affluence Scale.
*Comparison of sexes using 2-sided *t* tests for continuous variables and χ^2 test for categorical variables.
†Total number varies across variables owing to missing values.
‡Comparison of sexes using the Mann-Whitney *U* test.

lifestyles, we did not stratify or adjust the analysis for region. To study the effects of heterogeneity by sex, all the analyses were stratified for sex. Data management and data analysis were performed using Stata 15.1 (StataCorp, College Station, Texas). We used multiple imputation with chained equations to impute missing data (**Appendix 2**; available at www.jpeds.com).[18] This advanced method accounts for the uncertainty associated with missing data. Under the missing at random assumption, it provides unbiased and valid estimates of associations based on information from the available data yielding estimates similar to those calculated from full data.[19]

This study was performed in accordance with the Declaration of Helsinki, and ethics approval was granted by the review board of the Medical University of Innsbruck, Austria (approval number: AN 2015-0005 345/4.13). This study is registered with www.clinicaltrials.gov (registration number: NCT03929692). All study participants and their legal guardians gave written informed consent.

Results

A total of 1697 adolescents were assessed for eligibility. Owing to either nonattendance on the day of examination or lacking informed consent, 124 adolescents were excluded, leaving 1573 adolescents who were enrolled and constitute the EVA Tyrol baseline cohort. Fifty-three study participants were excluded from analysis as they were 18 years or older at the baseline examination (**Figure 1**).

The characteristics of the study participants according to sex are shown in **Table I**. The mean age of the boys was 15.52 ± 0.84 years, and of the girls 15.37 ± 0.77 years. Compared with boys, girls were slightly younger at baseline examination and were more likely to attend high school, but were less physically active and showed a distinctively higher prevalence of smoking. The mean BMI was 21.77 ± 3.69 in boys and 21.70 ± 3.50 in girls. In adolescence, the total proportion of overweight was 14.8%.

Figure 2 displays the trajectories of weight z-scores during the first 4 years of life stratified for adolescents with a BMI of greater than the 90th percentile vs normal weight. Birth weight z-scores were significantly higher in overweight adolescents (*P* = .0001). During the first 4 years of life, weight z-scores increased until the third month of age and decreased thereafter in both groups until the first year of life. Overweight adolescents had significantly higher mean weight z-scores at all time points throughout infancy and early childhood than did normal weight adolescents

	# Number of study participants in each group						
	Birth	1 month	3 months	7 months	1 year	2 years	4 years
# Number of study participants in each group							
BMI ≤90 percentile (n=1288)	939	733	718	708	709	618	554
BMI >90 percentile (n=225)	159	122	125	122	123	105	99
Mean difference in weight z-score between the two groups							
Mean difference (95% CI)	0.29 (0.14-0.45)	0.24 (0.06-0.41)	0.31 (0.13-0.48)	0.24 (0.07-0.40)	0.28 (0.12-0.45)	0.57 (0.38-0.76)	0.85 (0.65-1.05)
Comparison of means in weight z-score between the two groups							
p value	<0.001	0.006	<0.001	0.004	<0.001	<0.001	<0.001

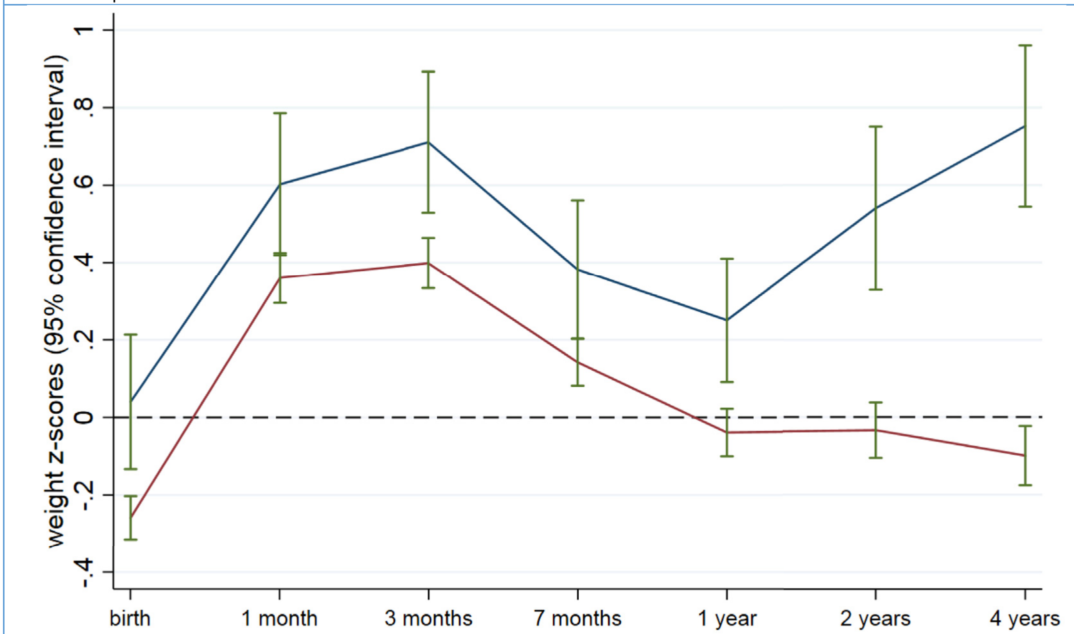

Figure 2. Trajectories of weight z-scores stratified for BMI at adolescence. #Total number varies across ages owing to missing values. Trajectories of weight z-scores in overweight and normal weight adolescents (blue, BMI >90th percentile; red, BMI ≤90 percentile; green, CI). The reference dataset for birth weight z-scores was based on Fenton et al and Kromeyer-Hauschild et al for all other weight z-scores.[11,12] The differences in means of weight z-scores between a BMI in greater than the 90th percentile and a BMI in the 90th percentile or lower at adolescence were significantly different when using the *t* test ($P < .005$) at all ages.

(Figure 2). The difference in z-scores between the groups was constant in the first year of life, but increased thereafter owing to increasing weight z-scores in the adolescent overweight group.

The prevalence of overweight in boys was 6.0%, 4.8%, 8.0%, 5.9%, 6.8%, 5.1%, and 3.5% at birth, 1 month, 3 months, 7 months, 1 year, 2 years, and 4 years, respectively. In girls, the respective prevalence of overweight was 3.6%, 5.9%, 8.0%, 9.1%, 7.3%, 3.5%, and 3.5% (Table II; available at www.jpeds.com).

Age of manifestation of overweight in overweight adolescents who provided the mother-child booklet is depicted in Figure 3 (available at www.jpeds.com). A total of 16% were already overweight at birth with a birthweight exceeding 4000 g, whereas 41% were not overweight during the first 4 years of life.

In multivariate analysis, we observed a significant positive association between weight z-scores at all ages except birth and BMI in adolescence (Figure 4, A). This analysis was adjusted for age, physical activity, socioeconomic status, alcohol and tobacco consumption, gestational age, breast feeding, mother's age at pregnancy, and mother's BMI at first trimester. Findings were comparable in both sexes. With advancing age, the strength of the associations increased. Figure 4, B, displays the association between conditional relative weight and adolescent BMI. Significant positive associations emerged for both sexes at each observed time point during the first 4 years of life, including birth (adjustment described above in this article). The β coefficients, CIs, and *P* values are provided in Table III (available at www.jpeds.com).

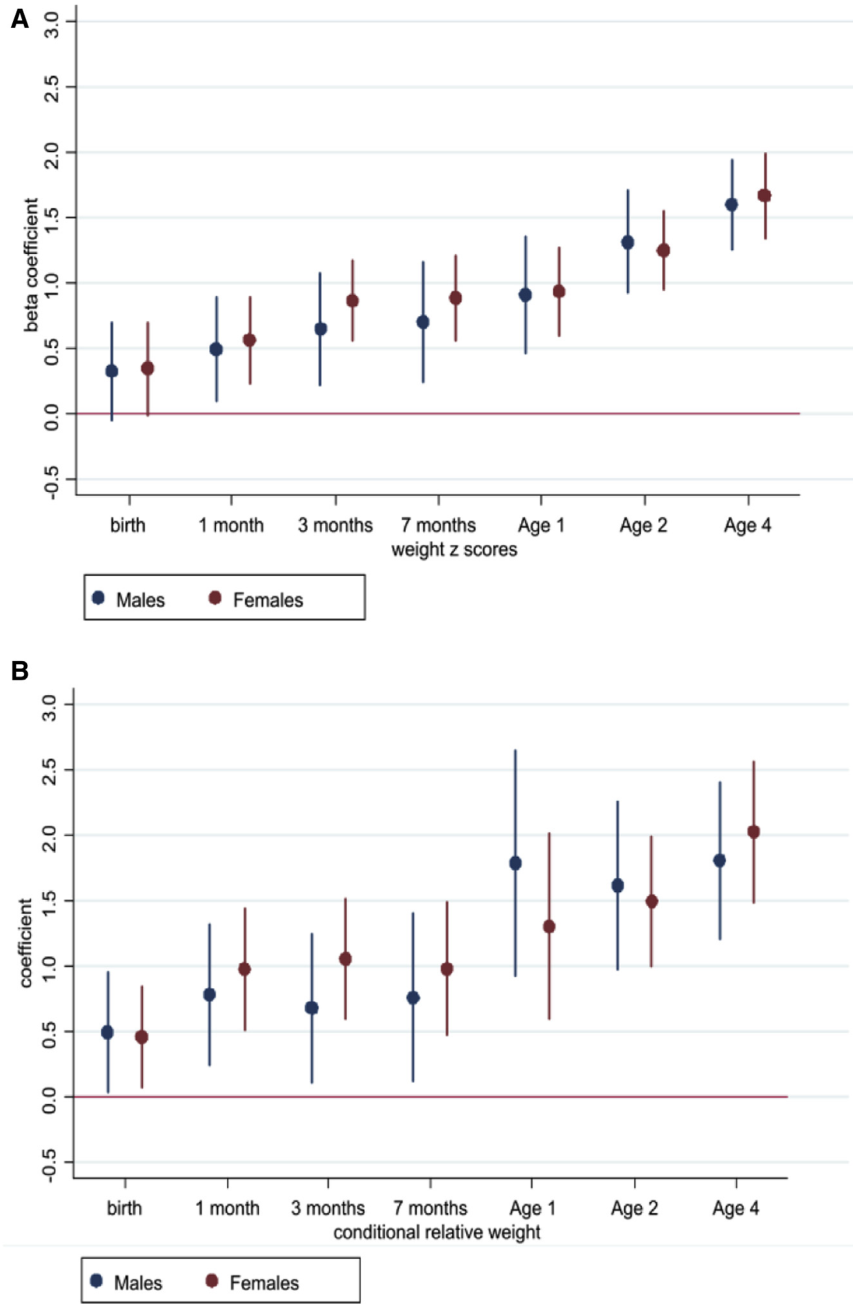

Figure 4. Association between conditional relative weight and weight z-score at birth, infancy, and early childhood and BMI at adolescence. **A,** Association between weight z-scores at birth, infancy, and early childhood and BMI at adolescence. ß represents unit change in BMI at adolescence with unit change in z weight at birth, infancy, or early childhood. Adjusted for current age, physical activity, socioeconomic status, alcohol and tobacco consumption, gestational age, breast feeding, mother's age at pregnancy, and mother's BMI at first trimester. **B,** Association between conditional relative weight at birth, infancy, and early childhood and BMI at adolescence. ß represents unit change in BMI at adolescence with unit change in conditional relative weight variable. Adjusted for current age, physical activity, socioeconomic status, alcohol and tobacco consumption, gestational age, breast feeding, mother's age at pregnancy, and mother's BMI at first trimester. ß (95% CI) is based on multiple imputation analysis.

Discussion

It is still not entirely clear during which phase in infancy and early childhood excessive weight gain is most relevant for the development of overweight in adolescence.

In our study, the mean BMI in male and female adolescents is in agreement with that reported in other European studies, as is the prevalence of overweight.[5,20,21] To implement adequate prevention programs, a detailed knowledge of weight development in infancy and early childhood is essential. By tracking BMI increments, early childhood (2-4 years) was identified as a possible initial period for the onset of sustained obesity.[6] However, BMI cannot discriminate between linear growth and soft tissue gain (fat mass and fat-free mass) and thus might not be the most sensitive tool for evaluating excessive weight gain. Conditional relative weight is a potential useful measure in this context.[9]

Excessive weight gain as represented by elevated conditional relative weight during any period in the first years of life is positively and significantly associated with an increased BMI in adolescence. Effects are strongest after the first year of life. These findings are in accordance with data from international low-to middle-income birth cohorts focusing on adult rather than adolescent BMI.[9,22] Adair et al showed a consistent, positive association between adult BMI and birthweight; conditional relative weight at 2 years of age; and conditional relative weight during mid-childhood.[9] The association increased in strength with age at measurement.[9] Antonisamy et al reported a positive association between adult BMI and conditional relative weight gain after the age of three months, especially after 6.5 years.[22] In addition, positive conditional relative weight gain during childhood was linked to a more unfavorable adult cardiovascular disease risk profile.[22]

Weight z-score trajectories were higher in overweight than in normal-weight adolescents throughout infancy and early childhood. Weight z-score trajectories of overweight adolescents paralleled those in normal weight adolescents and diverged after the first year of life. This finding suggests an early adiposity rebound, which is a correlate of future adiposity.[23] An early adiposity rebound is related to a higher risk for overweight and adiposity in young adulthood.[24] Similar to our results, Williams et al demonstrated that mean weight z-scores increase continuously until adulthood in early adiposity-rebound individuals, whereas they slightly decrease until the age of 11 years in individuals with average and late adiposity rebound.[25] They also reported a significant BMI difference of 4.8 kg/m^2 in males and 5.2 kg/m^2 in females in early adiposity-rebound individuals at the age of 26 years as compared with individuals with late rebound.[25]

Our findings concur with studies evaluating BMI dynamics from birth to adolescence, which identified separate BMI trajectories in overweight and obese children.[6,26] In these studies, overweight or obese adolescents had a significantly higher BMI SD score from the first year of life onwards than did normal or underweight adolescents.[6,26]

The mean birth weight in our study was within a normal range in male and female study participants with a mean gestational age of 39.26 $\pm$ 1.97 weeks in boys and 39.38 $\pm$ 1.99 weeks in girls. Of interest, weight z-scores were higher at birth in overweight than in normal weight adolescents. This finding is consistent with the finding from Geserick et al, who showed that almost one-half the children who were large for gestational age became overweight in adolescence.[6] However, a large literature review demonstrated that the effect of birth weight on later life overweight or obesity has yielded inconsistent results.[27]

As a limitation of this study, conditional relative weight gain cannot make a distinction between the gain in lean and fat mass. Yet, it is a mathematical tool for generating weight measurements that are independent of linear growth. Prenatal, infancy, and childhood data were extracted from mother-child booklets. Owing to unavailability of mother-child booklets, we had considerable missing data, which were addressed using the multiple imputation by chained equations method (**Appendix 2**). Although multiple imputation is a preferred approach considering that the present data are missing at random, it requires careful construction of models as the potential for model misspecification can be manifold.[28] As a further limitation information on father's BMI was not covered by mother-child booklets and was thus not available. Epidemiologic and animal studies indicate that also paternal BMI may influence the offspring's health and BMI.[29,30] Moreover, mother's BMI was imputed in 60% and thus we cannot claim that we have fully controlled for this variable.

Weight gain greater than expected during any period in the first 4 years of life is positively associated with BMI in adolescence. The effect is strongest after the first year of life. Therefore, dietary recommendations and close monitoring of weight gain should focus not only on infancy, but also on early childhood. ■

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Appendix 1

Additional members of the EVA Study Group

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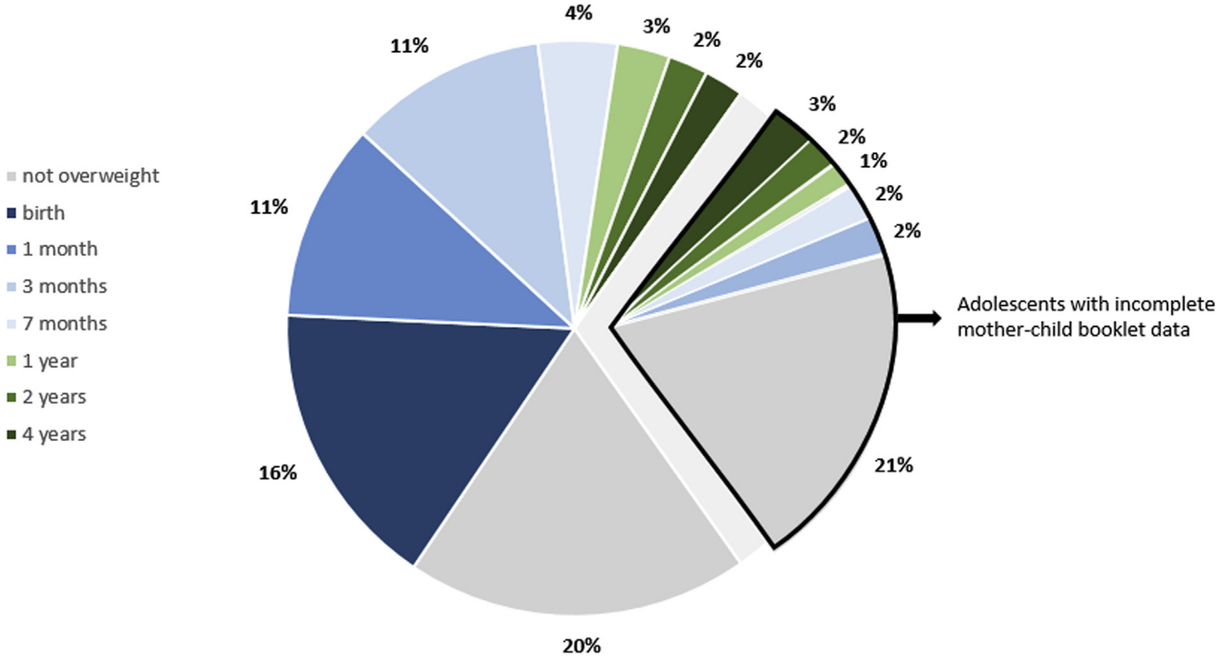

Figure 3. Age at manifestation of overweight in overweight adolescents (BMI > 90th percentile). The pie chart displays the age at manifestation of overweight. Subjects without mother-child booklets were not considered in this figure. In 69% of children, birth weight and BMI at all 6 follow-up time points were available, whereas 31% had missing values for 1 or more time points (separated pie). In the latter group, the first time point of documented overweight is displayed like in the group with complete data.

Table II. Prevalence of obesity in infancy and early childhood

Ages	Birth	1 mo	3 mo	7 mo	1 y	2 y	4 y
Total (n = 1520)*	71 (4.67)	82 (5.39)	121 (7.96)	117 (7.70)	107 (7.04)	64 (4.21)	53 (3.49)
Males (n = 667)*	40 (6.00)	32 (4.80)	53 (7.95)	39 (5.85)	45 (6.75)	34 (5.10)	23 (3.45)
Females (n = 853)*	31 (3.63)	50 (5.86)	68 (7.97)	78 (9.14)	62 (7.27)	30 (3.52)	30 (3.52)

Values are number (%).
*Total number varies across ages owing to missing values.

Table III. Association between conditional relative weight and weight z-score at birth, infancy, and early childhood and BMI at adolescence

	Boys		Girls	
Ages	ß (95% CI)	*P* value	ß (95% CI)	*P* value
Associations between weight z-scores and BMI*				
Birth	0.32 (−0.04 to 0.69)	.086	0.34 (−0.007 to 0.69)	.055
1 mo	0.49 (0.09 to 0.89)	.016	0.56 (0.23 to 0.88)	.001
3 mo	0.64 (0.22 to 1.07)	.003	0.86 (0.55 to 1.17)	<.001
7 mo	0.70 (0.24 to 1.16)	.003	0.88 (0.56 to 1.20)	<.001
1 y	0.90 (0.46 to 1.35)	<.001	0.93 (0.60 to 1.27)	<.001
2 y	1.31 (0.92 to 1.69)	<.001	1.24 (0.94 to 1.54)	<.001
4 y	1.59 (1.25 to 1.93)	<.001	1.66 (1.34 to 1.99)	<.001
Associations between conditional relative weight and BMI†				
Birth	0.49 (0.03 to 0.94)	.033	0.45 (0.07 to 0.83)	.019
1 mo	0.78 (0.24 to 1.31)	.004	0.97 (0.51 to 1.43)	<.001
3 mo	0.67 (0.11 to 1.24)	.019	1.05 (0.59 to 1.51)	<.001
7 mo	0.75 (0.11 to 1.39)	.021	0.97 (0.47 to 1.48)	<.001
1 y	1.78 (0.92 to 2.64)	<.001	1.30 (0.59 to 2.00)	<.001
2 y	1.61 (0.97 to 2.25)	<.001	1.49 (0.99 to 1.98)	<.001
4 y	1.80 (1.20 to 2.40)	<.001	2.02 (1.49 to 2.55)	<.001

ß (95% CI) is based on multiple imputation analysis.
*Association between weight z-scores at birth, infancy, and early childhood and BMI at adolescence. ß represents the unit change in BMI at adolescence with unit change in z weight at birth, infancy, or early childhood. Adjusted for current age, physical activity, socioeconomic status, alcohol and tobacco consumption, gestational age, breast feeding, mother's age at pregnancy, and mother's BMI at first trimester.
†Association between conditional relative weight at birth, infancy, and early childhood and BMI at adolescence. ß represents the unit change in BMI at adolescence with unit change in conditional relative weight. Adjusted for current age, physical activity, socioeconomic status, alcohol and tobacco consumption, gestational age, breast feeding, mother's age at pregnancy, and mother's BMI at first trimester.