# Association of prepubertal body composition in healthy girls and boys with the timing of early and late pubertal markers[1–3]

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## ABSTRACT

**Background:** It is controversial whether prepubertal body composition is implicated in the timing of puberty onset.

**Objective:** The objective was to investigate whether body composition in the 2 y preceding the start of the pubertal growth spurt—a marker of puberty onset—is associated with the attainment of early and late pubertal markers in healthy German boys and girls.

**Design:** Multivariate-adjusted regression analyses were performed in 215 participants of the DOrtmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study for whom body mass index (BMI) and its components fat mass/height$^2$ (FM/m$^2$) and fat-free mass/height$^2$ (FFM/m$^2$) 1 and 2 y before the onset of the pubertal growth spurt (age at takeoff; ATO) and information on early life exposures were available. In addition, age at peak height velocity (APHV) and menarche were examined.

**Results:** Higher BMIs and FM/m$^2$ $z$ scores 1 and 2 y before ATO showed modest associations with chronological age at ATO among girls only (girls: $P$ for = trend 0.05–0.1, adjusted for early life factors; boys: $P = 0.2$–$0.6$). FFM/m$^2$ $z$ scores were not related to age at ATO ($P$ for trend = 0.5–0.8). Conversely, prepubertal BMI and FM/m$^2$ more clearly predicted APHV and puberty duration (APHV minus ATO) in both sexes and age at menarche in girls (girls: adjusted $P$ for trend $<0.0001$–$0.03$; boys: $P = 0.01$–$0.046$).

**Conclusion:** This longitudinal study suggests that prepubertal body composition in healthy boys and girls may not be critical for the initiation of the pubertal growth spurt but instead affects the progression of pubertal development, which results in earlier attainment of later pubertal stages. *Am J Clin Nutr* 2009;89:221–30.


## INTRODUCTION

Whether body composition in childhood is implicated in the timing of puberty is currently a controversially debated issue (1, 2). Support for its relevance comes from many prospective studies, primarily conducted in girls, which showed that higher levels of adiposity in girls aged 5–9 y are related to an earlier menarche (3–13). By contrast, Demerath et al (14) showed that girls differed in relative weight only after menarche, ie, higher body mass indexes (BMI; in kg/m$^2$) are a consequence rather than a determinant of earlier puberty onset. In addition, the fact that birth weight and rapid weight gain during early life are strongly related to pubertal development (15) has been interpreted to indicate that prepubertal body composition and puberty onset are both influenced by factors operating nearer the time of birth and are hence related, but not causally (2, 14). Thus, further research to clarify whether there is a critical time window during which increased levels of body fatness will result in earlier puberty is needed and has been explicitly called for (1). The period 1 or 2 y before the earliest pubertal development may reasonably represent such a critical time window, because higher levels of adiposity at this time, and consequently higher leptin concentrations (16), could be permissive for puberty onset (17).

To date, very few studies have prospectively analyzed the relevance of prepubertal body composition for the timing of puberty in boys (18–21). These studies, as well as those conducted in girls, have mostly addressed a relatively late stage of pubertal development (ie, onset of menarche in girls and age at peak height velocity (APHV) or voice break in boys) (3–14, 18–22). In addition, the prepubertal time window of 5–9 y of age analyzed may have actually encompassed the onset of early pubertal signs. Alternatively, alignment of age to one of the earliest pubertal markers could allow insights into the association between body composition at a biologically comparable definitively prepubertal stage and subsequent pubertal development.

Therefore, the aim of this study was to use the prospectively collected and frequent height measurements of both girls and boys from the DOrtmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study to investigate whether chronological age at the initiation of puberty, as defined by the timing of the onset of the pubertal growth spurt (age at takeoff; ATO), was influenced by the level of BMI and the components of BMI, fat mass/height$^2$ (FM/m$^2$), and fat-free mass/height$^2$ (FFM/m$^2$) in the 2 preceding years, independently of early life factors. For comparative purposes with other studies, we also investigated whether body composition at this prepubertal stage was related to the chronological age at which later puberty markers (ie, PHV and menarche) occurred.

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## SUBJECTS AND METHODS

### DONALD study population

The DONALD Study is an ongoing, open-cohort study conducted by the Research Institute of Child Nutrition in Dortmund, Germany. This study was previously described in detail (23). Briefly, since recruitment began in 1985, detailed information on diet, growth, development, and metabolism between infancy and early adulthood has been collected from >1100 children. Every year, an average of 40–50 infants are newly recruited and first examined at the age of 3 mo. Each child returns for ≥3 visits in the first year, 2 in the second, and then once annually until early adulthood. During puberty, adolescents have also been asked to return for anthropometric measurements only at additional half-yearly intervals. The study was approved by the Ethics Committee of the University of Bonn, and all examinations are performed with parental consent.

Many DONALD participants have not yet reached adolescence. In addition, the ages of the children who were initially recruited into the DONALD Study were quite variable so that information on the first few years of life was not always available. Therefore, the number of children included in this analysis was derived as follows. Four hundred eleven term (37–42 wk gestation) singletons with a birth weight >2500 g had a minimum of both height measurements at 6 and 13 y and ≥5 measurements between these ages to allow estimation of ATO. The estimated ATO was considered plausible in 376 children (ie, it was between ≥5 and <13 y and in agreement with the visually inspected individual growth curve); 250 of these children also had information on rapid weight gain between birth and age 2 y. Finally, all children had to have complete information on breastfeeding and on maternal characteristics (BMI and educational status). Hence, the subcohort analyzed herein included 215 term singletons (49.8% female).

### Anthropometric measures

DONALD Study participants are measured at each visit according to standard procedures (24). They are dressed in underwear only and are barefoot. The trained nurses who conduct the measurements undergo an annual quality-control check during which inter- and intraobserver agreements are carefully monitored. Recumbent length in children aged <2 y is measured to the nearest 0.1 cm with a Harpenden (Holtain, Crymych, United Kingdom) stadiometer. From the age of 2 y onward, standing height is measured to the nearest 0.1 cm using a digital stadiometer. Weight is measured to the nearest 0.1 kg with an electronic scale (753 E; Seca, Hamburg, Germany). Skinfold thicknesses are measured from the age of 6 mo onward on the right side of the body to the nearest 0.1 mm with a Holtain caliper.

At the time of their child's admission to the study, parents are interviewed by the study pediatrician and weighed and measured by the study nurses using the same equipment as for children from age 2 y onward. Information on birth weight, length, and head circumference at birth as well as gestational age is abstracted from the *Mutterpass*, a standardized document given to all pregnant women in Germany.

### Anthropometric calculations

For the present analysis, we used those anthropometric measurements obtained as closely as possible to the 2 y before estimated ATO. Because not all participants had anthropometric measurements for all scheduled visits, these missing data were linearly imputed by using measurements before and afterward (maximum gap between 2 measurements was 1.5 y). The measurements closest to the ATO and 1 and 2 y before the ATO were then set to time = 0, −1, and −2, respectively. For each BMI, sex- and age-independent SD scores (SDS) were calculated by using the German reference curves (25). Percentage body fat (BF%) was calculated by using the Slaughter equations for prepubertal children (26). BF%, however, has recently been criticized to incorrectly reflect body-size-adjusted adiposity (27). Instead, it has been suggested to adjust FM for fat-free proxies of body size such as height (27). However, in the present study, the outcome ATO (and APHV) was itself derived from height measurements (*see* below). Because adjustments for height in multivariate analyses would hence be inappropriate, the components of BMI, FM/m$^2$ (FM = weight × BF%), and FFM/m$^2$ (FFM = weight − fat mass) as previously introduced by Maynard et al (28) were used as additional measures of body composition. Subsequently, $z$ scores of BMI-SDS, log-transformed FM/m$^2$, and FFM/m$^2$ were obtained by internal standardization to the sample in this analysis (mean = 0, SD = 1; by chronological age and sex).

### Puberty variables

All original height measurements were analyzed by using the parametric Preece and Baines model 1 (PB1) (29). The parameters of each child's growth curve were estimated by a nonlinear regression model (PROC NLIN in SAS; SAS Institute Inc, Cary, NC). The PB1 was fitted on various sex-specific age ranges of the height-for-age data, beginning with age 2 y, to determine the optimal range for our data. ATO was defined as the age at minimal height velocity (zero acceleration) at the onset of the pubertal growth spurt (30). Best fit was determined by *1*) graphical inspection of each child's individual growth curve, *2*) a comparison of the residual SDs (random error had to be smaller than the expected measurement error for height), and *3*) considering the plausibility and distribution of the pubertal variables estimated. On the basis of these 3 criteria the following age ranges were selected: all measurements from age 5 y onward for girls and from age 6 y onward for boys. The PB1 model also produced estimates of velocity at takeoff (VTO), APHV, and PHV. From these, we calculated the duration of the pubertal growth spurt (APHV − ATO), which in this article is termed "puberty duration."

Two other puberty variables were considered in this analysis for the sake of comparability with other studies: age at Tanner stage 2 for either breast or penis development in girls ($n$ = 75) and boys ($n$ = 66), respectively, and age at menarche in girls only ($n$ = 87). Tanner stage is visually assessed by one of the DONALD Study doctors at each visit after attainment of school age. After the age of 8 y, girls are also regularly asked whether menarche has already occurred, and if so, in which month and year.

### Early life factors

Birth weight was considered as both a continuous and as a categorical variable (ie, in those infants who weighed ≥2500 g but <3000 g compared with those who weighed ≥3000 g at birth). Other birth variables included gestational age, birth year, being firstborn (yes/no), and breastfeeding status (defined as those who had been fully breastfed for ≥2 wk). Growth patterns in infancy and early childhood were assessed by using rapid weight gain, which was defined as an increase in weight SDS >0.67 between birth and 24 mo (31) according to the German reference values (25). The following parental characteristics were also considered: maternal overweight status (BMI $\geq$ 25), high maternal educational status ($\geq$12 y of schooling), maternal age at birth, and smoking in the household (yes/no).

### Statistical methods

For description of the sample characteristics, 3 ATO groups were created by using the sex-specific distribution of ATO: early onset (<25th percentile), middle onset ($\geq$25th percentile and $\leq$75th percentile), and late onset (>75th percentile). Differences in characteristics between ATO groups were tested by using Kruskal-Wallis tests for continuous variables and chi-square tests for categorical variables.

Least-squares regression analyses were used to analyze the association of body composition with pubertal variables. Trend testing was performed with ATO as a continuous outcome and $z$ scores of BMI, FM/m$^2$, or FFM/m$^2$ as continuous influencing variables. Furthermore, the distributions of BMI, FM/m$^2$, or FFM/m$^2$ $z$ scores at 1 or 2 y before ATO were grouped to represent 3 sex-specific categories of body composition: low (<25th percentile), normal ($\geq$25th percentile and $\leq$75th percentile), and high (>75th percentile). In multivariate analysis, ATO was adjusted for potentially confounding early-life exposures. Each variable was initially considered separately, and those variables that had their own independent significant fixed effect in the basic models were included in the multivariate analyses. The adjusted means were the least-squares means predicted by the model when the other variables were held at their mean values. Similarly, multivariable models were constructed for APHV, puberty duration, and age at menarche. Finally, tracking of body composition from 1 y before ATO to APHV was analyzed by comparing the proportion of boys and girls grouped into the 3 categories of BMI, FM/m$^2$, or FFM/m$^2$ $z$ scores described above. A $\kappa$ value of $\geq$0.2 was selected to indicate the existence of poor tracking, $\geq$0.4 for moderate tracking, $\geq$0.6 for good tracking, and $\geq$0.8 for excellent tracking (32).

Because it has been suggested that the association between body composition and timing of puberty may differ between girls and boys (1), tests for sex interactions were performed. The association of the categories of BMI and FFM/m$^2$ with the chronological age at ATO was found to differ between boys and girls at 2 y before ATO (test for interaction: $P = 0.02$ and $P = 0.1$, respectively, in the full model), but not at 1 y before ATO (test for interaction: $P = 0.14$ and $P = 0.4$, respectively, in the full model). However, sex differences were also observed for associations of BMI with later puberty markers (test for interaction: $P = 0.1$ for associations between categories of BMI). Thus, all analyses were stratified by sex. A $P$ value <0.05 was considered statistically significant. All statistical analyses were carried out by using SAS version 8.2 (SAS Institute Inc).

## RESULTS

Early-life and familial characteristics of the 107 girls and 108 boys in this study are presented in **Table 1** by ATO group. Among girls whose puberty growth spurt began relatively early, a larger proportion were born light and had gained weight rapidly between birth and 24 mo in comparison with girls with later puberty onset. Similarly, boys entering puberty earlier tended to experience rapid weight gain more frequently and were less likely to have been fully breastfed for $\geq$2 wk than boys with later puberty onset.

Pubertal and anthropometric characteristics of the study sample are shown in **Table 2**. Children in the early ATO group experienced PHV and menarche (girls) at a significantly younger age than did the children in the other 2 ATO groups ($P < 0.0001$ for all of these variables). In girls only, those in the early ATO group also reached Tanner stage 2 at a younger age than did those girls in the other 2 ATO groups ($P < 0.0001$). Puberty duration was not clearly related to the timing of ATO; the girls and boys in the middle ATO group tended to experience the shortest puberty. In both boys and girls, there was a tendency for those in the late ATO group to have a lower BMI $z$ score 1 and 2 y before ATO. Similarly, girls in the late ATO group tended to have a lower FFM/m$^2$ $z$ score 1 and 2 y before ATO ($P = 0.06$–$0.1$).

The associations between BMI $z$ score 1 and 2 y before ATO and chronological age at ATO are presented in **Table 3**. In girls, a higher BMI $z$ score 1 and 2 y before ATO tended to be associated with an earlier pubertal growth spurt, ie, those with a high BMI $z$ score entered puberty approximately half a year earlier than did girls with a low BMI $z$ score. Among boys, there were no independent associations between BMI $z$ score 1 or 2 y before ATO and their chronological age at the time of their growth spurt.

Similarly, girls with higher FM/m$^2$ $z$ scores 1 or 2 y before ATO tended to be chronologically younger when they experienced their pubertal growth spurt than did girls with a lower FM/m$^2$ (**Table 4**). Again, there was no independent association between FM/m$^2$ $z$ scores in the 2 y preceding ATO and the chronological age at ATO among boys. In both sexes, FFM/m$^2$ $z$ scores in the 2 y preceding ATO were not related to the chronological age at ATO (**Table 5**).

The relevance of the BMI, FM/m$^2$ or FFM/m$^2$ $z$ scores 1 y before ATO for later pubertal variables is illustrated in the figures. Among girls (**Figure 1**), a higher BMI, FM/m$^2$, and FFM/m$^2$ $z$ score 1 y before their pubertal spurt was associated with a shorter puberty. Furthermore, PHV (Figure 1) and menarche (**Figure 2**) occurred significantly earlier in girls with a higher FM/m$^2$ $z$ score than in their counterparts with a lower FM/m$^2$ 1 y before their pubertal spurt. These associations were also—although less consistently —observed for BMI $z$ scores. Similarly, in boys (**Figure 3**), higher BMI, FM/m$^2$, and FFM/m$^2$ $z$ scores 1 y before ATO were associated with a shorter puberty, whereas an earlier PHV was seen only in those with higher BMI and FM/m$^2$ $z$ scores. Similar associations to later pubertal markers were observed with body-composition data at 2 y before ATO as the influencing variable (data not shown).

Of the girls and boys classified in the upper categories of BMI $z$ scores at 1 y before ATO, 84% of the girls and 76% of the boys were also classified as having a high BMI $z$ score at APHV (weighted $\kappa$: 0.68 and 0.71, respectively, indicated good tracking). For categories of FM/m$^2$ and FFM/ m$^2$ $z$ scores, moderate tracking between 1 y before ATO and APHV was observed in girls (weighted kappa: 0.58 and 0.58, respectively) and in boys (weighted $\kappa$: 0.60 and 0.41, respectively).

## DISCUSSION

The present longitudinal study in healthy free-living girls and boys does not suggest that body composition 1 or 2 y before the

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**TABLE 1**
Early life and familial characteristics of 107 girls and 108 boys from the DOrtmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study stratified by age at puberty onset (age at takeoff; ATO)

| | | ATO group[1] | | | |
|---|---|---|---|---|---|
| Variable | Total *n* | Early | Middle | Late | $P^2$ |
| Girls (*n*) | 107 | 26 | 54 | 27 | — |
| Early life characteristics | | | | | |
| Birth weight (g) | 107 | 3350 (2860, 3650)[3] | 3428 (3100, 3800) | 3450 (3100, 3650) | 0.5 |
| Birth weight <3000 g [*n* (%)] | 107 | 9 (34.5) | 8 (14.8) | 3 (11.1) | 0.05 |
| Gestational age (wk) | 107 | 40 (39, 41) | 39 (40, 41) | 40 (39, 41) | 1.0 |
| Fully breastfed ≥2 wk [*n* (%)] | 107 | 19 (73.1) | 38 (70.4) | 22 (81.5) | 0.6 |
| Rapid weight gain [*n* (%)] | 107 | 11 (42.3) | 9 (16.7) | 6 (22.2) | 0.04 |
| Birth year | 107 | 8 (30.8) | 13 (24.1) | 10 (38.5) | 0.8 |
| <1987 | 28 | 8 (30.8) | 25 (46.3) | 16 (29.6) | — |
| 1987–1990 | 44 | 10 (38.5) | 11 (40.7) | 9 (33.3) | — |
| >1990 | 35 | | | | |
| Family characteristics | | | | | |
| Firstborn [*n* (%)] | 103 | 15 (60.0) | 27 (52.9) | 17 (63.0) | 0.7 |
| Smoking exposure at home [*n* (%)] | 107 | 10 (38.5) | 17 (31.5) | 9 (33.3) | 0.8 |
| Maternal age at birth of the child (y) | 107 | 30 (28, 33) | 30 (28, 34) | 31 (28, 32) | 1.0 |
| Maternal overweight [*n* (%)] | 107 | 8 (30.8) | 19 (35.2) | 3 (11.1) | 0.07 |
| Maternal education ≥12 y schooling [*n* (%)] | 107 | 13 (50.0) | 28 (51.9) | 16 (59.3) | 0.8 |
| Boys (*n*) | 108 | 27 | 54 | 27 | — |
| Early life characteristics | | | | | |
| Birth weight (g) | 108 | 3440 (3300, 3800) | 3610 (3240, 3950) | 3750 (3500, 4150) | 0.08 |
| Birth weight <3000 g [*n* (%)] | 108 | 2 (7.4) | 3 (5.6) | 0 (0.0) | 0.4 |
| Gestational age (wk) | 108 | 40 (39, 41) | 40 (40, 41) | 40 (40, 41) | 0.9 |
| Fully breastfed ≥2 wk [*n* (%)] | 108 | 21 (77.8) | 35 (64.8) | 25 (92.6) | 0.02 |
| Rapid weight gain [*n* (%)] | 108 | 11 (40.7) | 13 (24.1) | 4 (14.8) | 0.09 |
| Birth year [*n* (%)] | 108 | 3 (11.1) | 13 (24.1) | 8 (29.6) | 0.3 |
| <1987 | 24 | 16 (59.3) | 22 (47.5) | 14 (51.9) | — |
| 1987–1990 | 52 | 8 (19.6) | 19 (35.2) | 5 (18.5) | — |
| >1990 | 32 | | | | |
| Family characteristics | | | | | |
| Firstborn [*n* (%)] | 103 | 16 (66.7) | 31 (57.4) | 13 (52.0) | 0.6 |
| Smoking exposure at home [*n* (%)] | 108 | 8 (29.6) | 15 (27.8) | 8 (29.6) | 1.0 |
| Maternal age at birth of the child (y) | 108 | 29 (27, 33) | 31 (28, 33) | 31 (28, 34) | 0.4 |
| Maternal overweight [*n* (%)] | 108 | 10 (37.0) | 16 (29.6) | 8 (29.6) | 0.8 |
| Maternal education ≥12 y schooling [*n* (%)] | 108 | 16 (59.3) | 30 (55.6) | 19 (70.4) | 0.4 |

[1] ATO groups were defined as follows: early (ATO < 25th percentile), middle (ATO ≥ 25th and ≤75th percentiles), and late (ATO > 75th percentile).
[2] Kruskal-Wallis or chi-square test for difference between the categories.
[3] All such values are unadjusted medians (quartile 1, quartile 3).

onset of the pubertal growth spurt is particularly critical for puberty onset. Instead, prepubertal body composition appears to influence how quickly girls and boys progress through puberty and is thus more strongly related to puberty duration and the age at which later pubertal characteristics occur than to the time at which the pubertal growth spurt is initiated.

This study was the first to analyze the body composition of both boys and girls at a comparable biological age before puberty onset for associations with many pubertal markers and hence allows us to disentangle potential prepubertal influences on earlier and later pubertal development. Previous studies investigating childhood body composition at different chronological ages for its association with later pubertal markers have been criticized because the age range investigated may still have encompassed the earliest pubertal developments (14). The present study overcomes this potential shortcoming by using body composition 1 and 2 y before the onset of the pubertal growth spurt—one of the earliest puberty markers.

Our finding that prepubertal body composition is associated with later puberty markers is in line with previous studies showing similar associations with childhood body composition at 5–9 y of age (3, 4, 6–8, 10–13, 18–21). Despite only investigating later puberty markers, these studies have commonly been interpreted to suggest that higher levels of body fat before puberty predispose to an earlier puberty onset (1, 12, 18, 19). However, the present study suggests only a weak association between prepubertal body composition and initiation of the pubertal growth spurt. Instead, children with higher prepubertal BMI or FM/m$^2$ values appeared to proceed more rapidly to PHV or menarche. Recent studies have provided new evidence of the obligatory role of hypothalamic kisspeptin in initiating puberty by disinhibiting the pulsatility of gonadotropin releasing hormone (33). It may well be that kisspeptin continues to be involved in the coordination between metabolic status and the reproductive axis, thus also influencing the rate of pubertal progression (34). Kisspeptin expression in turn may be regulated

**TABLE 2**

Pubertal and anthropometric characteristics of 107 girls and 108 boys from the DOrtmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study stratified by age at puberty onset (age at takeoff; ATO)[1]

| | | ATO group[2] | | | |
|---|---|---|---|---|---|
| Variable | Total *n* | Early | Middle | Late | $P^3$ |
| Girls | | | | | |
| ATO (y) | 107 | 7.5 (6.9, 7.8) | 8.7 (8.3, 9.1) | 9.8 (9.4, 10.0) | <0.0001 |
| Age at peak height velocity (y) | 104 | 10.5 (10.0, 10.8) | 11.5 (11.1, 11.9) | 12.6 (12.4, 13.0) | <0.0001 |
| Puberty duration (y) | 104 | 3.0 (2.8, 3.3) | 2.8 (2.6, 3.0) | 3.0 (2.7, 3.3) | 0.06 |
| Age at menarche (y) | 87 | 11.6 (11.0, 11.9) | 12.7 (12.2, 13:3) | 13.6 (13.3, 14.3) | <0.0001 |
| Age at Tanner stage 2 (y) | 75 | 9.5 (9.0, 10.3) | 10.5 (9.5, 11.0) | 11.5 (11.0, 12.1) | <0.001 |
| Anthropometric measures 1 y before ATO | | | | | |
| BMI ($kg/m^2$) | 107 | 15.4 (14.5, 16.5) | 15.9 (14.8, 17.8) | 15.2 (14.6, 17.4) | 0.2 |
| BMI (*z* score) | 107 | −0.08 (−0.69, 0.60) | 0.03 (−0.68, 0.97) | −0.64 (−0.95, 0.52) | 0.1 |
| Fat mass/height$^2$ ($kg/m^2$) | 107 | 2.6 (2.1, 3.3) | 2.6 (2.2, 4.2) | 2.6 (1.9, 3.4) | 0.6 |
| Fat mass/height$^2$ (*z* score) | 107 | −0.01 (−0.65, 0.72) | −0.17 (−0.55, 1.10) | −0.42 (−0.99, 0.26) | 0.2 |
| Fat-free mass/height$^2$ ($kg/m^2$) | 107 | 12.8 (12.3, 13.4) | 13.3 (12.4, 13.9) | 12.8 (12.5, 13.8) | 0.07 |
| Fat-free mass/height$^2$ (*z* score) | 107 | −0.15 (−0.67, 0.69) | 0.13 (−0.65, 0.85) | −0.54 (−0.93, 0.55) | 0.1 |
| Anthropometric measures 2 y before ATO | | | | | |
| BMI ($kg/m^2$) | 107 | 15.5 (14.5, 16.0) | 15.9 (14.8, 17.2) | 15.0 (14.2, 17.0) | 0.2 |
| BMI (*z* score) | 107 | 0.10 (−0.67, 0.46) | 0.12 (−0.42, 0.95) | −0.60 (−10.5, 0.54) | 0.07 |
| Fat mass/height$^2$ ($kg/m^2$) | 107 | 2.5 (2.3, 3.0) | 2.6 (2.2, 3.7) | 2.4 (1.7, 3.5) | 0.6 |
| Fat mass/height$^2$ (*z* score) | 107 | −0.03 (−0.40, 0.47) | −0.03 (−0.58, 1.01) | −0.42 (−1.30, 0.48) | 0.2 |
| Fat-free mass/height$^2$ ($kg/m^2$) | 107 | 12.7 (12.3, 13.4) | 13.2 (12.6, 13.7) | 12.7 (12.4, 13.6) | 0.2 |
| Fat-free mass/height$^2$ (*z* score) | 107 | −0.15 (−0.68, 0.65) | 0.24 (−0.45, 0.72) | −0.54 (−0.88, 0.37) | 0.06 |
| Boys | | | | | |
| ATO (y) | 108 | 9.2 (8.9, 9.5) | 10.3 (10.0, 10.5) | 11.1 (11.0, 11.5) | <0.0001 |
| Age at peak height velocity (y) | 104 | 12.5 (11.9, 12.8) | 13.4 (12.9, 13.7) | 14.3 (14.0, 14.7) | <0.0001 |
| Puberty duration (y) | 104 | 3.2 (3.0, 3.3) | 3.0 (2.9, 3.2) | 3.1 (3.0, 3.3) | 0.05 |
| Voice break (y) | 86 | 12.8 (12.6, 13.0) | 13.4 (12.9, 14.0) | 14.5 (14.1, 15.0) | <0.0001 |
| Age at Tanner stage 2 (y) | 66 | 10.5 (10.0, 10.8) | 10.6 (10.0, 11.2) | 10.5 (10.0, 11.0) | 0.4 |
| Anthropometric measures 1 y before ATO | | | | | |
| BMI ($kg/m^2$) | 108 | 16.4 (15.3, 18.2) | 16.9 (16.1, 18.7) | 16.1 (15.5, 18.0) | 0.4 |
| BMI (*z* score) | 108 | −0.04 (−0.62, 1.07) | 0.07 (−0.47, 0.81) | −0.64 (−1.02, 0.32) | 0.08 |
| Fat mass/height$^2$ ($kg/m^2$) | 108 | 2.3 (2.0, 4.1) | 2.7 (2.0, 4.3) | 2.3 (2.0, 3.4) | 0.4 |
| Fat mass/height$^2$ (*z* score) | 108 | −0.32 (−0.71, 1.38) | −0.08 (−0.79, 0.87) | −0.62 (−0.77, 0.25) | 0.3 |
| Fat-free mass/height$^2$ ($kg/m^2$) | 108 | 13.8 (13.1, 14.8) | 14.1 (13.3, 14.8) | 13.8 (13.5, 14.5) | 0.9 |
| Fat-free mass/height$^2$ (*z* score) | 108 | −0.19 (−0.90, 0.92) | −0.06 (−0.85, 0.69) | −0.42 (−0.75, −0.02) | 0.4 |
| Anthropometric measures 2 y before ATO | | | | | |
| BMI ($kg/m^2$) | 108 | 16.0 (15.0, 18.0) | 17.0 (15.4, 17.9) | 16.1 (15.2, 17.6) | 0.4 |
| BMI (*z* score) | 108 | −0.11 (−0.82, 1.16) | 0.30 (−0.59, 0.77) | −0.39 (−0.97, 0.35) | 0.1 |
| Fat mass/height$^2$ ($kg/m^2$) | 108 | 2.2 (1.8, 3.2) | 2.6 (2.0, 3.9) | 2.4 (2.0, 3.1) | 0.4 |
| Fat mass/height$^2$ (*z* score) | 108 | −0.25 (−0.76, 1.05) | 0.02 (−0.70, 1.00) | −0.43 (−0.79; 0.13) | 0.2 |
| Fat-free mass/height$^2$ ($kg/m^2$) | 108 | 13.7 (12.8, 14.9) | 14.0 (13.2, 14.5) | 13.9 (13.2, 14.8) | 0.6 |
| Fat-free mass/height$^2$ (*z* score) | 108 | 0.04 (−1.12, 1.21) | 0.03 (−0.71, 0.67) | −0.24 (−1.00, 0.67) | 0.7 |

[1] All values are unadjusted medians (quartile 1, quartile 3).

[2] ATO groups were defined as follows: early (ATO < 25th percentile), middle (ATO ≥ 25th and ≤75th percentiles), and late (ATO > 75th percentile).

[3] Kruskal-Wallis test for difference between the categories.

by adiposity signals such as leptin (35, 36), insulin (36), and the hunger hormone ghrelin (37). Because BMI and fatness clearly tracked from 1 y before ATO to APHV, it is conceivable that the relevance of prepubertal body composition for puberty duration seen in this study may at least be partly a consequence of the continuous prepubertal and peripubertal flux of endocrine signals from the periphery (eg, leptin and insulin) to the hypothalamus.

In this study, both the modest associations of prepubertal body composition with the start of the pubertal growth spurt and the stronger associations with later pubertal markers were seen independently of early life factors. In our view, this suggests that early life factors (15) and prepubertal body composition operate largely independently to influence puberty; thus, infancy and prepuberty are 2 critical periods during which the timing of pubertal events could be influenced. The potential to intervene may, however, be limited by a common genetic background regulating pubertal timing as well as growth during infancy and childhood (21).

It has been suggested that the link between body fat and timing of puberty may differ between girls and boys (1). In this study, the associations of prepubertal body composition with later pubertal markers were seen in both girls and boys. For boys, 3 recent prospective studies have also shown that those with higher childhood BMIs experience PHV (20, 21) and voice break (19) at an earlier age. Taken together, these data and our data provide evidence that prepubertal body composition in boys is related to later pubertal

**TABLE 3**
Associations between BMI (in kg/m$^2$) $z$ score 1 and 2 y before puberty onset and chronological age (in y) at puberty onset (age at takeoff; ATO) for 107 girls and 108 boys from the DOrtmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study[1]

| | Categories of BMI $z$ scores[2] | | | |
|---|---|---|---|---|
| | Low | Normal | High | $P$ for trend[3] |
| Girls ($n$ = 107) | | | | |
| 2 y before ATO | 8.9 (8.5, 9.3) | 8.5 (8.2, 8.8) | 8.6 (8.2, 9.0) | 0.06 |
| Unadjusted | | | | |
| Adjusted for early life factors[4] | 8.5 (8.1, 8.9) | 7.9 (7.5, 8.3) | 8.2 (7.7, 8.6) | 0.1 |
| 1 y before ATO | | | | |
| Unadjusted | 9.0 (8.6, 9.4) | 8.5 (8.2, 8.8) | 8.5 (8.1, 8.9) | 0.06 |
| Adjusted for early life factors[4] | 8.6 (8.2, 9.0) | 7.9 (7.5, 8.2) | 8.1 (7.7, 8.5) | 0.1 |
| Boys ($n$ = 108) | | | | |
| 2 y before ATO | | | | |
| Unadjusted | 10.2 (9.9, 10.6) | 10.4 (10.2, 10.6) | 10.0 (9.7, 10.3) | 0.5 |
| Adjusted for early life factors[4] | 10.0 (9.5, 10.5) | 10.2 (9.8, 10.7) | 9.7 (9.3, 10.2) | 0.6 |
| 1 y before ATO | | | | |
| Unadjusted | 10.5 (10.2, 10.8) | 10.3 (10.0, 10.5) | 10.0 (9.7, 10.3) | 0.2 |
| Adjusted for early life factors[4] | 10.3 (9.8, 10.8) | 10.1 (9.7, 10.5) | 9.8 (9.3, 10.3) | 0.2 |

[1] All values are least-squares means (95% CIs); missing values at 1 and 2 y before ATO were linearly imputed (*see* Subjects and Methods).
[2] Categories of BMI $z$ scores were defined as follows: low (BMI $z$ score < 25th percentile), normal (BMI $z$ score ≥25th and ≤75th percentiles), and high (BMI $z$ score > 75th percentile).
[3] From linear regression models with BMI $z$ scores as continuous variables.
[4] Rapid weight gain between 0 and 2 y, birth weight <3000 g, full breastfeeding for ≥2 wk, and maternal overweight.

markers in a similar way as in girls, which largely refutes previous suggestions of an opposite association in boys (38, 39).

Nonetheless, the modest association of prepubertal body composition with the initiation of puberty, ie, the start of the pubertal growth spurt, was primarily seen in girls (test for interactions: *see* Subjects and Methods). Furthermore, our study suggested that, among girls, APHV and age at menarche were somewhat more consistently related to FM/m$^2$ than to BMI (tests for interaction: *see* Subjects and Methods). These findings may be attributable, at least in part, to the fact that, in comparison

**TABLE 4**
Associations between fat mass/height$^2$ (FM/m$^2$) $z$ score 1 and 2 y before puberty onset and chronological age (in y) at puberty onset (age at takeoff; ATO) for 107 girls and 108 boys from the DOrtmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study[1]

| | Categories of FM/height$^2$ $z$ score[2] | | | |
|---|---|---|---|---|
| | Low | Normal | High | $P$ for trend[3] |
| Girls ($n$ = 107) | | | | |
| 2 y before ATO | | | | |
| Unadjusted | 9.1 (8.7, 9.5) | 8.5 (8.2, 8.8) | 8.4 (8.0, 8.8) | 0.02 |
| Adjusted for early life factors[4] | 8.6 (8.1, 9.0) | 8.1 (7.8, 8.4) | 8.0 (7.6, 8.5) | 0.05 |
| 1 y before ATO | | | | |
| Unadjusted | 9.0 (8.6, 9.4) | 8.5 (8.2, 8.8) | 8.5 (8.1, 8.9) | 0.01 |
| Adjusted for early life factors[4] | 8.5 (8.1, 9.0) | 8.0 (7.7, 8.4) | 8.2 (7.7, 8.6) | 0.05 |
| Boys ($n$ = 108) | | | | |
| 2 y before ATO | | | | |
| Unadjusted | 10.3 (10.0, 10.6) | 10.3 (10.1, 10.6) | 10.0 (9.7, 10.3) | 0.2 |
| Adjusted for early life factors[4] | 10.1 (9.6, 10.6) | 10.2 (9.7, 10.6) | 9.8 (9.3, 10.3) | 0.3 |
| 1 y before ATO | | | | |
| Unadjusted | 10.5 (10.2, 10.8) | 10.2 (10.0, 10.5) | 10.0 (9.7, 10.3) | 0.2 |
| Adjusted for early life factors[4] | 10.3 (9.8, 10.8) | 10.1 (9.7, 10.5) | 9.8 (9.4, 10.3) | 0.2 |

[1] All values are least-squares means (95% CIs); missing values at 1 and 2 y before ATO were linearly imputed (*see* Subjects and Methods).
[2] Categories of BMI $z$ scores were defined as follows: low (FM/m$^2$ $z$ score < 25th percentile), normal (FM/m$^2$ $z$ score ≥25th and ≤75th percentiles), and high (FM/m$^2$ $z$ score > 75th percentile).
[3] From linear regression models with FM/m$^2$ $z$ scores as continuous variables.
[4] Rapid weight gain between 0 and 2 y, birth weight <3000 g, full breastfeeding for ≥2 wk, and maternal overweight.

**TABLE 5**
Associations between fat-free mass/height$^2$ (FFM/m$^2$) *z* score 1 and 2 y before puberty onset and chronological age (in y) at puberty onset (age at takeoff; ATO) for 107 girls and 108 boys from the DOrtmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study[1]

| | Categories of FFM/m$^2$ *z* score[2] | | | |
|---|---|---|---|---|
| | Low | Normal | High | *P* for trend[3] |
| Girls ($n = 107$) | | | | |
| 2 y before ATO | | | | |
| Unadjusted | 8.9 (8.5, 9.3) | 8.5 (8.2, 8.8) | 8.6 (8.2, 9.0) | 0.3 |
| Adjusted for early life factors[4] | 8.5 (8.1, 8.9) | 8.0 (7.6, 8.3) | 8.2 (7.7, 8.6) | 0.5 |
| 1 y before ATO | | | | |
| Unadjusted | 8.8 (8.4, 9.3) | 8.5 (8.3, 8.8) | 8.6 (8.2, 9.0) | 0.5 |
| Adjusted for early life factors[4] | 8.4 (8.0, 8.9) | 8.0 (7.6, 8.3) | 8.2 (7.8, 8.7) | 0.7 |
| Boys ($n = 108$) | | | | |
| 2 y before ATO | | | | |
| Unadjusted | 10.2 (9.8, 10.5) | 10.3 (10.1, 10.5) | 10.2 (9.9, 10.5) | 1.0 |
| Adjusted for early life factors[4] | 10.0 (9.5, 10.4) | 10.1 (9.7, 10.6) | 10.0 (9.5, 10.5) | 0.8 |
| 1 y before ATO | | | | |
| Unadjusted | 10.2 (9.9, 10.6) | 10.3 (10.0, 10.5) | 10.2 (9.9, 10.5) | 0.6 |
| Adjusted for early life factors[4] | 10.0 (9.6, 10.5) | 10.1 (9.6, 10.5) | 10.0 (9.5, 10.5) | 0.8 |

[1] All values are least-squares means (95% CIs); missing values at 1 and 2 y before ATO were linearly imputed (*see* Subjects and Methods).
[2] Categories of BMI *z* scores were defined as follows: low (FFM/m$^2$ *z* score < 25th percentile), normal (FFM/m$^2$ *z* score ≥25th and ≤75th percentiles), and high (FFM/m$^2$ *z* score > 75th percentile).
[3] From linear regression models with FFM/m$^2$ *z* scores as continuous variables.
[4] Rapid weight gain between 0 and 2 y, birth weight <3000 g, full breastfeeding for ≥2 wk, and maternal overweight.

with boys, girls have a lower muscle mass (as indicated by 24-h creatinine excretion) per kilogram body weight (40) and a higher FM (41) already during childhood. Interestingly, in both girls and boys, higher lean mass (FFM/m$^2$) values before the pubertal growth spurt were—although unrelated to the timing of early or late pubertal marker—associated with a shorter duration of puberty. This indicates a potential relevance of muscle mass for puberty.

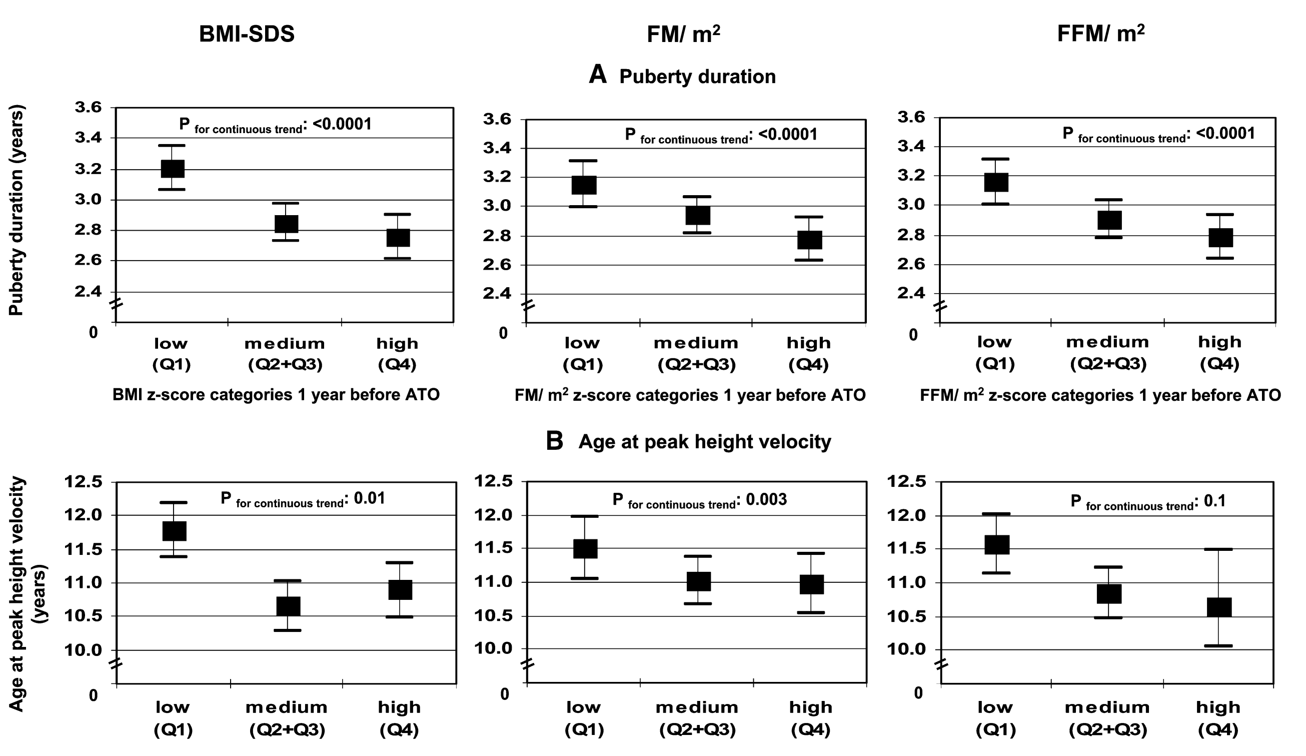


**FIGURE 1.** Duration of the pubertal growth spurt (age at peak height velocity minus age at takeoff; ATO) (A) and age at peak height velocity (B) by categories of BMI *z* scores (SD scores), fat mass/height$^2$ (FM/m$^2$) *z* scores, and fat-free mass/height$^2$ (FFM/m$^2$) *z* scores 1 y before ATO in 104 healthy girls. Data are means (95% CIs) adjusted for rapid weight gain between 0 and 2 y, birth weight <3000 g, full breastfeeding for ≥2 wk, and maternal overweight. *P* for continuous trend refers to the *P* values obtained in linear regression models with BMI, FM/m$^2$, and FFM/m$^2$ *z* scores as continuous variables. Q, quartile.

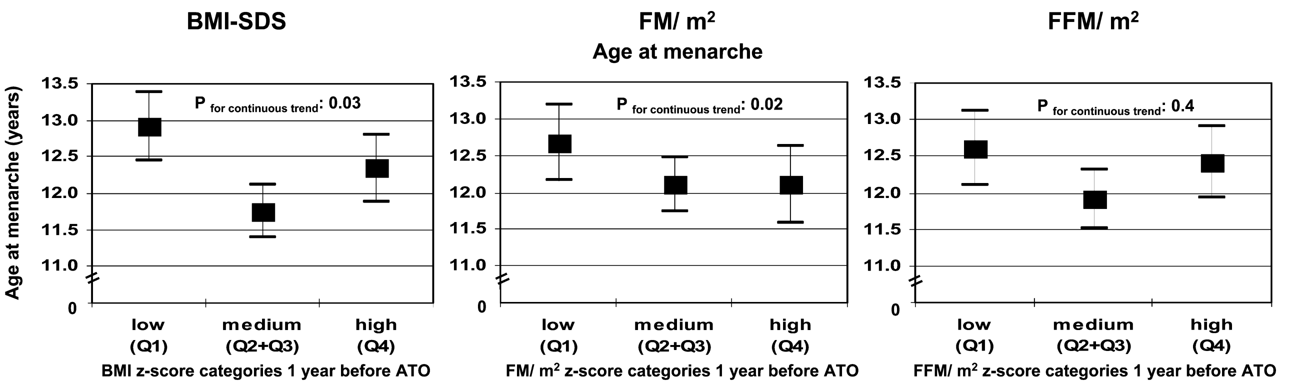


**FIGURE 2.** Age at menarche by categories of BMI *z* scores (SD scores), fat mass/height$^2$ (FM/m$^2$) *z* scores, and fat-free mass/height$^2$ (FFM/m$^2$) *z* scores 1 y before age at takeoff (ATO) in 87 healthy girls. Data are means (95% CIs) adjusted for rapid weight gain between 0 and 2 y, birth weight <3000 g, full breastfeeding for ≥2 wk, and maternal overweight. *P* for continuous trend refers to the *P* values obtained in linear regression models with BMI, FM/m$^2$, and FFM/m$^2$ *z* scores as continuous variables. Q, quartile.

The main strength of our study was its use of very detailed anthropometric data from early childhood until adolescence on a comparably large sample of both boys and girls. These data allowed the determination of both the initiation and the maximal growth spurt as indicators of somatic maturation. Alternatively, Tanner stages are commonly used to determine the initiation of puberty. However, these factors are difficult to assess and have been criticized as being subjective with considerable interobserver variability (42). The estimated values of ATO and APHV in our study are in accordance with values reported from other European studies (18, 20, 21) and showed an acceptable consistency with other pubertal markers assessed in the DONALD Study. Additional strengths of our study included our ability to control for the potential confounding effect of early life factors, particularly for rapid weight gain in the first 2 y of life, and the fact that we could investigate prepubertal BMI and its components FM/m$^2$ and FFM/m$^2$.

The main limitation of this study was the fact that the components FM/m$^2$ and FFM/m$^2$ were estimated from skinfold-thickness measurements, which are known to be more susceptible to measurement error than specialized research-based techniques, such as dual-energy X-ray absorptiometry, and may underestimate

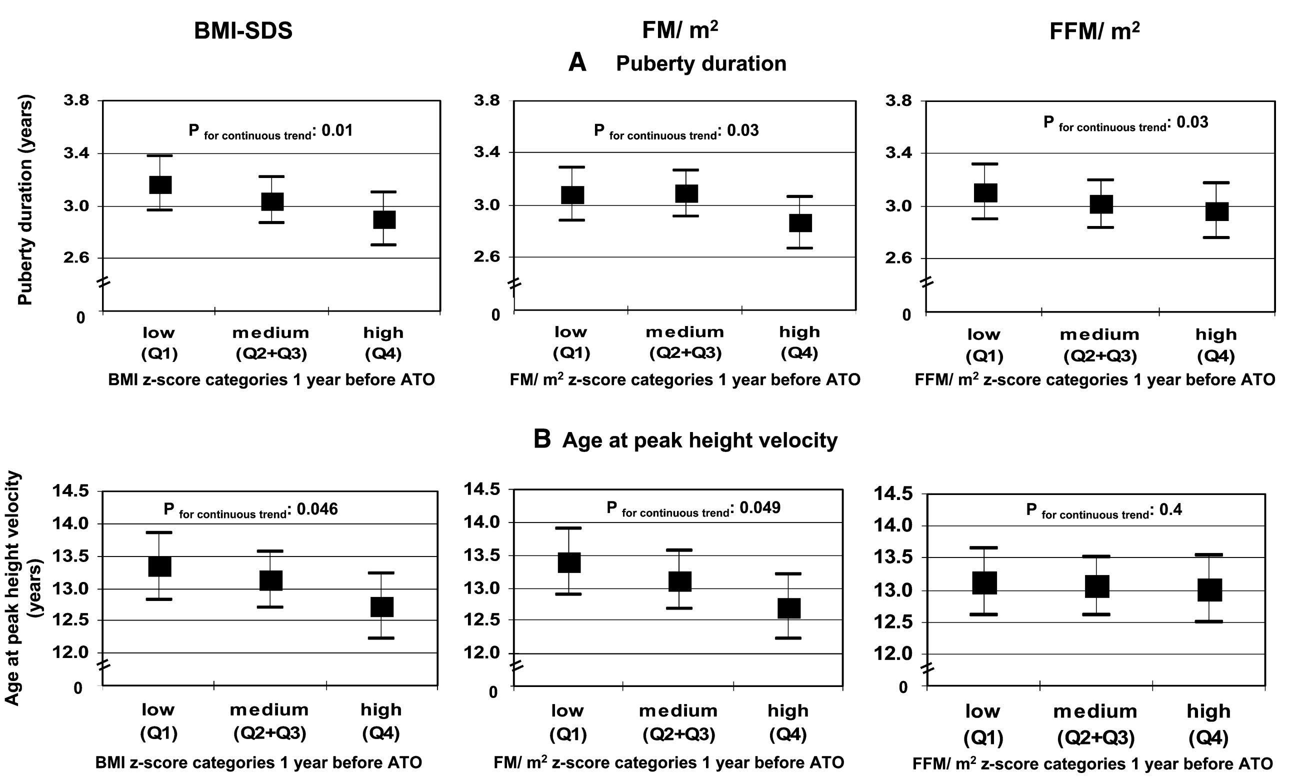


**FIGURE 3.** Duration of the pubertal growth spurt (age at peak height velocity minus age at takeoff; ATO) (A) and age at peak height velocity (B) by categories of BMI *z* scores (SD scores), fat mass/height$^2$ (FM/m$^2$) *z* scores, and fat-free mass/height$^2$ (FFM/m$^2$) *z* scores 1 y before ATO in 104 healthy boys. Data are means (95% CIs) adjusted for rapid weight gain between 0 and 2 y, birth weight <3000 g, full breastfeeding for ≥2 wk, and maternal overweight. *P* for continuous trend refers to the *P* values obtained in linear regression models with BMI, FM/m$^2$, and FFM/m$^2$ *z* scores as continuous variables. Q, quartile.

body fatness (43). However, intra- and interobserver variability are notably reduced when measurements are conducted by trained personnel, as was the case in our study (23). In addition, in the prepubertal DONALD participants, strong associations were observed between FFM estimated from skinfold-thickness measurements and independent measures of muscularity such as creatinine excretion, grip force, and forearm muscle area as assessed by peripheral quantitative computed tomography analysis (44). Finally, the elaborate design of the DONALD Study results in a select population with high educational attainment and socioeconomic status. Thus, our study does not include a large percentage of overweight ''at risk'' children. However, nonrepresentativeness is less relevant for the present longitudinal analyses of physiologic processes and will likely result in underestimation rather than overestimation of the true associations.

In conclusion, the present study does not suggest that prepubertal body composition is critical for the timing of puberty initiation, at least among healthy free-living boys and girls. Instead, higher prepubertal BMI or FM/$m^2$ values may influence how quickly both girls and boys progress through puberty and result in an earlier attainment of later pubertal stages.

The participation of all children and their families in the study is gratefully acknowledged. We also thank the staff of the Research Institute of Child Nutrition for carrying out the anthropometric measurements and for carrying out the medical examinations.

The authors' responsibilities were as follows—AEB and TR: conceived the project; AEB: conducted the statistical analyses and drafted the manuscript; and AEB, NK-D, and TR: contributed to the interpretation of the data and revision of the manuscript. None of the authors had any personal or financial conflicts of interest.

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