Infant BMI peak, breastfeeding, and body composition at age 3 y[1–4]

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ABSTRACT

Background: With the increasing focus on obesity, growth patterns in infancy and early childhood have gained much attention. Although the adiposity rebound has been in focus because of a shown association with adult obesity, not much has been published about the infant peak in body mass index (BMI).

Objective: This study links age and BMI at infant peak to duration of breastfeeding and body composition at 3 y of age.

Design: Frequent weight and height measurements for 311 Danish children in the SKOT (Complementary and Young Child Feeding – Impact on Short and Long Term Development and Health; in Danish) cohort were used to estimate BMI growth curves for the age span from 14 d to 19 mo by using a nonlinear mixed-effects model. BMI growth velocity before peak and age and BMI at peak were derived from the subject-specific models. Information about pregnancy and breastfeeding was assessed from background questionnaires. Assessment of body composition at age 3 y was made based on bioelectrical impedance, weight, and height.

Results: A longer duration of exclusive breastfeeding was associated with an earlier peak in infant BMI (P = 0.0003) and a lower prepeak velocity ($P < 0.0001$). BMI level at peak and prepeak velocity was positively associated with fat and fat-free mass at age 3 y (all $P < 0.0001$), whereas a later age at peak was associated with a lower fat mass, fat mass index, and fat-free mass index at age 3 y (all $P < 0.001$).

Conclusions: BMI peak characteristics are strongly associated with both duration of exclusive breastfeeding and body composition at 3 y of age. Thus, a better knowledge of characteristics and determinants of the early BMI peak is likely to improve our understanding of early development of obesity. *Am J Clin Nutr* 2015;101:319–25.

Keywords body composition, growth velocity, infant BMI peak, infant feeding, BMI growth curves

INTRODUCTION

Overweight and obesity in childhood has become an increasing burden, especially due to later complications such as type 2 diabetes mellitus, metabolic syndrome, and cardiovascular diseases. Many studies show strong associations between weight gain during infancy and later obesity (1–4). The risk of both childhood and adult obesity has been associated with growth with respect to rapid infant weight gain or increase in weight-for-age, weight-for-height, or BMI-for-age z scores (1–9), but there has not been much agreement concerning which periods during infancy are the most critical regarding rapid growth. Almost all age intervals between birth and 5 y of age have been suggested to be of the highest influence for subsequent obesity, but most critical periods are suggested to be within the first year of life (1, 5, 7–9). When estimating status or velocity of growth, most of these studies use weight or BMI at study-dependent fixed ages. This makes comparisons between studies difficult, but above all, this approach assumes a rather homogeneous group of children with similar development patterns. This is not a realistic assumption when it comes to childhood BMI.

Another approach to describe childhood BMI is by modeling individual BMI-for-age growth curves. For a typical individual, BMI increases until around age 7 mo, when it reaches a maximum, the infant BMI peak. It then decreases, reaching a minimum, the adiposity rebound, around age 6 y, before increasing once more (10). One feature of the growth curve, the adiposity rebound, has repeatedly been associated with later obesity (11–13). However, not much has been published about the infant peak in BMI.

BMI has been shown to track through life (14–17), with BMI and BMI gain in infancy correlated to adult adiposity and fat mass in industrialized populations (3, 8, 18). Two studies looked at correlations between infant BMI peak and later adiposity rebound and found no correlation between age at infant peak and age at adiposity rebound, as well as a moderate positive correlation between BMI at peak and BMI at adiposity rebound (16, 19), possibly explained by BMI tracking. One of the studies also found a negative correlation between growth velocity before BMI peak and velocity from BMI peak to adiposity rebound, suggesting it might be a result of regression toward the mean (16). However, the association between high BMI at peak and earlier and higher BMI at rebound has been found to depend on genetic disposition in the *FTO* locus, hereby identifying children who are not subject to BMI tracking (20).

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[3] Supplemental Material, Supplemental Table 1, and Supplemental Figure 1 are available from the "Supplemental data" link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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The aim of the present study is 3-fold: *1*) to fit BMI growth curves in this Danish cohort to estimate infant BMI peak and related growth characteristics, *2*) to find predictors of the BMI growth characteristics, and *3*) to relate the BMI growth characteristics to body composition at 3 y of age.

SUBJECTS AND METHODS

Study sample

Data are from a Danish observational cohort study on childhood nutrition and growth, the SKOT (Complementary and Young Child Feeding – Impact on Short and Long Term Development and Health; in Danish) cohort, which has previously been described in detail (21). In short, 330 children from the Copenhagen area were enrolled at age 7–8 mo to be examined at age 9, 18, and 36 mo. Exclusion criteria were children born before 37 wk of gestation or having a disease expected to affect either growth or food intake. Eighteen dropped out before the first visit, and one was excluded due to late manifestation of a severe chronic disease. Written consent was obtained from parents or guardians. The study was approved by the Committee on Biomedical Research Ethics of the Capital Region of Denmark (H-KF-2007-0003).

Measurements

Weight and length/height measurements were obtained at the 3 physical examinations at age 9 (±2 wk), 18 (±1 mo), and 36 mo (±3 mo), all taking place at the Department of Nutrition, Exercise and Sports, Copenhagen, Denmark. The procedure has been described previously (22). In short, weight at 9 and 18 mo was obtained by a digital pediatric scale to the nearest 0.001 kg. Weight at 36 mo was obtained by a digital scale to the nearest 0.1 kg. For all weight measurements, children wore a minimum of clothing. Recumbent length at 9 and 18 mo was obtained by using a digital measuring board as the average of 3 measurements to the nearest 0.05 cm. At 36 mo, standing height was measured by a stationary digital height measurer as the average of 3 measurements to the nearest 0.01 cm. As part of the free health care system in Denmark, all infants were offered a visit to their general practitioner at 5 wk, 5 mo, and 1 y. Also, the family received several visits at home from a nurse monitoring growth and well-being of the child and giving advice related to feeding patterns. The nurse usually visited the home within the first 2 wk. Weight and height measurements taken by nurses and general practitioners through infancy and childhood were recorded in a small book kept by the parents. These books were brought to the examinations by the parents and the information copied by the examiner. Birth weight and length were measured at the hospital/birth clinic. Gender-specific z scores for weight-for-age, height-for-age, weight-for-length, and BMI-for-age were calculated by using the WHO growth standards (10) and the WHO-Anthro software (23).

Body composition was assessed at 36 mo of age. Whole-body resistance was measured by a single-frequency (50-kHz) tetra polar bioelectrical impedance analysis with the child in a supine position. For a detailed description, see Ejlerskov et al. (24). Measurements were performed twice and the average used. A total of 250 completed a bioelectrical impedance analysis with success. For a subgroup of the children (n = 101), we further succeeded in obtaining a high-quality dual-energy X-ray absorptiometry scan at the 36-mo visit. We have previously developed prediction equations for fat mass (FM)[5] and fat-free mass (FFM) with bioelectrical impedance analysis, height, and weight as the independent variables with reference values from the dual-energy X-ray absorptiometry scans. The prediction equations for FFM and FM were as follows:

$$\mathrm{FFM} = 327.2\,\mathrm{RI} + 223.8\,\mathrm{weight} + 76.8\,\mathrm{height} + 417.6\,\mathrm{sex} - 2784.4 \quad (1)$$

$$\mathrm{FM} = (\mathrm{weight} \times 0.981 + 0.374) \times 1000 - \mathrm{FFM} \quad (2)$$

where FFM and FM were in grams, RI was the resistance index [height $(\mathrm{cm})^2$/resistance (Ω)], and weight was digital weight computed in kilograms. Height was in centimeters, and sex was recorded as male = 1 and female = 0.

At the 9-mo visit, parents filled out a background questionnaire containing, among other things, information about smoking during pregnancy, gestational weight gain, the child's gestational age at birth, age at introduction to different solids, and duration of exclusive breastfeeding. Exclusive breastfeeding was defined as receiving nothing but breast milk, water, or vitamins. Age at introduction to solids was defined as the earliest age at which the child received one of several different food categories.

Statistical analysis

The main analyses were performed in 3 steps: modeling subject-specific BMI curves, estimating curve characteristics, and examining associations to the different curve characteristics. Steps 1 and 2 are described in more detail in the section "Elaboration of statistical analysis" in the **Supplemental Material**.

Steps 1–2

Subject-specific BMI growth curves were fitted by using a nonlinear mixed model named SITAR (25, 26). The population curve was modeled by using a 4-degree polynomial, and flexibility on the subject level was obtained by inclusion of 3 random effects. Model checking was carried out by formal model diagnostics as well as visual inspection of the subject-specific curves.

We considered BMI data between 14 and 578 (19 mo) d of age to allow for a time lag before the outcome ascertainment (at 3 y) and to avoid the period of neonatal weight loss seen in the first 2 wk of life. All subjects with at least one BMI measurement in the studied age range were used to estimate the model (n = 311).

Estimated subject-specific BMI curves were obtained by combining the estimated fixed effects parameters and the predicted subject-specific random effects (Empirical Best Linear Unbiased Predictors). This resulted in a unique predicted curve for each subject. The amount of information available per subject was reflected in the degree of agreement between individual and population curves. If a given subject contributed to the overall

[5] Abbreviations used: FFM, fat-free mass; FFMI, fat-free mass index; FM, fat mass; FMI, fat mass index; FMP, fat mass percentage.

model with a single measurement only, strength was borrowed from the other subjects, and the corresponding subject-specific BMI curve became similar to the corresponding (sex-specific) population curve. Multiple measurements on the same subject implied much less agreement between the subject-specific and population curves (less shrinkage). Because we were interested in characteristics of the individual BMI growth curves and wanted to prevent including too many BMI curves following the population mean too closely, we extracted subject-specific growth curves from the full model only for children with at least 3 observations.

Age and level at the infant BMI peak were derived from the subject-specific BMI curves. Prepeak velocity was defined as the average linear BMI velocity from age 14 d to BMI peak and calculated as the difference in BMI divided by difference in time, with all numbers taken from the estimated subject-specific curves.

Step 3

Study sample characteristics were presented as means ± SDs or medians (IQRs) as appropriate. Sex differences and comparisons to the WHO growth standards were tested by 1- or 2-sample *t* test or Wilcoxon's rank-sum test.

Associations among sex, birth weight, birth length, gestational age at birth (12 missing), maternal weight gain during pregnancy (8 missing), smoking during pregnancy (yes/no) (3 missing), duration of exclusive (3 missing) or any (11 missing) breastfeeding, and age at introduction to solids and each of the growth curve characteristics were assessed with multiple weighted linear regression, with the number of BMI observations for each subject acting as weights to put more weight on the best predicted growth curves. Missing covariate values were imputed by using mean imputation before analysis (27). Adequacy of the model fits was assessed by residual and QQ plots. The association between duration of any breastfeeding and the 3 growth characteristics was explored in a subanalysis only including children with a BMI peak after end of all breastfeeding (n = 138) by exchanging duration of exclusive breastfeeding in the above models with duration of any breastfeeding.

We considered 5 different measures of body composition: FM; FFM; fat mass index (FMI), defined as FM/height^2; fat-free mass index (FFMI), defined as FFM/height^2; and fat mass percentage of total body weight (FMP). Associations between BMI growth curve characteristics and body composition at age 3 y were assessed by using weighted linear regression with the number of BMI observations for each subject acting as weights. All models were controlled for sex and exact age at 3-y measurements. Adequacy of the model fits was assessed by residual and QQ plots. Robust standard errors of regression coefficients were used, and P values were adjusted for multiple testing across outcomes by using the method proposed by Pipper et al. (28), which takes into account the correlation between test statistics. In a second analysis, we also controlled for duration of exclusive breastfeeding, birth weight, and birth length.

In all models with transformed outcome variables, estimates and confidence intervals were fitted on the transformed scale and back-transformed to the original scale, as suggested by Laursen et al. (29). All analyses were done by using the open-source statistical programming environment R version 3.0.2 (30) (http://www.r-project.org) and in particular the package *multcomp* (31). The overall significance level used was 0.05.

RESULTS

All 311 children had at least one observation on BMI in the studied time interval, but the number of BMI observations for each subject varied greatly between the children (median: 7; interquartile range: 5–9; range: 1–17). Of the observations, 26.4% were from the SKOT study, 30.8% were from the general practitioners, and 42.8% were from the home nurses. In addition, the distribution of measurement ages was far from uniform over the considered age interval, with 50% of the measurements occurring before 172 d after birth. Data are presented in more detail in **Supplemental Table 1** and **Supplemental Figure 1** in the online supplemental material.

Growth characteristics for all 311 children are presented by sex in **Table 1**. Boys were longer and heavier at birth than girls. Both sexes were at birth longer and heavier with a smaller weight-for-length and BMI-for-age compared with the WHO growth standards. At age 3 y, the cohort was still heavier than the WHO growth standards but now also with a higher weight-for-length and BMI-for-age z score. No sex differences were found for z scores at birth or age 3 y. Girls had a higher FM and lower FFM at age 3 y as measured in kilograms, index (FMI or FFMI; in kg/m^2), or as a percentage of total body mass.

Ten BMI growth curves showed a bad fit as judged by visual inspection (1 due to no pattern in the data and 9 due to a very late peak, of which 7 were after the end of the study period). These showed no differences from the rest with respect to birth measurements but had significantly higher weight-for-age, weight-for-height, and BMI z scores. Five children had only 1 or 2 observations on BMI and were also dismissed from the data. These 5 children did not differ from the remaining children in any of the anthropometric variables considered. For the remaining 296 children (153 girls, 52%), BMI growth curve characteristics are presented by sex at the bottom of Table 1.

Figure 1 shows population curves for boys and girls separately and the variation in data captured by the random intercept by means of ±2 SD. Sex-specific BMI curves differed significantly (P = 0.002). Girls had a lower BMI than boys at age 14 d (13.21 compared with 13.85) and showed a later peak in infant BMI than did boys (8.7 and 8.2 mo) at a lower level (16.96 and 17.31), but boys and girls did not differ significantly with respect to prepeak velocity (0.45 kg/m^2 per month) as shown in Table 1.

In multivariate models, children who were exclusively breastfed for a longer period had a lower prepeak velocity as well as an earlier peak (**Table 2** and **Figure 2**A). Children with a higher birth weight peaked earlier and at a higher BMI (Table 2 and Figure 2B). Children longer at birth had a later peak at a lower BMI. Mother's weight gain or smoking during pregnancy (7.8% smokers) did not influence the BMI growth characteristics in these multivariate models. Neither did gestational age at birth or age at introduction to solids. In a subanalysis, duration of any breastfeeding was not associated with any of the BMI growth characteristics.

In simple models, both BMI at peak and prepeak velocity were significantly positively associated with FFM, FM, FFMI, FMI, and FMP at age 3 y (**Table 3**). Age at peak was significantly negatively associated with FM, FFMI, FMI, and FMP. Sex

TABLE 1
Description of the study sample by sex[1]

	Boys		Girls		
	n	Value	*n*	Value	*P* value
Birth weight, kg	149	3.630 (3.400, 3.878)[2]	162	3.415 (3.164, 3.709)	<0.0001
Birth length, cm	149	52 (51, 54)	162	52 (50, 53)	<0.0001
Birth weight *z* score	149	0.57 (0.11, 1.04)*	162	0.39 (−0.15, 1.00)*	0.20
Birth length *z* score	149	1.12 (0.59, 2.17)*	162	1.53 (0.46, 2.07)*	0.05
Birth weight-for-length *z* score	149	−1.05 (−1.62, −0.23)*	162	−0.90 (−1.45, −0.44)*	0.60
Birth BMI *z* score	149	−0.28 (−0.80, 0.19)*	162	−0.43 (−0.85, 0.14)*	0.24
Weight-for-age *z* score at age 3 y	134	0.26 ± 0.82[3,*]	132	0.16 ± 0.79*	0.32
Length-for-age *z* score at age 3 y	132	0.09 ± 0.92	130	−0.10 ± 0.82	0.08
Weight-for-length *z* score at age 3 y	132	0.32 ± 0.84*	130	0.29 ± 0.85*	0.71
BMI-for-age *z* score at age 3 y	132	0.28 ± 0.84*	130	0.30 ± 0.88*	0.81
FFM at age 3 y, kg	110	12.60 (11.98, 13.30)	122	11.60 (11.00, 12.28)	<0.0001
FM at age 3 y, kg	110	2.19 (1.91, 2.69)	122	2.75 (2.18, 3.22)	<0.0001
FFMI at age 3 y, kg/m^2	110	13.56 (13.21, 14.02)	122	12.89 (12.58, 13.30)	<0.0001
FMI at age 3 y, kg/m^2	110	2.33 (2.12, 2.80)	122	2.97 (2.52, 3.60)	<0.0001
FMP at age 3 y	110	14.83 (13.24, 17.07)	122	18.64 (16.39, 21.69)	<0.0001
BMI at age 14 d, kg/m^2	143	13.85 (13.38, 14.38)	153	13.21 (12.58, 13.80)	<0.0001
Age at BMI peak, mo	143	8.2 (7.9, 8.4)	153	8.7 (8.4, 9.0)	<0.0001
BMI at peak, kg/m^2	143	17.31 (16.64, 17.98)	153	16.96 (16.19, 17.80)	0.02
Prepeak velocity[4]	143	0.44 (0.36, 0.53)	153	0.45 (0.38, 0.55)	0.26

[1]*Z* scores were calculated by using WHO standards. *P* values were determined by *t* test or Wilcoxon's rank-sum test as appropriate. *Significantly different from 0, $P < 0.05$; tested only for *z* score variables. FFM, fat-free mass; FFMI, fat-free mass index; FM, fat mass; FMI, fat mass index; FMP, fat mass percentage.
[2]Median; IQR in parentheses (all such values, not normally distributed).
[3]Mean ± SD (all such values, normally distributed).
[4]Presented as kg/m^2 per month.

differences were significant in all models with a higher FM, FMI, and FMP and lower FFM and FFMI in girls than in boys. Additional adjustment for duration of exclusive breastfeeding, birth weight, and birth length did not alter any conclusions or change the magnitude of estimates for BMI at peak or prepeak velocity considerably (all $P < 0.0001$). The magnitudes of the effect of age at peak were all reduced when including breastfeeding, birth weight, and birth length in the multivariate models but remained significant (all $P < 0.04$).

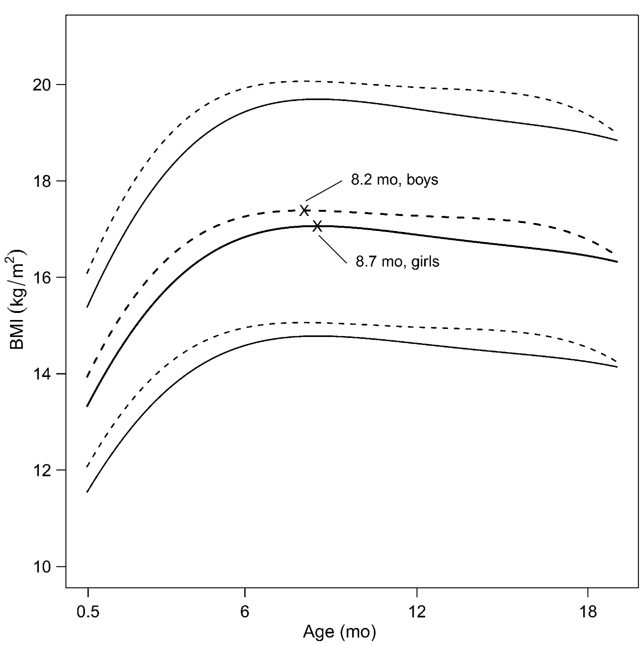

FIGURE 1 Flexibility of the model applied to the SKOT (Complementary and Young Child Feeding – Impact on Short and Long Term Development and Health; in Danish) data. Broken lines: boys. Full lines: girls. The thick lines indicate the population curves for girls (full line) and boys (broken line), respectively. The thin lines indicate the vertical shift in the curve by a ±2 SD value of the random effect α_i compared with the population curve for boys and girls, respectively.

DISCUSSION

This study found characteristics of the infant BMI peak to be associated with body composition at 3 y. Furthermore, sex differences were shown in timing of the peak and in prepeak velocity and as shown in other studies in all of the considered indices of body composition. Finally, a longer duration of exclusive breastfeeding was associated with an earlier peak in infant BMI. Our results suggest that timing of the infant BMI peak may play a role in the development of later childhood body composition and thereby overweight.

BMI growth characteristics and later body composition

In line with other studies (16, 32, 33), we found that girls were older and had lower BMI at peak. We did, however, not find girls to have a lower prepeak velocity, as found by Johnson et al. (33) and Wen et al. (16). This is probably explained by the fact that girls have a lower BMI at 14 d of age. We found girls to peak at age 8.7 mo and boys to peak at age 8.2 mo, whereas most other studies found later peaks for both girls (9–9.6 mo of age) and boys (8.8–9.1 mo of age) (19, 32, 33). The new Danish references (34) found earlier peaks: girls at 8.4 mo and boys at 7.7 mo. Duration of breastfeeding is higher in Denmark than in

TABLE 2
Estimated slopes for associations between predictors and BMI growth curve characteristics[1]

Covariate	Value at peak, kg/m^2	Age at peak, mo	Prepeak velocity[2]
Sex (F)	−0.09 (−0.16, −0.02)*	0.44 (0.35, 0.52)***	NS
Birth weight, kg	0.29 (0.18, 0.40)***	−0.52 (−0.65, −0.39)***	NS
Birth length, cm	−0.04 (−0.06, −0.01)*	0.05 (0.02, 0.08)**	NS
Excl. BF,[3] mo	NS	−0.05 (−0.07, −0.03)***	−0.02 (−0.02, −0.01)**

[1] n = 296. Estimated slope coefficients (95% CIs) from multiple linear regression models that included the nonsignificant variables: gestational age at birth, maternal gestational weight gain, smoking during pregnancy, and age at introduction to solids. A log transformation was applied to BMI and age at peak, and an inverse square root transformation was applied to prepeak velocity before analysis. *$P < 0.05$, **$P < 0.001$, ***$P < 0.0001$.

[2] Presented as kg/m^2 per month.

[3] Excl. BF, exclusive breastfeeding.

most other European countries (35). This might explain why we find earlier peaks than most other studies. The effect of breastfeeding might also explain the very early peak (both sexes peak at 6–7 mo) in the WHO growth standards, in which all children were exclusively breastfed for 4–6 mo and continued to breastfeed to 9–12 mo (10). One study of infancy BMI peak (16) found an earlier peak compared with findings of the present study for both girls and boys (7.4 and 7.2 mo), but no information on duration of breastfeeding was available.

We found girls to have more body fat (higher FM, FMI, and FMP) and less fat-free mass (lower FFM and FFMI) than boys at 3 y, both as unadjusted differences and in multivariate models including birth measurements and BMI peak characteristics. These early sex differences in body composition were also found in a review by Wells (36), who found sex differences to be more pronounced for FFM than for FM at this age. We speculate that differences in sex hormones, in particular testosterone, might explain parts of the sex differences seen at this age, because a small increase has been shown for boys from birth to around 3 mo of life (37).

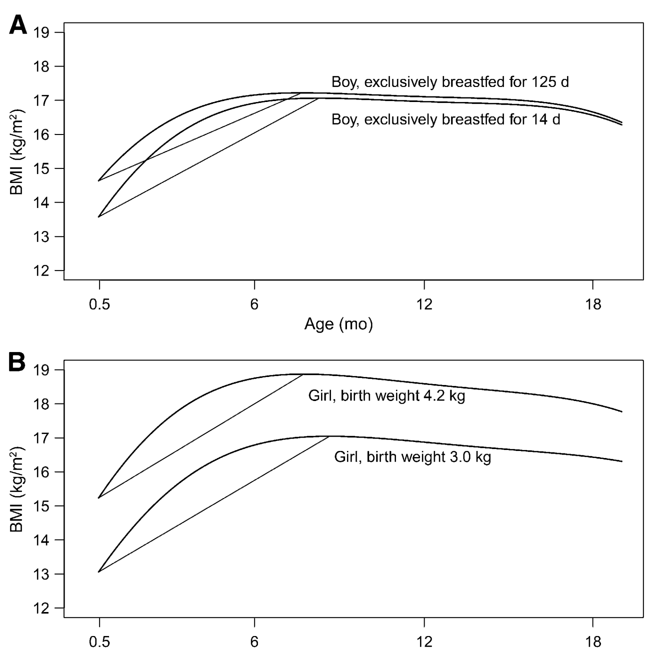

FIGURE 2 Examples of subject-specific BMI curves illustrating the effect of duration of breastfeeding (A) and birth weight (B) on the BMI growth curve characteristics. The subject-specific BMI curves were estimated by using a nonlinear mixed model with subject-specific random effects. The straight lines illustrate the prepeak velocity going from BMI at age 14 d to BMI at peak. Examples of BMI growth curves associated with a short and long duration of exclusive breastfeeding are shown in panel A. Children being exclusively breastfed for longer have a lower prepeak velocity (lower slope of the straight line) and an earlier peak. Examples of BMI growth curves associated with a high and low birth weight are shown in panel B. Children with a higher birth weight have an earlier peak at a higher BMI but a similar prepeak velocity.

Rapid growth in infancy, particularly rapid weight gain, has been associated with later obesity defined according to BMI in childhood as well as adulthood (3, 7, 38). We found that prepeak BMI velocity showed a positive association with FM, FFM, FMI, FFMI, and FMP at 3 y of age, and thereby BMI as FMI plus FFMI equals BMI. Because we did adjust for size at birth, this corresponds to centile crossing as explained by Cole (39). Sovio et al. (19) showed that BMI at peak was positively associated with adult BMI, suggesting a long-term association established early in life. We found this association to be present for both FFMI and FMI already at 3 y, which can be plausibly explained by BMI tracking (14, 15). Increasing evidence suggests systematic differences between the effects of infant weight gain on later body composition in industrialized and developing countries (18, 40), and these findings may therefore be valid only in industrialized populations.

Silverwood et al. (32) found a positive association between BMI at peak and later childhood BMI but also found a positive association between age at peak and later BMI in contrast to the negative association we found. This might be explained by the different timing of the measurements. We measured at 3 y (i.e., before adiposity rebound), and Silverwood et al. measured BMI at 5–13 y (i.e., after rebound). This may indicate that age at peak might be an indicator of tempo of growth. Because we did not have repeated measurements of body composition, it was not possible to establish whether age at BMI peak coincided with the timing of the infant peak in adiposity, but we did see associations with FM, FMI, and FMP at 3 y, suggesting an association with peak in adiposity in infancy.

Birth weight

We found birth weight to be positively associated with an earlier and higher BMI at peak. Others have found an association between higher birth weight z score and higher BMI at peak (16), but they also found a higher z score weight at birth to be associated with a lower velocity, which we did not see.

TABLE 3

Estimated slopes for associations between BMI growth curve characteristics and measures of body composition at age 3 y[1]

Outcome at age 3 y	BMI at peak, kg/m^2	Age at peak, mo	Prepeak velocity[2]
FFM, kg	0.26 (0.12, 0.40)***	−0.26 (−0.77, 0.25)	1.80 (0.79, 2.80)***
FM, kg	0.40 (0.33, 0.46)***	−0.39 (−0.67, −0.11)**	2.84 (2.13, 3.55)***
FFMI, kg/m^2	0.31 (0.23, 0.38)***	−0.36 (−0.63, −0.08)**	2.03 (1.27, 2.79)***
FMI, kg/m^2	0.44 (0.37, 0.51)***	−0.44 (−0.72, −0.15)**	3.14 (2.37, 3.92)***
FMP	1.96 (1.61, 2.31)***	−1.97 (−3.30, −0.64)*	14.12 (10.38, 17.87)***

[1] n = 220. Estimated slope coefficients (95% CIs) from multiple linear regression models that included adjustment for sex and exact age at examination of body composition. CIs and P values were adjusted for multiple testing. Square root transformations were applied to FM and FMI and a log-transformation was applied to FFM before analysis. *$P < 0.05$, **$P < 0.001$, ***$P < 0.0001$. FFM, fat-free mass; FFMI, fat-free mass index; FM, fat mass; FMI, fat mass index; FMP, fat mass percentage.

[2] Presented as kg/m^2 per month.

Breastfeeding

Several meta-analyses have found a protective effect of breastfeeding on later overweight and obesity (41–43). However, the effect seems to be modest, and some have suggested that there is no effect (44). We found that duration of exclusively breastfeeding was associated with an earlier peak in BMI and a lower prepeak velocity. Duration of breastfeeding has previously been shown to influence the BMI growth pattern. Chivers et al. (45) showed that children breastfed for longer than 4 mo had a later adiposity rebound at a lower level. Gale et al. (46) found that breastfed children had a lower FFM than did formula-fed children at age 8–9 mo and at 1 y but no differences in FM or FMP at this age. A longer duration of exclusive breastfeeding reduces age at peak, and formula-fed children will therefore be at a higher level at least in a short period after peak, which consequently, according to Gale et al. (46), is attributable to a higher amount of FFM. Although breastfed infants gain more FM in the first months of life, the lower prepeak velocity found for longer duration of breastfeeding might be explained by a lower FFM compared with formula-fed children at age 3–4 mo. Thompson and Lampl (47) found formula-fed girls to have higher amounts of testosterone in the first years of life both before and after introduction to solids compared with breastfed girls. For boys, they found no difference in testosterone amounts before introduction to solids but a lower amount of testosterone for those receiving formula compared with those receiving breast milk after introduction to solids. We found breastfeeding to be associated with an earlier peak, with girls peaking later than boys, who have slightly higher amounts of testosterone even at this young age. This might suggest that testosterone could explain some of the effect from exclusive breastfeeding on the BMI characteristics, which go in the same directions as the effects seen from sex.

We have seen duration of full breastfeeding to reduce the effect of early weight gain (0–5 mo) on FM in the same cohort (unpublished results). We did not see a reduction to the same extent here, probably because prepeak velocity covers a larger period going beyond the period of full breastfeeding.

Strength and limitations

A limitation of our study is that the measurements of weight and height through infancy were taken by different observers with varying degrees of accuracy and methods of measurements. This is, however, also a strength because it mimics the setting of any Danish child and provides us with a higher number of observations for each child.

In conclusion, all characteristics of the infant BMI peak are associated with body composition at 3 y, suggesting that characteristics and determinants of the BMI peak are of interest in understanding early obesity. The role of age and BMI at adiposity rebound have attracted much interest in understanding the development of overweight and obesity. More focus on the infant BMI peak might improve our understanding of the early development of overweight and obesity. The only modifiable factor we identified was duration of exclusive breastfeeding, but other factors such as gestational weight gain or age at introduction and composition of complementary feeding might also play a role.

The authors' responsibilities were as follows—KFM and CM: designed the study; KTE: managed the data collection; SMJ: performed the statistical analyses and prepared the first draft of the manuscript; CR: supervised the quality of the statistical analyses; SMJ and KFM: had responsibility for the final content; and all authors: contributed to the interpretation of results, commented on drafts, and approved the final version of the manuscript. The authors declared no conflicts of interest.

REFERENCES

1. Andersen LG, Holst C, Michaelsen KF, Baker JL, Sorensen TI. Weight and weight gain during early infancy predict childhood obesity: a case-cohort study. Int J Obes (Lond) 2012;36:1306–11.
2. McCarthy A, Hughes R, Tilling K, Davies D, Smith GD, Ben-Shlomo Y. Birth weight; postnatal, infant, and childhood growth; and obesity in young adulthood: evidence from the Barry Caerphilly Growth Study. Am J Clin Nutr 2007;86:907–13.
3. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. BMJ 2005;331:929.
4. Stocks T, Renders CM, Bulk-Bunschoten AM, Hirasing RA, van Buuren S, Seidell JC. Body size and growth in 0- to 4-year-old children and the relation to body size in primary school age. Obes Rev 2011;12:637–52.
5. Leunissen RW, Kerkhof GF, Stijnen T, Hokken-Koelega A. Timing and tempo of first-year rapid growth in relation to cardiovascular and metabolic risk profile in early adulthood. JAMA 2009;301:2234–42.
6. Monteiro PO, Victora CG. Rapid growth in infancy and childhood and obesity in later life—a systematic review. Obes Rev 2005;6:143–54.
7. Weng SF, Redsell SA, Swift JA, Yang M, Glazebrook CP. Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. Arch Dis Child 2012;97:1019–26.
8. Druet C, Stettler N, Sharp S, Simmons RK, Cooper C, Smith GD, Ekelund U, Levy-Marchal C, Jarvelin MR, Kuh D, et al. Prediction of childhood obesity by infancy weight gain: an individual-level meta-analysis. Paediatr Perinat Epidemiol 2012;26:19–26.

9. Young BE, Johnson SL, Krebs NF. Biological determinants linking infant weight gain and child obesity: current knowledge and future directions. Adv Nutr 2012;3:675–86.
10. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards: length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: methods and development. Geneva (Switzerland): World Health Organization; 2006; 1–312.
11. Rolland-Cachera MF, Deheeger M, Bellisle F, Sempe M, Guilloud-Bataille M, Patois E. Adiposity rebound in children: a simple indicator for predicting obesity. Am J Clin Nutr 1984;39:129–35.
12. Taylor RW, Grant AM, Goulding A, Williams SM. Early adiposity rebound: review of papers linking this to subsequent obesity in children and adults. Curr Opin Clin Nutr Metab Care 2005;8:607–12.
13. Whitaker RC, Pepe MS, Wright JA, Seidel KD, Dietz WH. Early adiposity rebound and the risk of adult obesity. Pediatrics 1998;101:E5.
14. Karlberg J, Kwan CW, Albertsson-Wikland K. Reference values for change in body mass index from birth to 18 years of age. Acta Paediatr 2003;92:648–52.
15. Stettler N. Nature and strength of epidemiological evidence for origins of childhood and adulthood obesity in the first year of life. Int J Obes (Lond) 2007;31:1035–43.
16. Wen X, Kleinman K, Gillman MW, Rifas-Shiman SL, Taveras EM. Childhood body mass index trajectories: modeling, characterizing, pairwise correlations and socio-demographic predictors of trajectory characteristics. BMC Med Res Methodol 2012;12:38.
17. Singh AS, Mulder C, Twisk JW, van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. Obes Rev 2008;9:474–88.
18. Wells JC, Chomtho S, Fewtrell MS. Programming of body composition by early growth and nutrition. Proc Nutr Soc 2007;66:423–34.
19. Sovio U, Kaakinen M, Tzoulaki I, Das S, Ruokonen A, Pouta A, Hartikainen AL, Molitor J, Jarvelin MR. How do changes in body mass index in infancy and childhood associate with cardiometabolic profile in adulthood? Findings from the Northern Finland Birth Cohort 1966 Study. Int J Obes (Lond) 2014;38:53–9.
20. Sovio U, Mook-Kanamori DO, Warrington NM, Lawrence R, Briollais L, Palmer CN, Cecil J, Sandling JK, Syvanen AC, Kaakinen M, et al. Association between common variation at the *FTO* locus and changes in body mass index from infancy to late childhood: the complex nature of genetic association through growth and development. PLoS Genet 2011;7:e1001307.
21. Madsen AL, Schack-Nielsen L, Larnkjaer A, Molgaard C, Michaelsen KF. Determinants of blood glucose and insulin in healthy 9-month-old term Danish infants: the SKOT cohort. Diabet Med 2010;27:1350–7.
22. Madsen AL, Larnkjaer A, Molgaard C, Michaelsen KF. IGF-I and IGFBP-3 in healthy 9 month old infants from the SKOT cohort: breastfeeding, diet, and later obesity. Growth Horm IGF Res 2011;21: 199–204.
23. World Health Organization. WHO Antro (version 3.2.2, January 2011) and macros. Geneva (Switzerland): World Health Organization; 2011.
24. Ejlerskov KT, Jensen SM, Christensen LB, Ritz C, Michaelsen KF, Molgaard C. Prediction of fat-free body mass from bioelectrical impedance and anthropometry among 3-year-old children using DXA. Sci Rep 2014;4:3889.
25. Beath KJ. Infant growth modelling using a shape invariant model with random effects. Stat Med 2007;26:2547–64.
26. Cole TJ, Donaldson MD, Ben-Shlomo Y. SITAR—a useful instrument for growth curve analysis. Int J Epidemiol 2010;39:1558–66.
27. White IR, Thompson SG. Adjusting for partially missing baseline measurements in randomized trials. Stat Med 2005;24:993–1007.
28. Pipper CB, Ritz C, Bisgaard H. A versatile method for confirmatory evaluation of the effects of a covariate in multiple models. J R Stat Soc Ser C Appl Stat 2012;61:315–26.
29. Laursen RP, Dalskov SM, Damsgaard CT, Ritz C. Back-transformation of treatment differences—an approximate method. Eur J Clin Nutr 2014;68:277–80.
30. R Core Team. R: A language and environment for statistical computing. Vienna (Austria): R Foundation for Statistical Computing; 2013.
31. Hothorn T, Bretz F, Westfall P. Simultaneous inference in general parametric models. Biom J 2008;50:346–63.
32. Silverwood RJ, De Stavola BL, Cole TJ, Leon DA. BMI peak in infancy as a predictor for later BMI in the Uppsala Family Study. Int J Obes (Lond) 2009;33:929–37.
33. Johnson W, Choh AC, Lee M, Towne B, Czerwinski SA, Demerath EW. Characterization of the infant BMI peak: sex differences, birth year cohort effects, association with concurrent adiposity, and heritability. Am J Hum Biol 2013;25:378–88.
34. Tinggaard J, Aksglaede L, Sorensen K, Mouritsen A, Wohlfahrt-Veje C, Hagen CP, Mieritz MG, Jorgensen N, Wolthers OD, Heuck C, et al. The 2014 Danish references from birth to 20 years for height, weight and body mass index. Acta Paediatr 2014;103:214–24.
35. Børnedatabasen SSI. Danish Child Registry: Version 2012 [Internet]. Copenhagen (Denmark): Statens Serum Institut [cited 2014 Mar 20]. Available from: http://www.ssi.dk/Sundhedsdataogit/Registre%20og%20kliniske%20databaser/De%20nationale%20sundhedsregistre/Graviditet%20fodsler%20born/Bornedatabasen.aspx.
36. Wells JC. Sexual dimorphism of body composition. Best Pract Res Clin Endocrinol Metab 2007;21:415–30.
37. Forest MG, Cathiard AM, Bertrand JA. Evidence of testicular activity in early infancy. J Clin Endocrinol Metab 1973;37:148–51.
38. Brands B, Demmelmair H, Koletzko B. How growth due to infant nutrition influences obesity and later disease risk. Acta Paediatr 2014; 103:578–85.
39. Cole TJ. Children grow and horses race: is the adiposity rebound a critical period for later obesity? BMC Pediatr 2004;4:6.
40. Wells JC. Adaptive variability in the duration of critical windows of plasticity: implications for the programming of obesity. Evol Med Public Health 2014;2014:109–21.
41. Arenz S, Ruckerl R, Koletzko B, von Kries R. Breast-feeding and childhood obesity—a systematic review. Int J Obes Relat Metab Disord 2004;28:1247–56.
42. Harder T, Bergmann R, Kallischnigg G, Plagemann A. Duration of breastfeeding and risk of overweight: a meta-analysis. Am J Epidemiol 2005;162:397–403.
43. Owen CG, Martin RM, Whincup PH, Smith GD, Cook DG. Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. Pediatrics 2005;115:1367–77.
44. Casazza K, Fontaine KR, Astrup A, Birch LL, Brown AW, Bohan Brown MM, Durant N, Dutton G, Foster EM, Heymsfield SB, et al. Myths, presumptions, and facts about obesity. N Engl J Med 2013;368: 446–54.
45. Chivers P, Hands B, Parker H, Bulsara M, Beilin LJ, Kendall GE, Oddy WH. Body mass index, adiposity rebound and early feeding in a longitudinal cohort (Raine Study). Int J Obes (Lond) 2010;34:1169–76.
46. Gale C, Logan KM, Santhakumaran S, Parkinson JR, Hyde MJ, Modi N. Effect of breastfeeding compared with formula feeding on infant body composition: a systematic review and meta-analysis. Am J Clin Nutr 2012;95:656–69.
47. Thompson AL, Lampl A. Prenatal and postnatal energetic conditions and sex steroids levels across the first year of life. Am J Hum Biol 2013;25:643–54.