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The impact of early growth patterns and infant feeding on body composition at 3 years of age

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Abbreviations:

BAZ: BMI-for-age z-score

BIA: Bioelectrical impedance analysis

BWZ: Birth weight z-score

DXA: Dual-energy X-ray absorption

FFM: Fat-free mass

FFMI: Fat-free mass index

FM: Fat mass

FMI: Fat mass index

HAZ: Height/length-for-age z-score

WAZ: Weight-for-age z-score

WFH: Weight-for-height/length z-score.

Abstract:

Early excessive weight gain is positively associated with later obesity, yet the effect of weight gain during specific periods and the impact of infant feeding practices are debated. The objective of this study was to examine the impact of weight gain in periods of early childhood on body composition at 3 years and whether infant feeding modified the relationship between early growth and body composition at 3 years. We studied 233 children from the prospective cohort study, SKOT. Birth weight z-scores (BWZ) and change in weight-for-age z-scores (WAZ) from 0-5, 5-9, 9-18, and 18-36 months were analysed for relations with body composition (anthropometry and bioelectrical impedance) at 3 years by multivariate regression analysis. BWZ and change in WAZ from 0-5 months were positively associated with BMI, fat mass index (FMI), and fat-free mass index (FFMI) at 3 years. Full breastfeeding for 4-5 months (compared to less than 1 month) attenuated the effect of early growth on FMI by 47 % ($p = 0.05$), while full breastfeeding for 6 months eliminated the effect of early growth ($p = 0.002$). Full breastfeeding for 6 months (compared to less than 1 month) also eliminated the positive relation between BWZ and FMI ($p = 0.002$). No effect modification of infant feeding was found for FFMI. In conclusion, high birth weight and rapid growth from 0-5 months were associated with increased FMI and FFMI at 3 years. Longer duration of full breastfeeding reduced the effect of birth weight and early weight gain on fat mass.

Introduction

Many studies have shown highly significant associations between weight gain during the first months or years of life and later adiposity[1;2]. The first 4–9 months of life have been identified as a sensitive period for the influence of rapid growth on fat mass (FM) at later ages [3-5] and later risk of obesity[6-8]. Alternatively, other studies have found excessive weight gain in the period 2–6 years [5;9] and no specific period (from birth to 15 years) at all[10] to be of particular importance.

Nutrition in infancy is thought to be particularly influential on later risk of obesity, as growth patterns and changes in body composition in early infancy are closely linked with feeding patterns [3;11-13]. Breastfed infants show slower weight gains in the first year of life [11;12] and have lower FM at 12 months compared to formula-fed infants[13]. Three meta-analyses have shown breastfeeding to be associated with a small but consistently reduced risk of obesity determined by BMI [14-16], while breastfeeding does not seem to reduce mean BMI[17]. However, less consistency has been found with regard to the relationship between infant feeding and FM and fat–free mass (FFM) at later ages. Three studies have found an inverse relationship between duration of breastfeeding and FM at 4 years[18], 9–10 years[19], and 16 years of age[20], one study found an inverse effect in 9-year-old girls but not boys [21], and three studies found no differences at 2 years[22], 5 years[23], and 18 years of age[24].

Supporting the theory that early overnutrition leads to increased risk of obesity at later ages, two randomised controlled trials demonstrated increased growth rates and higher FM at 5–8 years of age in a group of children born small for gestational age who had received nutrient-enriched formula versus control formula until 6–9 months of age[3]. However, fewer studies have focused on the relation between the timing of the introduction of solids and later risk of obesity, and the findings that exist are inconsistent[25;26]. Early introduction to solids has been found to be associated with higher energy intake [27;28] and earlier introduction to unhealthy foods[29].

Breastfeeding, formula feeding, and complementary feeding practices are three highly related components, and it can be difficult to distinguish which component is responsible for certain effects. Therefore, both breastfeeding and information on complementary feeding should be included in analyses of early diet and body composition in later childhood[18;23]. Although large variations in body composition exist within a given BMI[30], most studies of both early growth and early feeding have used BMI or BMI standard deviation scores as indirect measures of adiposity at later age stages[1;2;14–17]. In this study, however, we supplement anthropometric measurements and BMI with fat mass index (FMI) and fat–free mass index (FFMI) estimated from bioelectrical impedance analysis. In order to elucidate the mechanisms behind rapid growth and to improve prevention strategies of childhood obesity, it is important to identify the age window that is most impacted in this regard and modifiable factors that influence growth in this period. The main aim of this study was to undertake a detailed investigation of how weight gain in four periods, spanning birth to 3 years of age, influences body composition at 3 years of age. Our secondary aim was to examine the impact of breastfeeding and age of introduction to solids on FMI and FFMI.

Subjects and Methods

Study design and participants

The data of this study comes from the SKOT cohort (in Danish: Småbørns Kost og Trivsel), a prospective observational cohort study that monitored healthy Danish children at 9, 18, and 36 months of age. This study has previously described in detail by Madsen et al.[31]. In brief, the inclusion criteria for the study included singleton term infants (at a gestational age of 37–42 weeks) without any diseases expected to affect growth or food intake. Recruitment took place from April 2007 to May 2008, with 2,211 families randomly selected from the National Danish Civil Registry to be invited to participate. Out of these, 330 families accepted and were enrolled in the study. The 36-month examinations took place from October 2009 to October 2010.

Anthropometry

Birth weight and weight at 5 months were obtained from health records kept by the parents of the study participants. All other anthropometric measurements, including weight, height, and skin folds, were obtained from physical examinations of 9-week (±2 weeks), 18-month (± 1 months), and 36-month (± 3 months) children at the Department of Nutrition, Exercise, and Sports, Copenhagen, Denmark. The procedures for the anthropometric measurement of 9- and 18-month children have been described previously by Madsen et al.[32]. At 36 months, naked body weight was measured to the nearest 0.1 kg on a yearly calibrated digital scale (Tanita WB-100MA, Tanita Corporation, 1-14-2, Maeno-chi, Itabashi-ku, Tokyo, Japan), and height was measured by a stationary digital height measurer (235 Heightronic Digital Stadiometer, Issaquah, WA, USA) to the nearest 0.01 cm. Triceps and subscapular skinfolds were measured by a Harpenden skinfold calliper (Chasmors Ltd, London, UK) and recorded to the nearest 0.1 mm. Except for weight, all measurements were performed in triplicate, and averages were used in analysis. Following standardized procedures, four well-trained observers conducted the examinations. Weight and height/length were entered into the software WHO Anthro 2005 [33] to achieve gender-specific z–scores. The number of overweight and obese children at 3 years of age was determined according to the cut-off values of the IOTF [34] and according to WHO growth standards [35].

Body composition assessment at 3 years of age

Body composition at 36 months was measured using bioelectrical impedance analysis (BIA) (described in detail by Ejlerskov et al.[36]). Whole body resistance, reactance, and impedance were measured with the child in a supine position using a single-frequency (50 kHz) tetra polar BIA (Quantum III, RJL Systems, Michigan, USA). On the right foot, the signal electrode (LMP3 Diagnostic Tab Electrodes, Kendall, Covidien, Mansfield, USA) was placed over the distal portion of the second metatarsal (the base of the second toe), and the detecting electrode was placed at the anterior ankle on an imaginary line bisecting the medial malleolus. On the right hand, the signal electrode was placed above the metacarpophalangeal joint of the middle finger. The detecting electrode on the right hand was placed on an imaginary line bisecting the ulnar head, as specified by the manufacturer. These measurements were performed twice consecutively, and the mean values of resistance, reactance, and impedance were registrered. A prediction equation for the FFM of the study's cohort of 3-year-old children was prior developed using BIA, height, and weight, with dual–energy x–ray analysis (DXA) as a reference method[36]. In short, high quality DXA scans were achieved for a sub-group of the SKOT children (n = 101), and a prediction equation was obtained via linear regression models using a 10–fold cross validation approach with BIA, weight, height, and gender as independent variables (adjusted $R^2 = 0.84$)[36]. FFM and FM were calculated using the following equations:

$$FFM = 327.2\ RI + 223.8\ weight + 76.8\ height + 417.6\ sex - 2784.4$$

$$FM = (weight * 0.981 + 0.374)*1000 - FFM$$

where FFM and FM are in grams, RI is the resistance index (height (cm)^2/resistance (Ω), weight is digital weight computed in kg, height is in cm, and sex is recorded as male = 1 and female = 0.

Feeding patterns and other information

At the 9 month examination, the participants' parents filled out questionnaires on yearly household income, age, height, and weight of parents, infant gestational age at birth, gestational weight gain, and smoking during pregnancy. In all three examinations, parents filled out follow-up questionnaires with updated information regarding their educational status, from which a variable of the mothers' educational levels at time of the 3-year examination was generated. At the 36 month examination, we measured the height and weight of the accompanying parent using the same measuring equipment as used for the children. Data on feeding patterns, including duration of full and partial breastfeeding and age of introduction to complementary foods, were obtained in interviews at each examination. Full breastfeeding was defined as receiving only breast milk, water, and vitamins, though allowed for exceptional bottle feeding (e.g., if a child had been babysat for a single night), which increased the duration of full breastfeeding for 15 infants. Partial breastfeeding was defined as a baby receiving some breast milk along with other food, weaning foods, or formula milk. Age of introduction to solids was defined as the earliest age in months at which an infant first received one of 19 food categories. Information on formula intake (g/day) at 9 months was derived from pre-coded dietary records developed for infants (described in Gondolf et al.[37]).

Ethics

The parents of all participants received verbal and written information about the study and written consent was obtained from all. The study was approved by The Committees on Biomedical Research Ethics for the Capital Region of Denmark (H–KF–2007–0003).

Statistical analysis

The dataset only includes children with information on FM and FFM. Missing values were considered missing at random, and available-cases analyses were carried out.

To account for natural variation in FM and FFM due to body size, we calculated FMI as FM/height (kg/m^2) and FFMI as FFM/height (kg/m^2)[38]. Linear regression confirmed that FMI and FFMI were not associated with height ($p > 0.5$). In the absence of well–established reference data for FM or FMI to identify cut-off values for overweightness in young children, we grouped FMI and FFMI according to gender-specific quartiles.

Differences between the weight-for-age z–scores (WAZ), height/length-for-age z-scores (HAZ), weight-for-height/length z-scores (WFH), and the BMI-for-age z-scores (BAZ) in the study sample, as well as the WHO standard, were evaluated using one-sample *t*-tests. Differences in the feeding patterns between genders were assessed either using *t*-tests or, if not normally distributed, Wilcoxon rank tests. Anthropometry at 3 years of age, parental characteristics, and infant feeding practices were evaluated according to FMI and FFMI quartiles using means ± SD and median + interquartile range (IQR) (if not normally distributed). Testing of trends across quartiles of FMI and FFMI was based on linear regression.

Associations between body composition at 3 years of age and weight gain in four age intervals (0–5 months, 5–9 months, 9–18 months, and 18–36 months) were analysed using multiple linear regression. Body composition outcomes were regressed on change in WAZ in each of the four age intervals in both a simple model, only adjusting for gender and birth weight z–score (BWZ), and in a fully adjusted model controlling for gender, BWZ, household income, educational level of mother, smoking during pregnancy, gestational weight gain, and parental BMI or height or weight according to outcome of interest. The educational level of the mother was grouped into five categories: “no education above school level”, “trainee or vocational education”, “short academic education < 3 years of age”, “academic education 3–4 years”, and “long academic education > 4 years”. Data on household incomes were collected in categories ranging from “less than 200,000 DKK” to “more than 800,000 DKK”, with 14 intervals of 50,000 DKK (≈ 8700 US$) between, and these groupings were used as quantitative variables in the analyses. As only few mothers reported smoking in pregnancy, this variable was included as a dichotomous variable (yes/no). Model assumptions were evaluated using residual and normal probability plots. Robust standard errors were employed in case substantial departures were found.

For each quartile of FMI, the development of mean WAZ across the four time points was visualised in scatter plots. The same was done for each quartile of FFMI. Differences between quartiles of mean WAZ over time were evaluated using linear mixed models while controlling for gender, household income, educational level of mother, smoking during pregnancy, gestational weight gain, and parental BMI, including child-specific random effects.

To identify the impact of birth weight and early growth on FMI and FFMI, we grouped birth weight into four categories: "< 3000 g" (n = 23), "3000–3499 g" (n = 92), "3500–3999 g" (n = 83), and "≥ 4000g" (n = 35). Only two children were born with a weight below 2500 g. Change in WAZ from 0–5 months was also divided into four categories: "<-0.67", "-0.67–0", "0–0.67", and "> 0.67". A change in WAZ exceeding 0.67 represents upward centile crossing at standard growth curves, which is a threshold that has been found clinically relevant[39]. Differences in the proportion of children in the highest quartile of FMI and FFMI across the categories were tested using X^2-tests.

Associations between FMI or FFMI, duration of full and partial breastfeeding, and age of introduction to solids were assessed using multiple regression in simple models adjusted only for gender and in fully adjusted models while controlling for BWZ, WAZ change from 0–5 months, household income, educational level of mother, smoking during pregnancy, gestational weight gain, and parental BMI. We included the combined effects corresponding to the BWZ-modified effect of full breastfeeding, the BWZ-modified effect of age of introduction to solids, the effect modification of full breastfeeding by WAZ change from 0–5 months, and the effect modification of age of introduction to solids by WAZ change from 0–5 months in a fully adjusted regression model with FMI or FFMI as outcome variables. For these analyses, full breastfeeding was categorized as "< 1 month" (< 31 days, n = 36), "1–3 months" (31–120 days, n = 39), "4–5 months" (121–180 days, n = 137), and "6 months" (>180 days (range 183–197), n = 21). Age of introduction were grouped as "3–4 months" (n = 138), "5 months" (n = 63), and "6 months" (n = 32). Backwards stepwise elimination was used for removing non-significant combined effects one at a time by means of likelihood-ratio tests. The same procedure was applied to a similar model with the variables of partial breastfeeding used in interaction terms ("< 4 months" [< 121 days; n = 30], "4–5 months" [121–182 days, n = 30], "6–8 months" [183–273 days; n = 60], "9–11 months" [274–364 days, n = 56], and "≥ 12 months" [> 365 days, n = 54]).

The study's data were analysed using STATA version 11.0 (StataCorp LP, Texas, USA). The significance level was set at α = 0.05.

Results

Out of the 330 children initially recruited for SKOT, 263 (79.7%) completed the 36-month examination. FFM and FM were calculated for the 233 children with complete BIA, height, and weight data. Children without BIA data were higher at 3 years of age than children with complete BIA data ($p = 0.008$, data not shown), yet no differences were seen in terms of weight and BMI at 3 years of age. Data for weight and length at 5 months was missing for 66 children. A comparison of the children with or without 5-month values showed no differences in weight and length at birth and 9 months of age (data not shown).

Sample characteristics

The mean WAZs of the SKOT children were above average compared with WHO growth standards in all examinations (all $p < 0.001$) (**Table 1**). HAZ was measured at birth and 5 months by midwifes and practitioners and was substantially higher than the WHO standards, most likely due to inaccurate length measures in the primary healthcare sector. At 3 years of age, 19 children were overweight (8.2%) and none were obese according to the IOTF criteria. Forty-six children (19.7 %) were at risk of becoming overweight (with a BAZ of above 1 SD), 4 children (1.7 %) were overweight with a BAZ above 2 SD, and none were obese according to the WHO growth standards. One hundred fifty-eight children (67.8 %) were fully breastfed for 4 months or more, while 99 children (42.5 %) were still partially breastfed at 9 months. Five children (2 %) were introduced to solids earlier than 4 months, 133 (57 %) at 4 months, 63 children (27 %) at 5 months, and 32 children (14 %) at 6 months.

Feeding patterns were found to not differ between boys and girls (all $p > 0.3$, data not shown), however, infants that were no longer fully breastfed at 4 months were introduced to solids earlier than infants fully breastfed at 4 months ($p < 0.001$) (data not shown). No trends across FMI or FFMI quartiles were found for the majority of the infant feeding variables (**Table 2 and 3**), yet a negative trend across FMI quartiles was seen for the number of children fully breastfed at 4 months ($p = 0.028$) (Table 2). There was also a trend of higher maternal BMIs in the higher FMI quartiles ($p = 0.07$). Maternal age, height, gestational weight gain, smoking during pregnancy, parental educational level, paternal height and BMI, and household incomes were not related to the FMI quartiles (all, $p > 0.13$, data not shown). Positive trends across FFMI quartiles were seen for parental BMI (both $p < 0.02$), while negatives trends were seen for parental education (both $p < 0.05$, data not shown). Maternal age, height, gestational weight gain, smoking during pregnancy, paternal height and household incomes were not related to the FFMI quartile (all, $p > 0.18$, data not shown).

Association between early weight gain and body composition at 3 years of age

BWZ and change in WAZ from 0–5 months were found to be positively related to height, weight, BMI, FMI, and FFMI at 3 years of age in both the simple and adjusted models (**Table 4**). In addition to this, change in WAZ from 0–5 months was positively associated with the sum of skin folds ($p < 0.001$). The different growth patterns over time for the mean WAZs according to the FMI quartiles are shown in **Figure 1a.** There was significant interaction between the FMI quartiles and time ($p < 0.001$), with the most evident difference existing between growth patterns from 0–5 months. Controlling for the educational level of the mother, smoking during pregnancy, gestational weight gain, and parental BMI, differences between the quartiles showed that the mean WAZ of the highest FMI quartile was significantly higher than that of the other FMI quartiles at 5 months ($p < 0.002$) and 9 months ($p < 0.05$). At 18 months, only the WAZs of the first and second FMI quartiles were significantly lower than the highest ($p < 0.002$). At 36 months, the third FMI quartile was only just lower than the fourth FMI quartile ($p = 0.08$), yet the others remained even lower ($p < 0.001$). Growth patterns over time did not differ between the FFMI quartiles ($p = 0.17$), but the mean WAZ of the fourth quartile was significantly higher than all the other quartiles ($p < 0.001$) (**Figure 1b)**.

FMI and FFMI according to birth weight and early weight gain

The probability of being in the highest quartile of FMI and FFMI according to birth weight and early weight gain is shown in **Table 5.** We categorised birth weight into four categories and analysed the share of children from each category that were placed in the highest quartile of FMI and FFMI at 3 years of age. The same approach was taken for change in WAZ from 0–5 months. More children with a birth weight above 4000 g were placed in the highest quartile of FMI compared to children with birth weights from 3000–3500 g (40% compared to 17%, $p < 0.007$). For the group of children undergoing rapid growth in their first five months of life (change in WAZ > 0.67), 49% were placed in the highest quartile of FMI at 3 years of age, which was more than children with weight gains not exceeding 0.67 WAZ from 0–5 months (all groups, $p < 0.031$). A significantly larger proportion of the children with birth weights above 4000 g compared to 3000–3500 g and less than 3000 g were in the highest FFMI quartile at 3 years of age (40% compared to 17% and 13%, respectively, both $p < 0.04$). WAZ change from 0–5 months did not affect the probability of being in the highest FFMI quartile at 3 years of age.

Associations between early feeding practices and body composition at 3 years of age

Both in the unadjusted and adjusted regression analyses, full breastfeeding, partial breastfeeding, age of introduction to solids, and age of introduction to cow's milk were found to be not related to FMI or FFMI at 3 years of age (data not shown). However, when testing for possible interactions between early feeding practices and early growth, we found two effect modifications of duration of full breastfeeding (**Table 6**). The effect of BWZ on FMI was eliminated by full breastfeeding for 6 months compared to less than 1 month (from β = 0.69 to β = – 0.07, p = 0.002) (Table 6 & **Figure 2a**). A duration of full breastfeeding for 4–5 months attenuated the positive effect of change in WAZ from 0–5 months on FMI by 47% compared to less than 1 month (from β = 0. 81 (0.46 – 1.17) to β = 0.43 (0.05 – 0.81), p = 0.05), while 6 months of full breastfeeding eliminated the effect of WAZ on FMI (β = –0. 15 (–0.76 – 0.45), p = 0.002) (Table 6 & **Figure 2b**). A borderline effect modification on WAZ change from 0–5 months due to full breastfeeding for 1–3 months was also seen (45 % reduction, β = 0.45 (0.04 – 0.85), p = 0.08) (Table 6). The effect of age of introduction to solids on FMI did not interact with duration of full breastfeeding ($p > 0.25$), and no interactions were found between gender and age of introduction to solids or duration of full breastfeeding ($p > 0.23$).

Neither age of introduction to solids or duration of partial breastfeeding modified the effect of BWZ or change in WAZ from 0–5 months on FMI ($p > 0.3$). No interactions were found between BWZ, WAZ change from 0–5 months and early feeding practice on FFMI ($p > 0.6$).

Discussion

In this prospective cohort, we found that high birth weight and rapid growth in the first 5 months of life independently affected body composition and measures of adiposity at 3 years of age, while there were no effects of weight gain in the following age periods. Full breastfeeding for 4–6 months considerably attenuated the effect of birth weight and weight gain from 0–5 months on FMI at 3 years compared to less than 1 month. Our results indicate that longer durations of full breastfeeding, which is a modifiable factor, can attenuate the effect of birth weight and early growth on FM at 3 years of age.

After controlling for parental height, weight or BMI, gestational weight gain, mother's educational level, and smoking during pregnancy, our results show that birth weight and growth in the first 5 months of life are strong predictors of body composition at 3 years of age. A birth weight above 4000 g increased the probability of being in the highest quartile of FMI and FFMI at 3 years of age by approximately 50% compared to children with birth weights ranging from 3000–3500 g. Rapid weight gain above 0.67 *z*–scores from 0–5 months were strongly related to FMI but not FFMI. Other studies have also found rapid early weight gain to be associated with FM rather than FFM [3-5;40-42], though studies on the effect of birth weight on later body composition support a stronger association with FFM than FM [43;44]. It is possible that low birth weight is particularly responsible for a smaller proportion of FFM later in life [43]. However, one reason that we found birth weight to be equally related to FFM and FM could be due to the low number of children with birth weights below 2500 g in this cohort.

Length measures of the children at 0 and 5 months resulted in very high HAZ scores, most likely due to a tendency by midwifes and general medical practitioners to overestimate length measurements in the primary healthcare sector, as has been demonstrated by other studies[45]. The WAZ values were found to be above the WHO standards at all ages. Disregarding WFH and BAZ at birth and 5 months, WFH and BAZ values were also found to be above WHO standards at 9, 18, and 36 months of age. Part of the explanation for this is that the cohort of this study included infants that had only been breastfed for a short period. However, we have previously shown that the WAZ and BAZ of children from the SKOT cohort who were breastfed at 9 months were closer to the median of the WHO growth standards at 9 and 18 months or less compared to children that were no longer breastfed at 9 months [32]. However, duration of full or partial breastfeeding was not found to be directly associated with BMI, FMI, or FFMI at 3 years of age in this study.

Early feeding patterns as effect modifiers

The effect of birth weight on FMI at 3 years of age was eliminated if the child had been fully breastfed for 6 months. No effect modification was found for less than 6 months' duration of full breastfeeding. A 4–6 month duration of full breastfeeding was found to have a considerable modifying effect on the impact of early growth on FMI at 3 years of age, indicating that, aside from the direct effect of breastfeeding on early growth [11;12;32], a longer duration of full breastfeeding directly influences the extent to which early rapid weight gain adversely affects FM development. The DONALD study[46] showed a similar protective effect of full breastfeeding for at least 4 months with respect to body fat percentage among 249 infants ranging from 2–5 years of age with early rapid weight gain. Preliminary data from the PROBIT study also showed a strong relationship between early rapid weight gain and obesity at 6–7 years of age to be higher among children who had been exclusively formula fed from 1 month of age compared to other infants[47].

As the present study is observational, we cannot say if the found effect modifications can be explained by physiology, decisions made by parents, or advice given by healthcare workers. The duration of full breastfeeding and age of introduction to solids are by nature interdependent. Infants in the SKOT cohort still partially breastfed at 9 months had been introduced to complementary foods later than non-breastfed infants a 9 months[37]. Moreover, at 9 months, non-breastfed infants in this cohort had a higher intake of protein in their complementary diet compared to partially breastfed infants [37] also found to modify the effect of early growth on FM development[46]. The fact that we did not see a direct association between early feeding and FMI could be due to insufficient power and a low number of overweight children in our study.

The relationships between FFMI, birth weight, and early growth were not affected by infant nutrition in this study. Thus, we speculate that factors in pregnancy, the child's level of physical activity, and dietary quality beyond infancy have a greater impact on FFMI.

Strengths and limitations

In this study, FM and FFM were predicted using predictive equations generated from a large number of DXA scans in the same cohort. This was done to be able to include more children in the analyses, as we had acceptable DXA scans from only 101 children, bioelectrical impedances of 233 children[36]. Compared with FFM and FM measured by DXA, the predicted FFM and FM showed a prediction error of 2.8% (333 g) for FFM, and a prediction error of 11.3% (284 g) for FM[36]. We find it likely that FMI in 3-year-old children is a good predictor of later risk of obesity. Other studies have shown a high level of tracking of FM from 2–7 years [41] and 4–9 years[48], with a higher increase among those who acquired a high fat percentage earlier in life [41;48]. A strength of this study is the prospective and detailed information it obtained with regard to growth. The study's data on the duration of breastfeeding and age of introduction to solids was collected retrospectively at 9 months. Unfortunately, however, the data on age of introduction to solids was crude (in months) and did not allow for a more detailed grouping of the ages of introduction. The main limitation of our study is its small number of children fully breastfed for 6 months (n = 21), as this group appears to drive the significant effect modifications. With an observational study design, it will always be a risk that the children breastfed for 6 months differs from children being breastfed for a shorter period of time with other characteristics.

The families in the SKOT study are characterized by extensive educations and high incomes and associated with durations of breastfeeding, ages of introduction to solids, and complementary diets [19] that may possibly reduce extremes in infant feeding practices. In contrast to other studies [28;29], most children in the SKOT study were introduced to solids at 4 months of age or later. Despite this relative homogeneity, infant feeding practices were found to modify the effect of early growth. The effect modifications of early feeding are likely to depend on alternatives to breastfeeding that differ from country to country, and therefore we encourage other studies to investigate similar effect modifications of infant feeding on early growth to extend the generalizability of this study to populations of different characteristics.

Conclusion

In conclusion, birth weight and weight gain in the first 5 months of life had a strong influence on later body composition both in terms of FM and FFM. None of the other periods, from 5 months to 3 years of age, showed significant relations with FM and FFM at 3 years of age.

Moreover, we have demonstrated that full breastfeeding for 4–6 months attenuated the impact of early growth on FMI at 3 years of age, while full breastfeeding for 6 months eliminated the impact of high birth weight on FMI. This complex relation suggests that breastfeeding has an additional protective effect aside from a direct effect on early growth. Infant feeding was found not to modify the effect of early growth on FFMI. Our results suggest that early feeding can be important to modify the effect of high birth weight and excessive weight gain in early infancy, and support current recommendations concerning the duration of full breastfeeding.

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Conflicts of interest:

None.

Authorship:

The study was designed by KFM, CM, and KTE and LBC conducted the 3-year data collection examination. KTE, KFM, and CM formulated the research question. KTE analysed data and wrote the first draft of the manuscript. SMJ and CR supervised the quality standards of the statistical analyses. All authors contributed to interpretation of the results and commented on drafts. KTE have primary responsibility for the final content. All authors have read and approved the final manuscript.

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Table 1. Anthropometric characteristics in the SKOT cohort according to WHO z-scores[35].

	Mean (range)	P-value
At birth (n = 233)*		
WAZ	0.48 (-1.98 - 2.71)	< 0.001
HAZ	1.39 (-3.84 - 4.29)	< 0.001
WFH	-0.95 (-4.71 - 2.54)	< 0.001
BAZ	-0.35 (-3.99 - 2.63)	< 0.001
At 5 months (n = 167)†		
WAZ	0.32 (-2.00 - 3.29)	< 0.001
HAZ	1.21 (-1.12 - 4-21)	< 0.001
WFH	-0.40 (-2.57 - 2.89)	< 0.001
BAZ	-0.48 (-2.62 - 2.88)	< 0.001
At 9 months (n = 233)		
WAZ	0.40 (-1.62 - 3.00)	< 0.001
HAZ	0.25 (-1.94 - 2.84)	< 0.001
WFH	0.43 (-1.52 - 4.21)	< 0.001
BAZ	0.35 (-1.75 - 4.37)	< 0.001
At 18 months (n = 229)		
WAZ	0.41 (-2.02 - 2.58)	< 0.001
HAZ‡	0.11 (-2.91 - 2.53)	0.07
WFH‡	0.49 (- 1.86 - 3.00)	< 0.001
BAZ‡	0.49 (-1.69 - 3.14)	< 0.001
At 36 months (n = 233)		
WAZ	0.17 (-2.06 - 2.04)	< 0.001
HAZ	-0.05 (-2.09 - 2.36)	0.34
WFH	0.28 (-1.76 - 2.36)	< 0.001
BAZ	0.27 (-1.78 - 2.44)	< 0.001

Values are means [minimum-maximum]. Differences between WAZ, HAZ, WFH, and BAZ in the study sample, as well as the WHO standards, were evaluated by means of one-sample *t*-tests. WAZ, weight-for-age z-score; HAZ, height/length-for-age z-score; WFH, weight-for-height/length z-score; BAZ, BMI-for-age z-score.

* Measured by midwifes at the hospital.

† Measured by general medical practitioner.

‡ Missing values for 3 children.

Table 2. Characteristics of the SKOT children according to FMI quartile at 3 years of age

		n	Overall	3-year FMI quartile				P for trend
				1 (n = 58)	2 (n = 58)	3 (n = 59)	4 (n = 58)	
Anthropometric characteristics								
FM (kg)*	Girls	122	2.71 (0.74)	1.82 (0.34)	2.44 (0.23)	3.00 (0.21)	3.61 (0.43)	<0.001
	Boys	111	2.29 (0.65)	1.56 (0.38)	2.03 (0.16)	2.41 (0.20)	3.13 (0.38)	<0.001
FFM (kg)*	Girls	122	11.65 (0.90)	11.26 (0.93)	11.33 (0.76)	11.97 (0.76)	12.05 (0.88)	<0.001
	Boys	111	12.67 (1.01)	12.46 (1.06)	12.41 (1.06)	12.67 (0.78)	13.14 (0.99)	0.008
BMI (kg/m^2)		233	15.8 [15.1;16.6]	14.8 [14.3;15.3]	15.4 [15.1;15.8]	16.0 [15.7;16.4]	17.4 [16.9;17.9]	< 0.001
Skin folds triceps (mm)		224	9.3 [8.1;10.4]	8.2 [7.6;9.3]	8.8 [8.0;10.3]	9.4 [8.3;10.4]	10.4 [9.4;11.8]	< 0.001
Skin folds subscapular (mm)		230	6.3 [5.5;7.2]	5.8 [5.2;6.4]	6.1 [5.4;6.7]	6.3 [5.7;7.2]	7.7 [6.3;8.7]	< 0.001
Infant feeding								
Days of exclusive BF		233	126 [91;152]	125 [122;152]	135 [117;166]	122 [61;143]	129 [61;152]	0.20
Fully BF at 4 mo, % (n)		233	67.8 (158)	77.2 (44)	74.6 (44)	56.9 (33)	62.7 (37)	0.028
Days of any BF		230	274 [183;349]	304 [212;357]	284 [183;365]	227 [152;318]	265 [196;365]	0.98
Partial BF at 9 mo, % (n)		233	42.5 (99)	50.9 (29)	42.4 (25)	34.5 (20)	42.4 (25)	0.31
Formula at 9 mo (g/d)		233	169 [0;410]	93 [0;334]	169 [7;401]	269 [11;449]	138 [0;447]	0.15

Introduction to solids (mo)	233	4.0 [4.0;5.0]	4.0 [4.0;5.0]	4.0 [4.0;5.0]	4.0 [4.0;5.0]	4.0 [4.0;5.0]	0.95

Data presented as mean (SD) or median [IQR] if not normally distributed. Trends across FMI quartiles were assessed using linear regression models adjusted for gender. FMI, fat mass index (kg/m^2); FM, fat mass; FFM, fat-free mass; BF, breastfed; mo, months.

* Not adjusted for gender.

Table 3. Characteristics of the SKOT children according to FFMI quartile at 3 years of age

		n	Overall	3-year FFMI quartile				P for trend
				1 (n = 57)	2 (n = 59)	3 (n = 59)	4 (n = 58)	
Anthropometric characteristics								
FM (kg)*	Girls	122	2.71 (0.74)	2.37 (0.59)	2.46 (0.62)	2.78 (0.65)	3.24 (0.76)	< 0.001
	Boys	111	2.29 (0.65)	1.99 (0.48)	2.28 (0.51)	2.19 (0.78)	2.69 (0.59)	< 0.001
FFM (kg)*	Girls	122	11.65 (0.90)	11.22 (0.85)	11.31 (0.82)	11.77 (0.80)	12.30 (0.73)	< 0.001
	Boys	111	12.67 (1.01)	12.03 (0.89)	12.49 (0.83)	12.79 (0.90)	13.38 (0.95)	< 0.001
BMI (kg/m^2)		233	15.8 [15.1;16.6]	14.8 [14.4;15.2]	15.6 [15.2;16.0]	15.9 [15.5;16.6]	17.3 [16.7;17.9]	< 0.001
Skin folds triceps (mm)		224	9.3 [8.1;10.4]	8.6 [7.7;9.9]	9.0 [8.0;10.2]	9.4 [8.3;10.7]	9.7 [8.8;11.1]	< 0.001
Skin folds subscapular (mm)		230	6.3 [5.5;7.2]	5.9 [5.2;6.7]	6.3 [5.4;6.9]	6.4 [5.7;7.4]	6.9 [5.9;8.2]	< 0.001
Infant feeding								
Days of exclusive BF		233	126 [91;152]	132 [105;152]	136 [115;152]	122 [44;152]	122 [75;152]	0.24
Fully BF at 4 mo, % (n)		233	67.8 (158)	70.7 (41)	74.1 (43)	62.7 (37)	63.8 (37)	0.26
Days of any BF		230	274 [183;349]	274 [183;335]	318 [197;365]	244 [173;335]	274 [183;365]	0.99
Partial BF at 9 mo, % (n)		233	42.5 (99)	48.3 (28)	48.3 (28)	33.9 (20)	39.7 (23)	0.19
Formula at 9 mo (g/d)		233	169 [0;410]	253 [14;429]	89 [0;316]	231 [0;432]	146 [0;422]	0.83

Introduction to solids (mo)	233	4.0 [4.0;5.0]	4.0 [4.0;5.0]	4.0 [4.0;5.0]	4.0 [4.0;5.0]	4.0 [4.0;5.0]	0.52

Data presented as mean (SD) or median [IQR] if not normally distributed. Trends across FFMI quartiles were assessed using linear regression models adjusted for gender. FFMI, fat-free mass index (kg/m^2); FM, fat mass; FFM, fat-free mass; BF, breastfed; mo, months.

* Not adjusted for gender.

Table 4. Relation between weight gain during four time periods (Δ weight-for-age z-score) and body composition outcomes at 3 years of age expressed as regression coefficients

	Outcomes at 3 years of age											
		Height (cm)		Weight (kg)		BMI (kg/m^2)		FMI (kg/m^2)	FFMI (kg/m^2)		∑ SF (mm)
	n	β (SE)	N	β (SE)	n	β (SE)	n	β (SE)	β (SE)	n	β (SE)
Simple model											
BWZ	233	0.80 (0.23)[c]	233	0.59 (0.10)[c]	233	0.38 (0.08)[c]	233	0.21 (0.05)[c]	0.15 (0.04)[c]	223	0.32 (0.23)
Δ WAZ, 0–5 mo	167	0.83 (0.30)[b]	167	0.85 (0.11)[c]	167	0.66 (0.09)[c]	167	0.42 (0.06)[c]	0.22 (0.05)[c]	161	1.33 (0.22)[c]
Δ WAZ, 5–9 mo	167	1.34 (0.38)[c]	167	0.68 (0.19)[c]	167	0.29 (0.15)	167	0.12 (0.10)	0.15 (0.09)	161	0.09 (0.35)
Δ WAZ, 9–18 mo	229	0.72 (0.42)	229	0.12 (0.21)	229	-0.10 (0.16)	229	-0.18 (0.10)	0.08 (0.08)	219	-0.46 (0.37)
Δ WAZ, 18–36 mo	229	1.66 (0.47)[c]	229	0.72 (0.21)[c]	229	0.24 (0.18)	229	0.14 (0.11)	0.08 (0.09)	219	0.10 (0.38)
Adjusted model											
BWZ	217	0.68 (0.21)[c]	215	0.52 (0.10)[c]	215	0.35 (0.08)[c]	215	0.21 (0.05)[c]	0.13 (0.05)[b]	206	0.24 (0.25)
Δ WAZ, 0–5 mo	153	0.70 (0.28)[a]	155	0.78 (0.10)[c]	152	0.64 (0.09)[c]	152	0.42 (0.06)[c]	0.20 (0.06)[c]	147	1.43 (0.26)[c]
Δ WAZ, 5–9 mo	153	1.26 (0.46)[b]	155	0.56 (0.21)[b]	152	0.10 (0.17)	152	-0.02 (0.11)	0.10 (0.10)	147	-0.30 (0.45)
Δ WAZ, 9–18 mo	213	0.94 (0.46)[a]	211	0.19 (0.21)	211	-0.10 (0.16)	211	-0.17 (0.10)	0.07 (0.08)	202	-0.47 (0.43)
Δ WAZ, 18–36 mo	213	1.09 (0.44)[a]	211	0.62 (0.21)[b]	211	0.22 (0.18)	211	0.10 (0.12)	0.10 (0.10)	202	0.04 (0.41)

Each cell represents a multiple regression model with body composition at 3 years of age as the dependent variable and the left row showing explanatory variables. The simple model was adjusted for gender and BWZ. The adjusted model was adjusted for gender, BWZ, income, mother's educational level, smoking during pregnancy, and gestational weight gain. Height was also adjusted for parental height, weight was adjusted for parental weight, and BMI, FMI, FFMI, and sum of skinfolds were all adjusted for parental BMI.

FMI, fat mass index; FFMI, fat-free mass index; ∑ SF, sum of triceps and subscapular skin folds; BWZ, birth weight z-score; mo, months; WAZ, weight-for-age z-score.

[a] $p < 0.05$.

[b] $p \leq 0.01$.

[c] $p \leq 0.001$.

Table 5: Prevalence of children in the fourth quartile of FMI and FFMI according to birth weight and WAZ change from 0–5 months

	n	n placed in fourth quartile of FMI (%)	P*	n placed in fourth quartile of FFMI (%)	P*
Birth weight (g)					
< 3000	23	5 (21.7)	0.17†	3 (13.0)	0.039†
3000–3499	92	16 (17.4)	0.007	16 (17.4)	0.007
3500–3999	83	23 (27.7)	0.19	25 (30.1)	0.30
≥ 4000	35	14 (40.0)	reference	14 (40.0)	reference
Δ WAZ, 0-5 months					
< -0.67	49	7 (14.3)	0.001	10 (20.4)	0.47
-0.67–0	41	6 (14.6)	0.001	7 (17.1)	0.29
0–0.67	40	10 (25.0)	0.031	9 (22.5)	0.65
> 0.67	37	18 (48.7)	reference	10 (27.0)	reference

FMI, fat mass index (kg/m^2); FFMI, fat-free mass index (kg/m^2); Δ WAZ, change in weight-for-age z-score.

* Comparison of group difference against reference by Pearson X^2.

† Comparison by Fischer's exact.

Table 6: Multiple regression model of the association between birth weight, weight gain from 0–5 months, infant feeding, and FMI at 3 years of age (n = 152).

Risk factor	Estimate	SE	P
Intercept	2.42	0.64	< 0.001
BWZ	0.69	0.15	< 0.001
Δ WAZ 0-5 months	0.81	0.18	< 0.001
Sex (0, female; 1, male)	-0.59	0.09	< 0.001
Full breastfeeding			
< 1 months	reference		
1–3 months	-0.03	0.20	0.88
4–5 months	-0.07	0.15	0.66
6 months	-0.29	0.31	0.34
Age of introduction			
3–4 months	reference		
5 months	0.14	0.12	0.23
6 months	0.44	0.28	0.12
Maternal BMI	0.00	0.02	0.85
Gestational weight gain	-0.01	0.01	0.34
Maternal educational level			
No education above school level	reference		
1–2 years	0.53	0.35	0.13
Further education < 3 years of age	0.45	0.32	0.15
Further education 3–4 years	0.35	0.30	0.24
Further education > 4 years	0.40	0.31	0.20
Smoking during pregnancy (0, No; 1, Yes)	0.07	0.29	0.80
Paternal BMI	0.00	0.02	0.88
Household income	0.00	0.01	0.88
BWZ x full breastfeeding			
< 1 months	reference		

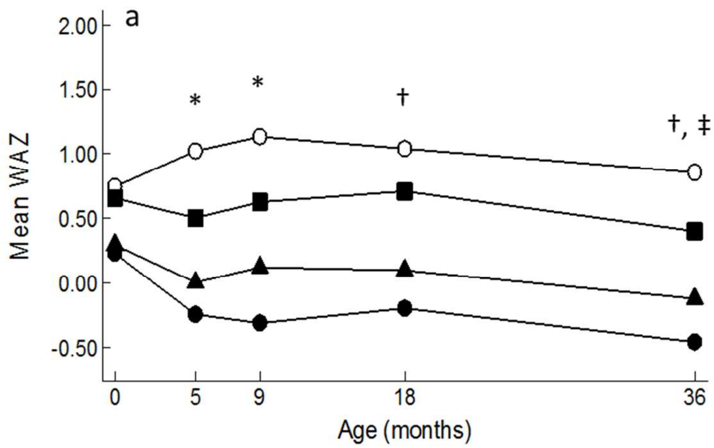
1–3 months	-0.09	0.22	0.67
4–5 months	-0.17	0.17	0.33
6 months	-0.76	0.24	0.002
Δ WAZ 0-5 months x full breastfeeding			
< 1 months	reference		
1–3 months	-0.37	0.20	0.08
4–5 months	-0.38	0.19	0.05
6 months	-0.97	0.30	0.002

A multiple regression model with FMI (kg/m^2) at 3 years of age as the dependent variable with explanatory variables listed in the left row. The intercept represents the mean value of FMI at 3 years of age in the reference groups. FMI, fat mass index; BWZ, birth weight z-score; WAZ, weight-for-age z-score.

Figures Legend

Figure 1: Change in WAZ (weight-for-age z-scores) from 0–36 months according to (a), fat mass index (FMI), and (b), fat-free mass index (FFMI) quartiles at 3 years of age. 1st quartile (●), 2nd quartile (▲), 3rd quartile (■), 4th quartile (○). Differences between quartiles were assessed via mixed model analyses controlling for the educational level of the mother, smoking during pregnancy, gestational weight gain, household income, and parental BMI.*4th quartile (reference) higher than all other quartiles ($p < 0.05$). †4th quartile higher than 1st and 2nd quartiles ($p < 0.002$). ‡4th quartile borderline higher than 3rd quartile ($p < 0.08$).

Figure 2: Predicted mean fat mass index (FMI, kg/m^2) at 3 years of age according to (a), birth weight z-score (BWZ), and (b), change in weight-for-age z-scores (WAZ) from 0–5 months categorized into subgroups of breastfeeding duration in 152 children in the SKOT cohort. Figure lines are drawn from the coefficients in question derived from the multiple regression model presented in Table 6. (a) illustrates the interaction between BWZ and duration of full breastfeeding, and (b) illustrates the interaction between WAZ change from 0–5 months and duration of full breastfeeding. Duration of full breastfeeding < 1 months (●, n = 36), 1–3 months (▲, n = 39), 4–5 months (■, n = 137) and 6 months (○, n = 21).



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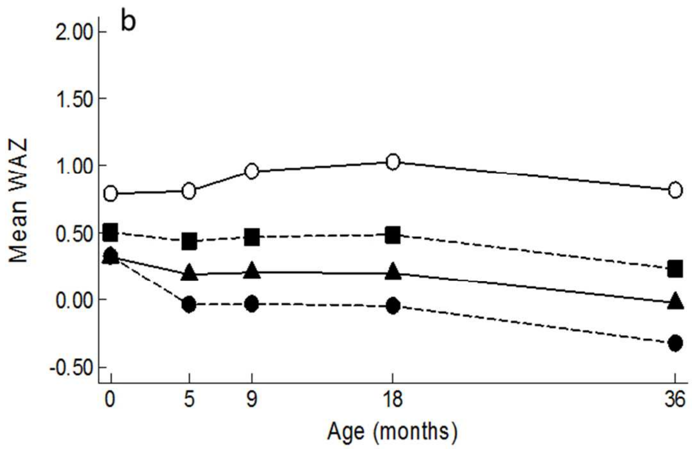

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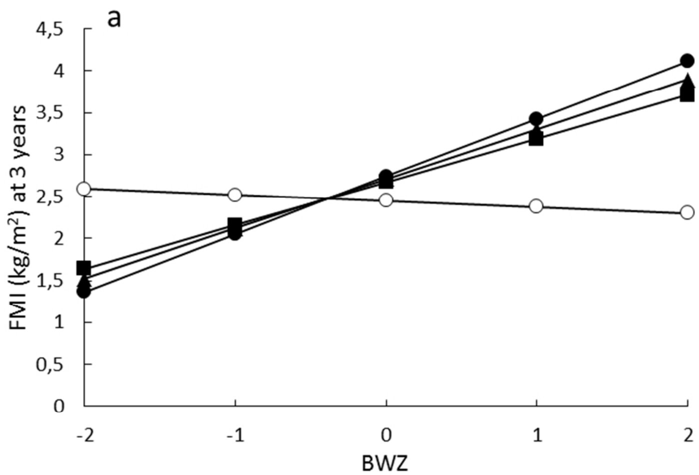

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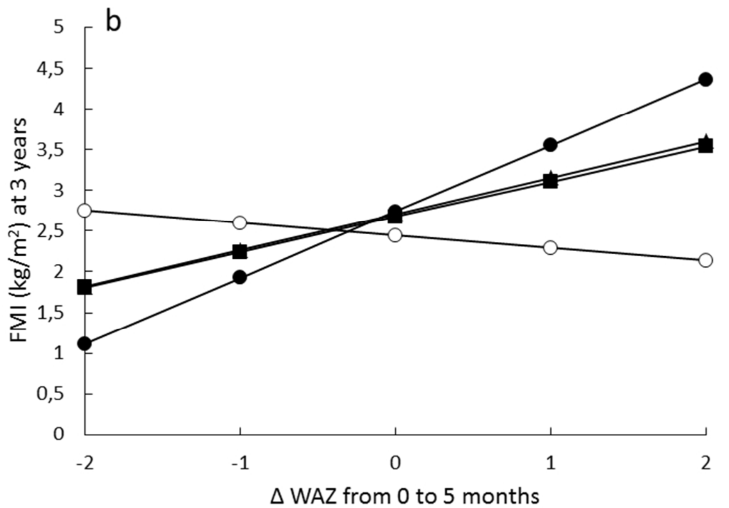

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