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Fat mass and fat-free mass track from infancy to childhood: New insights in body composition programming in early life

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Abstract

Objective: Early life is a critical window for adiposity programming. This study investigated whether fat mass percentage (FM%), fat mass index (FMI), abdominal fat, and fat-free mass (FFM) in early life track into childhood and whether there are sex differences and differences between infant feeding types.

Methods: Detailed body composition was longitudinally measured by air-displacement

plethysmography, dual-energy x-ray absorptiometry, and abdominal ultrasound in 224 healthy, term-born children. Measurements were divided into tertiles. Odds ratios (OR) of remaining in the highest tertile of FM%, FMI, abdominal subcutaneous and visceral fat, and FFM index (FFMI) were calculated from early life to age 4 years. **Results:** High FM% and FMI tracked from age 3 and 6 months to age 4 years (OR = 4.34 [p = 0.002] and OR = 6.54 [p < 0.001]). High subcutaneous abdominal fat tracked from age 6 months to age 4 years (OR = 2.30 [p = 0.012]). High FFMI tracked from age 1, 3, and 6 months to age 4 years (OR = 4.16 [p = 0.005], 3.71 [p = 0.004], and 3.36 [p = 0.019]). In non-exclusively breastfed infants, high FM% tracked from early life to age 4 years, whereas this was not the case for exclusively breastfed in-

Conclusions: Infants with high FM%, FMI, subcutaneous abdominal fat, and FFMI in early life are likely to remain in the highest tertile at age 4 years. Exclusive breastfeeding for 3 months is potentially protective against having high FM% at age 4 years.

fants. There was no tracking in visceral fat or sex differences.

INTRODUCTION

Childhood obesity is a global public health threat with an alarming rising incidence. Globally, 38 million children under the age of 5 years had overweight or obesity in 2019 (1). Obesity at a young age has direct adverse consequences as well as long-term morbidity, such as cardiovascular disease, insulin resistance, and type 2 diabetes mellitus. Without intervention, children with overweight or obesity have a high risk of having overweight or obesity as adults (1).

Therefore, it is important to unravel which period during childhood has a great influence on adiposity programming.

It has been reported that weight-to-height and BMI SD score (SDS) track from childhood into adulthood (2). A high BMI at age 5 years and a fast increase in BMI SDS in early childhood are predictive for overweight and obesity in adolescence (3). Our research group found that rapid weight gain in the first months of life is an important risk factor for having overweight or obesity and having an unfavorable metabolic profile in early adulthood (4). This indicates that the

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first months of life especially are a critical window for adiposity programming and development of noncommunicable diseases later in life (4,5). However, it has been demonstrated that infants and young children with a comparable weight or BMI have a highly variable body composition and fat distribution (6-9). Excessive fat mass and visceral fat accumulation are important contributors to the development of an unfavorable metabolic outcome (10,11). We found that infants with a rapid rise in fat mass in the first 6 months of life have higher fat mass trajectories until 2 years of age (12). Despite the development of accurate methods for body composition measurement in infants and young children, such as air-displacement plethysmography (ADP) (13,14), data about tracking of high fat mass and fat-free mass (FFM) from infancy to childhood are not yet available.

Therefore, we evaluated the tracking of high fat mass percentage (FM%) and abdominal fat distribution, measured as high abdominal subcutaneous and visceral fat, in our prospective cohort from age 1, 3, and 6 months until the age of 4 years. We also determined whether high FFM index (FFMI) would track from infancy to childhood. We hypothesized that infants with high FM%, abdominal subcutaneous fat, or visceral fat in early infancy would continue to have high body fat measures at 4 years of age. In addition, we investigated whether this tracking would be different between boys and girls or between types of infant feeding.

METHODS

Participants

This current study was embedded in the Sophia Pluto study, a birth cohort study of healthy infants aiming to provide detailed data on body composition from early life to childhood (6,12). Infants were recruited from several maternity wards in Rotterdam, the second largest city in The Netherlands, between 2013 and 2017. All participants met the following inclusion criteria: born term (≥37 weeks' gestation) and singleton, with an uncomplicated neonatal period and without severe asphyxia (defined as an Apgar score below 3 after 5 minutes), sepsis, or the need for respiratory ventilation, and at least 4 years of age with complete follow-up.

Exclusion criteria were maternal disease or medication that could interfere with fetal growth, including maternal corticosteroids and diabetes mellitus, known congenital or postnatal disease, or intrauterine infection that could interfere with growth. The Medical Ethics Committee of Erasmus University Medical Center approved the study, and written informed consent was given by all parents or caregivers with parental authority.

Data collection and measurements

Outpatient clinic visits were scheduled at 1, 3, and 6 months and at 4 years. Birth data were taken from hospital and midwife records. Maternal and paternal characteristics and feeding type and habits

Study Importance

What is already known?

- ► Early life may be a critical window for adiposity programming.
- ► A rapid rise in fat mass percentage (FM%) in the first 6 months of life is associated with higher FM% trajectories until the age of 2 years.

What does this study add?

- ► Infants with high FM%, fat mass index, abdominal subcutaneous fat, and fat-free mass index in the highest tertile during the first 6 months of life are more likely to remain in the highest tertile at 4 years of age.
- ► In non-exclusively breastfed infants, FM% in the highest tertile in early life tracks significantly to the highest tertile at 4 years of age, whereas this is not the case for exclusively breastfed infants.

How might these results change the direction of research or the focus of clinical practice?

 Our results support the presence of a critical window of adiposity and fat-free mass programming in the first 6 months of life.

were obtained by interviews at the clinic visits and completed questionnaires from both parents. Infant feeding mode was categorized as exclusive breastfeeding (EBF) if infants had EBF for at least the first 3 months of life. Exclusive formula feeding (EFF) was defined as starting EFF before 1 month of age. Mixed feeding was defined as starting a combination of breastfeeding and formula feeding between 1 and 3 months of age.

Anthropometrics

Weight was measured to the nearest 5 g by an electronic infant scale (Seca 717) at 1, 3, and 6 months and by a flat scale (Seca 876) at 4 years. Length was measured twice in the supine position to the nearest 0.1 cm by an Infantometer (Seca 416) at 1, 3, and 6 months and in the upright position by a stadiometer (Seca 213) at 4 years. BMI was calculated as weight in kilograms divided by height in meters squared.

Body composition

Body composition was measured with ADP by Pea Pod (Infant Body Composition System, COSMED) during the visits at 1, 3, and

6 months of age, as described in detail elsewhere (6). ADP was conducted using the same machine. The machine was used and calibrated daily according to the user's manual (15). ADP was validated earlier against a reference four-compartment model, and reliability was determined with a percent coefficient of variance of 7.9% for FM% (14).

When the infant exceeded the weight limit of 8 kg at 6 months, body composition was measured by dual-energy x-ray absorptiometry (DXA) scan (GE Prodigy Advance R000279, GE Healthcare; enCORE software version 14.1). A vacuum cushion was used to avoid movement artifacts, which we have reported to have similar results at age 6 months compared with ADP (16). At age 4 years, body composition was determined using the same DXA machine without a vacuum cushion. Children wore only underwear and they were swaddled in a cotton blanket. During the study, the same DXA machine was used and calibrated daily according to the protocol recommended by the supplier (17). Percent coefficient of variance for FM% was determined earlier to be between 0.39% and 4.49% (18).

FM% was calculated as fat mass in kilograms divided by total body weight in kilograms times 100%. Fat mass index (FMI) was calculated as fat mass in kilograms divided by length in meters squared. FFMI was calculated as FFM in kilograms divided by length in meters squared.

Abdominal fat

Abdominal subcutaneous and visceral fat was determined as single plane depth in centimeters at every visit, starting from 3 months, using ultrasound (ProSound 2 ultrasound with a UST-9137 convex transducer; Hitachi Aloka Medical, Ltd.) (19). Both were measured in the supine position, placing the transducer on the intercept of the xiphoid line and the waist circumference measurement plane. Visceral fat was measured in the longitudinal plane from the peritoneal boundary to the corpus of the lumbar vertebrae with a probe depth of 9 cm and subcutaneous fat in the transverse plane from the cutaneous boundary to the linea alba with a probe depth of 4 cm. Minimal pressure was applied. Validity and reproducibility of measurements were confirmed previously (19). The relative interobserver technical error of measurement was 3.2% for visceral fat and 3.6% for subcutaneous fat.

Statistical analysis

SDS for birth length and birth weight was calculated and corrected for gestational age and sex. SDS for length and weight was calculated at every visit, based on Dutch references, using Growth Analyser software (http://www.growthanalyser.org) (20). Using World Health Organization (WHO) classification, overweight at age 4 years was defined as weight-for-length > 2 SDS, and obesity was defined as

weight-for-length > 3 SDS (1). Underweight was defined as weight-for-age < -2 SDS (21).

Baseline characteristics and body composition measurements are expressed as mean (SD). Not-normally distributed values are expressed as median (interquartile range). Independent Student t test was used to determine differences in the baseline characteristics and body composition measurements between boys and girls. Because of the lack of longitudinal reference values for FM%, FMI, FFMI, and abdominal subcutaneous and visceral fat measured by ultrasound from infancy until 4 years of age, we used categorical outcomes. Boys and girls were divided at each time point into sexspecific tertiles for FM%, FFMI, abdominal subcutaneous and visceral fat, and BMI SDS, and these were subsequently merged into group tertiles for "high," "moderate," and "low." Logistic regression models were used to calculate the odds ratio (OR) for having high FM%, FMI, FFMI, abdominal subcutaneous and visceral fat, or BMI SDS at 4 years of age, based on being in the high group at 1, 3, and 6 months. OR was calculated using the low group at 4 years of age as the reference category. An OR above 1 for remaining in the high group over time was considered as significant tracking. All logistic regression models were corrected for infant feeding mode until age 3 months. Additional adjustment for sex did not change the results and thus was not included in the final models. If infant feeding type was a significant factor in one of the models, logistic regression models were conducted for EBF and non-EBF infants separately. In order to determine differences between sex, logistic regression models were performed for boys and girls separately.

Statistical tests were performed with SPSS Statistics version 25.0 (IBM Corp.). Results were regarded as statistically significant if p < 0.05.

RESULTS

Clinical characteristics are presented in Table 1. The total group consisted of 224 infants, and 53.6% were male. Weight and length were different between boys and girls at 1, 3, and 6 months of age. Based on the WHO criteria, most children at 4 years of age had normal weight, and only eight (3.6%) children had overweight or obesity. FM%, FFMI, abdominal subcutaneous and visceral fat, and BMI SDS were divided into "high," "moderate," and "low" groups. Distribution of these groups is presented in Table 2.

Tracking of FM% and FMI

High FM% tracked from age 3 and 6 months to 4 years, with OR = 4.34 (p = 0.002) and OR = 6.54 (p < 0.001), respectively (Table 3). High FMI also tracked from age 3 and 6 months to 4 years, with OR = 2.62 (p = 0.027) and OR = 5.68 (p = 0.001), respectively. There was no tracking from age 1 month to 4 years, and there was no difference in tracking of high FM% or FMI between boys and girls (data not shown).



TABLE 1 Child characteristics

	Boys (n = 120; 53.6%)	Girls (n = 104: 46.4%)	p value
Birth	120, 33.070	104, 40.470)	p value
Gestational age (wk)	39.58 (1.26)	39.86 (1.08)	0.080
Weight SDS	0.29 (1.01)	0.14 (1.05)	0.270
Length SDS*	0.70 (1.14)	0.63 (1.15)	0.724
Ethnicity (%)	0.70 (1.14)	0.03 (1.13)	0.064
Caucasian	69.2	65.4	0.004
Black	1.7	10.6	
Asian	0.8	1.0	
Latin	0.8	0	
Other	22.5	19.2	
		3.8	
Missing	5.0	3.8	0.000
Delivery mode (%)	(0.0	74.0	0.080
Vaginal	60.8	74.0	
Cesarean section	39.2	26.0	
Age 1 month	4.07.70.55	4.00 (0.51)	0.00
Weight (kg)	4.36 (0.55)	4.09 (0.51)	<0.001
Weight-for-length SDS	-0.05 (0.86)	-0.03 (0.88)	0.896
Length (cm)	54.93 (2.12)	53.85 (2.21)	<0.001
Length SDS	0.11 (0.91)	-0.02 (0.90)	0.284
Age 3 months			
Feeding mode until age 3 months (%)			0.783
EBF	40.8	43.3	
EFF	29.2	25.0	
Mix	30.0	31.7	
Weight (kg)	6.19 (0.67)	5.73 (0.58)	<0.001
Weight-for-length SDS	0.26 (0.90)	0.20 (0.93)	0.630
Length (cm)	61.95 (2.10)	60.41 (1.97)	<0.001
Length SDS	0.42 (0.85)	0.26 (0.80)	0.146
Age 6 months			
Weight (kg)	7.92 (0.82)	7.34 (0.75)	<0.001
Weight-for-length SDS	0.10 (0.94)	0.07 (0.96)	0.813
Length (cm)	68.67 (2.17)	66.70 (2.09)	<0.001
Length SDS	0.24 (0.87)	0.10 (0.82)	0.244
Age 4 years			
Weight (kg)	17.52 (2.16)	17.18 (2.12)	0.221
Weight-for-length SDS at age 4 y	0.18 (1.18)	0.22 (0.92)	0.745
Underweight (%)	8 (6.7)	2 (1.9)	0.188
Normal weight (%)	106 (88.3)	100 (96.2)	
	4 (3.3)	1 (1.0)	
Overweight (%)			
Overweight (%) Obesity (%)	2 (1.7)	1 (1.0)	
_	2 (1.7) 104.98 (3.91)	1 (1.0) 104.31 (4.28)	0.233

Data expressed as mean (SD). Significant data are bold. Abbreviations: EBF, exclusive breastfeeding; EFF, exclusive formula feeding; Mix, mixed feeding; SDS, SD score.

Tracking of FFMI

High FFMI tracked from age 1, 3, and 6 months to 4 years, with OR = 4.16 (p = 0.005), OR = 3.71 (p = 0.004), and OR = 3.36 (p = 0.019), respectively (Table 3). We found no difference in tracking of high FFMI between sexes.

Tracking of abdominal fat

Median visceral and subcutaneous abdominal fat decreased with age. High abdominal subcutaneous fat tracked from age 6 months to 4 years, with OR = 2.30 (p = 0.035) (Table 3). No tracking of visceral fat was found. There was no sex difference in tracking of high abdominal fat.

Tracking of BMI

For the sake of comparison with literature data, we also evaluated the tracking of BMI SDS (Table 3). High BMI SDS tracked from 1, 3, and 6 months to 4 years, with OR = 3.15 (p = 0.012), OR = 6.50 (p < 0.001), and OR = 7.74 (p < 0.001), respectively. No sex differences in tracking of high BMI SDS were found.

Influence of infant feeding type

Tracking of high FM% was influenced by infant feeding type. We analyzed tracking of FM% separately for EBF infants and non-EBF infants (children with EFF and mixed feeding; Table 4). In the EBF infants, there was no significant tracking of high FM% from early life to 4 years of age. However, in non-EBF infants, we found tracking from age 3 and 6 months to 4 years, with OR = 4.00 (p = 0.006) and OR = 7.33 (p = 0.001), respectively.

There was no influence of infant feeding type in tracking of high FFMI, abdominal subcutaneous and visceral fat, and BMI SDS to 4 years of age.

DISCUSSION

In the present study, we show that infants in the highest tertile of FM%, FMI, abdominal subcutaneous fat, and FFMI in early life had high odds to remain in the highest tertile at 4 years of age. In contrast to EBF infants, non-EBF infants tracked in the highest FM% tertile from early life to 4 years of age, indicating a difference in tracking between infant feeding types.

High FM% and FMI tracked from age 3 and 6 months to 4 years, indicating that infants with high FM% and FMI in the first 6 months of life are more likely to still have high FM% and FMI at 4 years of age. Previously, others have found a moderate association between FM% and FMI at 3 and 4 months and 4 years of age (22,23). Our

^{*}Birth length was available in 71 boys and 60 girls.



TABLE 2 "High" and "low" groups of FM%, FMI, FFMI, abdominal subcutaneous and visceral fat, and BMI SDS

		FM%	FMI (kg/m²)	FFMI (kg/m²)	Abdominal subcutaneous fat (cm)	Visceral fat (cm)	BMI SDS (kg/m²)
Age 1 month							
High	ð	>18.03	>2.57	>12.41	NA	NA	>0.77
	P	>18.80	>2.60	>11.91	NA	NA	>0.74
Low	ð	<14.27	<2.09	<11.65	NA	NA	<-0.19
	Q	<14.50	<2.01	<11.35	NA	NA	<-0.02
Age 3 months							
High	ð	>24.23	>3.91	>12.77	>0.45	>2.59	>0.68
	φ	>25.73	>4.18	>12.31	>0.43	>2.55	>0.60
Low	ð	<21.20	<3.29	<12.11	<0.36	<2.07	<-0.10
	Q	<20.43	<3.10	< 11.65	<0.34	<1.99	<-0.17
Age 6 months							
High	ð	>26.00	>4.33	>13.13	>0.47	>2.44	>0.55
	Q	>28.03	>4.69	>12.47	>0.47	>2.39	>0.52
Low	ð	<21.40	<3.42	<12.36	<0.37	<2.00	<-0.18
	Q	<23.50	<3.74	<12.00	<0.37	<1.84	<-0.17
Age 4 years							
High	ð	>28.63	>4.64	>11.95	>0.41	>2.31	>0.62
	φ	>31.80	>5.18	>11.41	>0.42	>2.48	>0.74
Low	ð	<25.23	<3.90	<11.36	<0.32	<1.83	<-0.28
	φ	<27.63	<4.25	<10.64	<0.31	<1.89	<-0.12

Abbreviations: BMI SDS, BMI SD score; FM%, fat mass percentage; FMI, fat mass index; FFMI, fat-free mass index; NA, not applicable; 3, boys; 9, girls.

research group showed that accelerated gain in weight-for-length during the first 6 months of life was associated with increased FM% at 21 years (4). We found previously, in the Sophia Pluto study, that a rapid rise in FM% in the first 6 months of life and not thereafter was associated with higher FM% trajectories until the age of 2 years (12). Altogether, these findings support the presence of a critical window for adiposity programming in the first 6 months of life.

High FFMI tracked from age 1, 3, and 6 months to 4 years. Our results are in line with those of an Ethiopian birth cohort study showing a positive association between FFM at birth with FFMI at 4 years of age (24) and FFM at the age of 5 years measured by ADP (25). However, tracking of high FFM from infancy to childhood has never been described. As high FFMI tracked from early life to childhood, this could indicate that the first months of life are not only a critical window for adiposity programming but also for FFM programming. In contrast to FM%, we found tracking of high FFMI from age 1 month to 4 years. This might suggest that FFMI tracks from an earlier age than FM%. A systematic review reported consistent associations between birth weight and lean body mass in term-born children, adolescents, and adults, whereas this consistent association was not found for fat mass (26). A study in preterm infants reported a similar FM% at 52 weeks postmenstrual age as in term-born infants, whereas the lower FFM persisted (27). This could indicate that the last trimester of pregnancy is potentially also an important period for the programming of FFM, particularly as we showed that FFMI already tracks from 1 month of age.

We found tracking of high abdominal subcutaneous fat from age 6 months to 4 years, but there was no tracking of abdominal visceral fat to 4 years. In older children and adults, especially truncal and visceral fat largely contribute to an unfavorable metabolic health profile (28,29). Some research groups have found abdominal subcutaneous fat to be associated with an unfavorable metabolic profile in children (11,30). However, these findings are contradictive, as others showed that abdominal subcutaneous fat might have a protective effect against the adverse effects of visceral fat (31). We found tracking of abdominal subcutaneous fat from infancy to childhood, which might suggest that subcutaneous fat is also programmed during the first months of life. In contrast, we did not find tracking of visceral fat from early life to 4 years of age. Other research groups have measured visceral fat by ultrasound or computed tomography in 6- to 8-year-old children or reported tracking of abdominal visceral fat from age 2 to 6 years (32-34). Altogether, this suggests that the visceral fat depot develops at an older age than the abdominal subcutaneous depot, which would potentially explain why we did not find tracking of visceral fat from early life to 4 years of age.

Our results show that infant feeding influences tracking of FM%. EBF infants had lower odds of having high FM% at 4 years compared with infants with EFF or mixed feeding. We also found tracking to be different between EBF and non-EBF infants. EBF infants had no significant tracking of FM% from early life, whereas non-EBF infants had a high OR to track from 3 and 6 months to 4 years of age. An explanation could be that adiposity programming is different

TABLE 3 Odds ratio for body composition tracking from age 1, 3, and 6 months to age 4 years

	At age 4 years					
	High FM%	High FMI	High FFMI	High abdominal subcutaneous fat High visceral fat	High visceral fat	High BMI SDS
Age 1	Age 1 month					
High	High 1.70 (0.72-3.98), $p = 0.225$	1.48 (0.63-3.48), $p = 0.369$	4.16 (1.52-11.36), p = 0.005 NA	NA	NA	3.15 (1.29-7.66), p = 0.012
Age 3	Age 3 months					
High	High 4.34 (1.72-10.92), $p = 0.002$	2.62 (1.12-6.16), p = 0.027	3.701 (1.50-9.15) , $p = 0.004$ 1.76 (0.79-3.95), $p = 0.168$	1.76 (0.79-3.95), p = 0.168	1.03 (0.50-2.14), p = 0.932	6.50(2.45-17.28), p < 0.001
Age 6	Age 6 months					
High	High 6.54 (2.37-18.07), $p < 0.001$ 5.68 (1.96-16.45), $p = 0.001$	5.68 (1.96-16.45), p = 0.001	3.36 (1.22-9.23), p = 0.019	3.36 (1.22-9.23), p = 0.019 $2.30 (1.06-4.99), p = 0.035$	1.63(0.74-3.62), p = 0.228	1.63(0.74-3.62), p = 0.228 $7.74(2.67-22.45), p < 0.001$

Values are odds ratio (95% confidence interval) and p value for having high body composition outcome at 4 years of age, adjusted for feeding mode until age 3 months and estimated by logistic regression group as reference category. Significant data are bold with the "low"

fat mass index; FFMI, fat-free mass index; BMI SDS, BMI SD score; NA, not applicable Abbreviations: FM%, fat mass percentage; FMI,

TABLE 4 Odds ratio for FM% tracking from age 1, 3, and 6 months to age 4 years in EBF and non-EBF infants

	At and Avegre	
	At age 4 years	
	EBF	Non-EBF
	FM% high	FM% high
Age 1 month		
FM% high	1.00 (0.42-2.40),	1.33 (0.56-3.16),
	p = 1.00	p = 0.514
Age 3 months		
FM% high	1.429 (0.54-3.75),	4.00 (1.50-10.66),
	p = 0.469	p = 0.006
Age 6 months		
FM% high	2.20 (0.76-6.33),	7.33 (2.20-24.50),
	p = 0.144	p = 0.001

Values are odds ratio (95% confidence interval) and *p* value for FM% at 4 years of age in EBF and in non-EBF infants, estimated by logistic regression with the "low" group as reference category. EBF refers to EBF until age 3 months, and non-EBF refers to exclusive formula feeding or mixed feeding until age 3 months. Significant data are bold. Abbreviations: EBF, exclusive breastfeeding; FM%, fat mass percentage.

in EBF and non-EBF infants. Our research group found earlier that appetite-regulating hormones were different between EBF and EFF infants at age 3 months (35). Also, differences in gut microbiota and serum metabolic profile have been reported between EBF and EFF infants in early life, which all could potentially influence adiposity programming (36,37). It has been described that EBF is protective for the development of childhood obesity (38). Our findings support that EBF in early life has a potentially protective effect on adiposity programming later in life.

Tracking of FM%, FMI, and FFMI was not different between girls and boys. It is known that girls have a higher FM% and lower FFM from early age onward (6,39), but present findings show that tracking of body composition until age 4 years does not have sex differences.

For the sake of comparison with literature data, we also investigated the tracking of BMI SDS. High BMI SDS tracked from age 1, 3, and 6 months to 4 years, which is in line with previous data (2,3). However, it is known that children with a comparable weight or BMI might have different body fat or fat distribution (6-8). Therefore, tracking in BMI is not predictive for later body fat and fat distribution.

This is one of the first studies, to our knowledge, reporting tracking of FM%, FMI, FFMI, and abdominal fat distribution from early life to 4 years of age. The strengths of this study are the longitudinal and detailed measurements of body composition in a large group of 224 healthy, term-born children for a period of 4 years. Although ADP by Pea Pod (COSMED) and DXA had a very small difference in FM% of 0.9% at age 6 months, these measurements were considered similar, as there was no proportional bias (16). Therefore, it is very unlikely tracking results were influenced by the measuring methods used. A limitation is the lack of longitudinal reference values for FM%, FMI, FFMI, and abdominal subcutaneous and visceral fat measured by ultrasound from infancy until

4 years of age. Therefore, we used categorical outcomes to investigate tracking from infancy to young childhood. We did not investigate tracking of abdominal subcutaneous and visceral fat from 1 month of age because performing ultrasound measurements at 1 month of age has proven to be very exhausting for the infants. Because we did not find tracking of abdominal subcutaneous and visceral fat from age 3 months to 4 years, we did not expect to find tracking of abdominal fat from 1 month to 4 years of age.

CONCLUSION

FM% and FMI in the highest tertiles tracked from age 3 and 6 months to 4 years, high abdominal subcutaneous fat tracked from 6 months to 4 years of age, and high FFMI tracked from age 1, 3, and 6 months to 4 years. High FM% tracked from 3 and 6 months to 4 years in non-EBF infants, whereas tracking was not significant in EBF infants. Our longitudinal data support the presence of a critical window of adiposity and FFM programming in the first 6 months of life and a protective effect of EBF on adiposity programming.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

AUTHOR CONTRIBUTIONS

The study concept was developed by ACSHK and LMB. Research was conducted by IALPVB, KSDF, and LMB. Data analysis and drafting the manuscript was primarily done by IALPVB and ACSHK. All authors were involved in writing the manuscript and had final approval of the submitted version.

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REFERENCES

 World Health Organization. Report of the Commission on Ending Childhood Obesity. World Health Organization; 2016.

- 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;9:474-488.
- Geserick M, Vogel M, Gausche R, et al. Acceleration of BMI in early childhood and risk of sustained obesity. N Engl J Med. 2018;379:1303-1312.
- 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;301:2234-2242.
- Druet C, Stettler N, Sharp S, et al. Prediction of childhood obesity by infancy weight gain: an individual-level meta-analysis. *Paediatr Perinat Epidemiol*. 2012;26:19-26.
- Breij LM, Kerkhof GF, De Lucia RE, et al. Longitudinal fat mass and visceral fat during the first 6 months after birth in healthy infants: support for a critical window for adiposity in early life. *Pediatr Obes*. 2017;12:286-294.
- Freedman DS, Sherry B. The validity of BMI as an indicator of body fatness and risk among children. *Pediatrics*. 2009;124(suppl 1):S23-S34.
- Freedman DS, Wang J, Maynard LM, et al. Relation of BMI to fat and fat-free mass among children and adolescents. *Int J Obes (Lond)*. 2005:29:1-8.
- Breij LM, Steegers-Theunissen RP, Briceno D, Hokken-Koelega AC. Maternal and fetal determinants of neonatal body composition. Horm Res Paediatr. 2015;84:388-395.
- Gesta S, Tseng YH, Kahn CR. Developmental origin of fat: tracking obesity to its source. Cell. 2007;131:242-256.
- Botton J, Heude B, Kettaneh A, et al. Cardiovascular risk factor levels and their relationships with overweight and fat distribution in children: the Fleurbaix Laventie Ville Sante II study. *Metabolism*. 2007;56:614-622.
- de Fluiter KS, van Beijsterveldt I, Breij LM, Acton D, Hokken-Koelega ACS. Association between fat mass in early life and later fat mass trajectories. JAMA Pediatr. 2020;174:1141-1148.
- 13. Ma G, Yao M, Liu Y, et al. Validation of a new pediatric air-displacement plethysmograph for assessing body composition in infants. *Am J Clin Nutr.* 2004;79:653-660.
- 14. Ellis KJ, Yao M, Shypailo RJ, Urlando A, Wong WW, Heird WC. Body-composition assessment in infancy: air-displacement pleth-ysmography compared with a reference 4-compartment model. *Am J Clin Nutr.* 2007;85:90-95.
- COSMED Pea Pod Brochure ENGLISH. Published 2021. Accessed July 02, 2021. https://www.cosmed.com/hires/Pea_Pod_Broch ure_EN_C03838-02-93_A4_print.pdf
- de Fluiter KS, van Beijsterveldt IALP, Goedegebuure WJ, et al. Longitudinal body composition assessment in healthy term-born infants until 2 years of age using ADP and DXA with vacuum cushion. Eur J Clin Nutr. 2020;74:642-650.
- 17. GE Healthcare. Frequently asked questions: Advanced body composition application overview. 2012.
- Guo Y, Franks PW, Brookshire T, Antonio TP. The intra- and interinstrument reliability of DXA based on ex vivo soft tissue measurements. Obes Res. 2004;12:1925-1929.
- De Lucia Rolfe E, Modi N, Uthaya S, et al. Ultrasound estimates of visceral and subcutaneous-abdominal adipose tissues in infancy. J Obes. 2013;2013:951954. doi:10.1155/2013/951954
- Talma H, Schonbeck Y, Bakker B, Hirasing RA, Sv B. Growth Charts 2010: Guide to Measuring and Weighing Children and Completing Growth Charts. TNO; 2010.
- World Health Organization. Nutrition Landscape Information System (NLIS) Country Profile Indicators: Interpretation Guide. World Health Organization: 2019.
- Forsum E, Eriksson B, Flinke E, Henriksson H, Henriksson P, Lof M. Fat and fat-free mass of healthy Swedish children show tracking during early life, but there are differences. Acta Paediatr. 2019;108:1704-1708.

- Scheurer JM, Zhang L, Gray HL, Weir K, Demerath EW, Ramel SE. Body composition trajectories from infancy to preschool in children born premature versus full-term. J Pediatr Gastroenterol Nutr. 2017;64:e147-e153.
- 24. Admassu B, Wells JCK, Girma T, et al. Body composition during early infancy and its relation with body composition at 4 years of age in Jimma, an Ethiopian prospective cohort study. *Nutr Diabetes*. 2018;8:46. doi:10.1038/s41387-018-0056-7
- Wibaek R, Vistisen D, Girma T, et al. Associations of fat mass and fatfree mass accretion in infancy with body composition and cardiometabolic risk markers at 5 years: the Ethiopian iABC birth cohort study. PLoS Med. 2019;16:e1002888. doi:10.1371/journal.pmed.1002888
- Wells JC, Chomtho S, Fewtrell MS. Programming of body composition by early growth and nutrition. *Proc Nutr Soc.* 2007:66:423-434.
- Hamatschek C, Yousuf El, Möllers LS, et al. Fat and fat-free mass of preterm and term infants from birth to six months: a review of current evidence. Nutrients. 2020;12:288. doi:10.3390/nu12020288
- Fox CS, Massaro JM, Hoffmann U, et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation. 2007;116:39-48.
- Slyper AH. Childhood obesity, adipose tissue distribution, and the pediatric practitioner. *Pediatrics*. 1998;102:e4. doi:10.1542/ peds.102.1.e4
- Gonzalez-Alvarez C, Ramos-Ibanez N, Azprioz-Leehan J, Ortiz-Hernandez L. Intra-abdominal and subcutaneous abdominal fat as predictors of cardiometabolic risk in a sample of Mexican children. Eur J Clin Nutr. 2017;71:1068-1073.
- Tamura A, Mori T, Hara Y, Komiyama A. Preperitoneal fat thickness in childhood obesity: association with serum insulin concentration. Pediatr Int. 2000;42:155-159.
- 32. Mook-Kanamori DO, Holzhauer S, Hollestein LM, et al. Abdominal fat in children measured by ultrasound and computed tomography. *Ultrasound Med Biol.* 2009;35:1938-1946.

- Liem ET, De Lucia RE, L'Abee C, Sauer PJ, Ong KK, Stolk RP. Measuring abdominal adiposity in 6 to 7-year-old children. Eur J Clin Nutr. 2009;63:835-841.
- 34. Vogelezang S, Gishti O, Felix JF, et al. Tracking of abdominal subcutaneous and preperitoneal fat mass during childhood. The Generation R Study. *Int J Obes (Lond)*. 2016;40:595-600.
- 35. de Fluiter KS, Kerkhof GF, van Beijsterveldt IALP, et al. Appetiteregulating hormone trajectories and relationships with fat mass development in term-born infants during the first 6 months of life. Eur J Nutr. 2021;60:3717-3725. doi:10.1007/s00394-021-02533-z
- 36. Prentice P, Koulman A, Matthews L, Acerini CL, Ong KK, Dunger DB. Lipidomic analyses, breast- and formula-feeding, and growth in infants. *J Pediatr.* 2015;166(2):276-281 e6.
- Ihekweazu FD, Versalovic J. Development of the pediatric gut microbiome: impact on health and disease. Am J Med Sci. 2018;356(5):413-423.
- 38. Yan J, Liu L, Zhu Y, Huang G, Wang PP. The association between breastfeeding and childhood obesity: a meta-analysis. *BMC Public Health*. 2014;14(1):1267. doi:10.1186/1471-2458-14-1267
- Davis SM, Kaar JL, Ringham BM, Hockett CW, Glueck DH, Dabelea D. Sex differences in infant body composition emerge in the first 5 months of life. J Pediatr Endocrinol Metab. 2019;32(11):1235-1239.

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