An observational cohort study of weight- and length-derived anthropometric indicators with body composition at birth and 5 mo: the Healthy Start study

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ABSTRACT

Background: Despite widespread use of weight- and length-based anthropometric indexes as proxies for adiposity, little is known regarding the extent to which they correspond with fat mass (FM) or fat-free mass (FFM) during infancy.

Objective: This study aimed to examine associations of 3 derived indicators—weight-for-age *z* score (WFAZ), weight-for-length score (WFLZ), and body mass index *z* score (BMIZ)—with FM, percentage of FM, and FFM measured by air-displacement plethysmography during the first 5 mo of life.

Design: Applying prospectively collected data from 1027 infants in a Colorado prebirth cohort, we used multivariate regression to evaluate associations between the derived indicators and body composition at birth and at 5 mo, and with change (Δ) during follow-up.

Results: At birth, all 3 derived indicators were more strongly associated with FFM than with FM. Each unit of WFAZ corresponded with 0.342 kg FFM (95% CI: 0.331, 0.351 kg FFM), compared with 0.121 kg FM (95% CI: 0.114, 0.128 kg FM) ($P < 0.0001$); similar trends were observed for WFLZ and BMIZ. By 5 mo, WFLZ and BMIZ were more strongly associated with FM than with FFM, whereas WFAZ correlated similarly with the 2 components of body composition. ΔWFLZ and ΔBMIZ were both more strongly related to ΔFM than to ΔFFM; however, a direct comparison of the 2 indexes with respect to change in the percentage of FM indicated that ΔBMIZ was the optimal proxy of adiposity gain ($P < 0.0001$, pairwise difference).

Conclusions: Weight- and length-based indexes are poor surrogates for newborn adiposity. However, at 5 mo, WFLZ and BMIZ are suitable proxies of FM. When assessing adiposity gain, ΔBMIZ is the best indicator of fat accrual during the first 5 postnatal months. This trial was registered at clinicaltrials.gov as NCT02273297. *Am J Clin Nutr* 2017;106:559–67.

Keywords: neonatal adiposity, fat mass, fat-free mass, lean mass, body composition, air-displacement plethysmography

INTRODUCTION

Body composition in early life—in particular, fat mass (FM)—is thought to play a key role in the programming of obesity and obesity-related diseases including hypertension, stroke, type 2 diabetes, and cardiovascular disease (1, 2). In infants, body composition has been historically assessed by serial measurements of weight and length; little is known about the extent to which common adiposity indicators, such as weight for age (3), weight for length (3, 4) and BMI for age (3, 5, 6), represent adipose tissue mass as opposed to bone or muscle mass—an important distinction given that fat and lean mass have differential implications for future cardiovascular and metabolic health (7, 8).

Air-displacement plethysmography (ADP) has been championed as a safe, valid, and accurate method for assessing body composition in infants (9–11). Despite a flurry of investigations that used ADP to characterize patterns of fat and lean mass gain during infancy (12–14), few studies, to our knowledge, have formally assessed the relation between derived anthropometric indexes and directly measured body composition. So far, only a few small cross-sectional analyses of data from both term and preterm infants reported poor correlations of birth weight, as well as weight- and length-based indexes, with neonatal FM (15–17). To our knowledge, no study to date has evaluated whether or how changes in derived indexes correlate

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Supplemental Tables 1 and 2 and Supplemental Figure 1 are available from the "Online Supporting Material" 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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Abbreviations used: ADP, air-displacement plethysmography; AGA, appropriate for gestational age; BMIZ, BMI-for-age *z* score; BW/GA, birthweight-for-gestational age; FFM, fat-free mass; FM, fat mass; LGA, large for gestational age; RA, research assistant; SGA, small for gestational age; WFAZ, weight-for-age *z* score; WFLZ, weight-for-length *z* score; %FM, percentage of fat mass.

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with changes in body composition during infancy. Finding an adequate proxy for research measures of body composition during infancy would have important methodologic ramifications for future developmental origins studies relating growth in early life to long-term health outcomes.

Here, we used data from singleton infants in a Colorado prebirth cohort to examine the extent to which 3 weight- and length-derived anthropometric indicators—weight-for-age z score, weight-for-length z score, and BMI-for-age z score—serve as proxies for ADP-measured body composition, namely, FM, fat-free mass (FFM), and percentage of FM (%FM). We evaluated these associations in 3 situations: at birth, at 5 mo, and with a change in body composition between birth and 5 mo. As secondary endpoints, we also examined associations of the derived anthropometric indicators with skinfold thickness, which is often used in research settings as a proxy for subcutaneous adiposity, and length z score, which is considered to be a proxy for lean mass.

METHODS

Study population

This study included participants in Healthy Start, an ongoing study of a Colorado-based cohort of pregnant women and their children. Enrollment procedures and eligibility criteria have been published (18–20). Briefly, we recruited pregnant women from obstetric clinics at the University of Colorado from 2009 to 2014 to participate in research visits at medians of 17 and 27 wk of gestation, and at a median of 1 d after delivery (hereafter referred to as the "delivery visit"). At the visits during pregnancy, we collected information from the women on sociodemographic characteristics, medical history, and lifestyle characteristics during pregnancy; at the delivery visit, trained clinical assistants carried out anthropometric assessments. Participants consented to the use of their medical records, including maternal perinatal characteristics such as gestational glucose tolerance, delivery mode, and gestational weight gain, and infant's weight and length. At a median of 5.2 mo postpartum ("5-mo visit"), we invited the women and their children to participate in a postnatal research visit, during which we collected updated information on sociodemographic and lifestyle characteristics from the mothers, and assessed anthropometric characteristics and body composition of the infants. All participants provided written informed consent before enrollment, and all procedures were conducted in accordance with established ethical standards of the Colorado Multiple Institutional Review Board. The Healthy Start study was registered as an observational study at clinicaltrials.gov (identifier NCT02273297).

Of the 1410 mother-infant pairs in Healthy Start, we excluded 177 in which the infant was born before 37 wk of gestation, as preterm infants may exhibit fundamentally different growth patterns than those of term infants (21), 130 pairs in which the infants were missing data on anthropometry (weight, length), and an additional 76 with infants who were missing ADP measures at birth. This yielded 1027 infants with complete data at the delivery visit. Of these, we had weight and length data for 727 at the 5-mo visit. After excluding 21 infants missing ADP measures of body composition, a total of 706 infants had complete weight, length, and body- composition data at 5 mo of age. No notable differences were found in maternal, perinatal, or sociodemographic characteristics between the participants with complete data at birth and those with complete data at 5 mo (**Table 1**). **Supplemental Figure 1** shows the study participant flow.

Measurements

Weight and length

At the delivery and 5-mo visits, trained clinical assistants used whole-body ADP (PeaPod device; COSMED) (25) to calculate the infant's weight as a sum of FM and FFM (the details of procedures are described in Body-composition assessment below). Trained research assistants (RAs) measured length at birth and 5 mo using a recumbent length board, which has a fixed perpendicular headpiece and a sliding foot-piece that forms a 90° angle with the measurement surface. Two RAs measured length with this instrument, applying a standard protocol as the infant lay supine on the measuring board (26). We measured each infant twice; if the measurements differed by >0.5 cm, then a third measurement was taken. For the analysis, we used the mean of the 2 closest measurements. We used these values to calculate the sex-specific weight-for-age z score (WFAZ), weight-for-length z score (WFLZ), BMI-for-age z score (BMIZ), and length-for-age z score using the WHO growth standard (23, 24).

Skinfold thicknesses

At the delivery and 5-mo visits, trained RAs measured the triceps, subscapular, and midthigh skinfold thicknesses to the nearest 1 mm using skinfold calipers (Lange; Beta Technology) according to standard procedures (26). For this analysis, we took the sum of the 3 skinfolds as a measure of overall subcutaneous adiposity (27).

Body-composition assessment

At the delivery and 5-mo visits, clinical personnel used the ADP device (25) to estimate FM (kilograms of adipose tissue) and FFM (comprising water, muscle, and bone, in kilograms), as well as the %FM calculated as a proportion of the FM divided by total mass. We carried out 2 measurements/infant, and obtained a third if %FM differed by $>2\%$; the mean of the 2 closest readings was used for analysis.

Statistical analysis

First, as a descriptive assessment of the associations, we calculated Spearman correlations between pairs of anthropometric indicators at birth and at 5 mo, and among changes in the indicators from birth to 5 mo. The anthropometric measures include the 3 derived indicators (WFAZ, WFLZ, and BMIZ); sum of the skinfolds; ADP-assessed FM, %FM, and FFM; and length-for-age z score. We examined correlations for all children, separately for boys and girls, and separately for infants born to non-Hispanic white, non-Hispanic black, and Hispanic mothers. Because associations within each of these comparisons could differ by race, sex, or the exact age at the time of assessment, we also adjusted correlations for these characteristics. Doing so did not substantially change correlations; thus we show unadjusted correlations for all infants.

TABLE 1
Background characteristics of 1027 Healthy Start participants with complete data at birth and the subsample of 706 participants with complete data at 5 mo[1]

	Complete data	
	At birth (n = 1027)	At 5 mo (n = 706)
Family and sociodemographic characteristics		
Maternal age at enrollment, y	28.4 ± 6.1	28.9 ± 6.1
Annual household income <$40,000	28.5 (293)	28.3 (200)
Infant male sex	50.7 (521)	49.4 (349)
Maternal race/ethnicity		
Non-Hispanic white	54.3 (558)	55.8 (394)
Hispanic	24.5 (252)	24.4 (172)
Non-Hispanic black	15.0 (154)	14.2 (100)
Other	6.1 (63)	5.7 (40)
Perinatal characteristics		
Maternal BMI before pregnancy, kg/m^2	25.7 ± 6.2	25.7 ± 6.3
Gestational weight gain[2]		
Inadequate	21.1 (217)	23.4 (165)
Adequate	28.3 (291)	29.8 (210)
Excessive	50.5 (519)	46.9 (331)
Gestational diabetes mellitus	4.0 (39)	3.7 (25)
Mother smoked during pregnancy	8.3 (85)	6.7 (47)
Cesarean delivery	20.6 (212)	20.4 (144)
Characteristics at the delivery visit		
Gestational age at delivery, wk	39.6 ± 1.1	—
Weight-for-age z score[3]	−0.31 ± 0.89	−0.33 ± 0.88
Weight-for-length z score[3]	−0.34 ± 0.92	−0.32 ± 0.91
BMI-for-age z score[3]	−0.42 ± 0.90	−0.41 ± 0.91
Sum of skinfolds,[4] mm	15.0 ± 3.4	15.3 ± 3.5
Fat mass, kg	0.29 ± 0.15	0.30 ± 0.15
Fat-free mass, kg	2.8 ± 0.3	2.8 ± 0.3
% Fat mass	9.1 ± 3.9	9.2 ± 3.9
Length z score[3]	−0.13 ± 1.08	−0.13 ± 1.11
Characteristics at the 5-mo visit		
Age, mo	—	5.1 ± 1.2
Weight-for-age z score[3]	−0.40 ± 0.95	−0.49 ± 0.91
Weight-for-length z score[3]	−0.24 ± 1.03	−0.25 ± 1.02
BMI-for-age z score[3]	−0.34 ± 1.01	−0.35 ± 1.02
Sum of skinfolds,[4] mm	37.8 ± 8.2	37.1 ± 8.0
Fat mass, kg	1.7 ± 0.5	1.7 ± 0.5
Fat-free mass, kg	5.2 ± 0.6	5.2 ± 0.6
% Fat mass	24.1 ± 5.4	24.1 ± 5.4
Length z score[3]	−0.40 ± 1.00	−0.39 ± 1.00

[1] Data are means ± SDs or percentages (n).
[2] According to the Institute of Medicine 2009 guidelines (22).
[3] According to the WHO 0–2-y growth standard (23, 24).
[4] Sum of the subscapular, triceps, and thigh skinfolds.

Next, using a 2-step approach we examined associations of each weight- and length-derived z-score indicator, skinfold sum, and length z-score with FM and FFM. First, we fit a general linear model regressing each derived indicator on maternal race/ethnicity as a surrogate for infant race/ethnicity. For sum of the skinfolds, we also included age and sex as covariates; this was not necessary for the z score indicators because they were standardized with respect to age- and sex-specific reference data. The residuals from this model were then used as the independent variables in the second model, which was a linear multivariate model with FM and FFM as the outcomes. This approach not only allowed us to examine whether a particular derived indicator is associated with FM and/or FFM; it also enabled us to compare the magnitude (β estimate) and significance of the association between the derived indicator and FM or FFM (e.g., whether the indicator is more strongly associated with FM or FFM based on the Hotelling-Lawley trace test).

We used the same approach to examine change (Δ) in anthropometric characteristics from birth to 5 mo. However, we also included an additional analysis using a linear multivariate model where the residuals of Δ%FM regressed on age, sex, and mother's race/ethnicity as the independent variables and ΔWFAZ, ΔWFLZ, and ΔBMIZ as the outcomes. This method enabled us to compare directly the utility of each derived indicator as a proxy for adiposity gain over time according to %FM, a measure of relative FM that is complementary to FFM. To test for an overall difference in the relation of Δ%FM with change in the z score indicators, we carried out a multivariate

ANOVA. If we found evidence of an overall difference ($P < 0.05$, multivariate ANOVA, Hotelling-Lawley trace), we then used contrast statements to carry out pairwise comparisons of β estimates for the relation between Δ%FM and pairs of derived indicators (e.g., $\beta_{\Delta\%FM \rightarrow \Delta WFAZ}$ compared with $\beta_{\Delta\%FM \rightarrow \Delta WFLZ}$; $\beta_{\Delta\%FM \rightarrow \Delta WFAZ}$ compared with $\beta_{\Delta\%FM \rightarrow \Delta BMIZ}$; and $\beta_{\Delta\%FM \rightarrow \Delta WFLZ}$ compared with $\beta_{\Delta\%FM \rightarrow \Delta BMIZ}$).

Because associations of the derived indicators with body composition may differ with respect to fetal growth and, accordingly, birth size, we also performed all analyses separately for infants who were small for gestational age [SGA; birthweight-for-gestational age (BW/GA) z score <10th percentiles of age and sex], appropriate for gestational age (AGA; BW/GA z score in the 10th to 90th percentiles), and large for gestational age (LGA; BW/GA z score >90th percentile) (28).

Finally, we conducted some sensitivity analyses. Children of women with abnormal glucose tolerance may exhibit altered patterns of intrauterine (29, 30) and postnatal growth (31), so we reran all analyses after excluding 55 infants whose mothers had gestational diabetes mellitus (GDM). We also assessed the potential impact of perinatal characteristics known to be associated with infant growth (e.g., maternal BMI before pregnancy, maternal age, and household income) on our findings by including each covariate in the calculation of residuals in the first step of our 2-step approach. Taking the example of prepregnancy BMI, we regressed the derived indicator of interest, say WFAZ, on maternal BMI before pregnancy and mother's race/ethnicity, then used the residuals as the independent variable in a multivariate model where FM and FFM were the outcomes. Neither exclusion of infants whose mothers had GDM nor the addition of the above-mentioned characteristics substantially altered the direction (negative or positive), magnitude (<20% change in the estimates of association), or significance ($P < 0.05$, z test, for exclusion of mothers with GDM; $P < 0.05$, F test, for inclusion of covariates) of our results. Therefore, we show results for all participants and did not include the perinatal characteristics in the models because the objective of this study is to evaluate the utility of the derived indicators as proxies of adiposity, rather than to disentangle upstream etiological causes of the observed associations. All analyses were conducted by using SAS 9.4.

RESULTS

Study sample characteristics

Of the 1027 infants with complete data at birth, 54.3% were non-Hispanic white, 24.5% were Hispanic, and 15.0% were non-Hispanic black. Approximately half were male (50.7%). Mean ± SD gestational age at delivery was 39.6 ± 1.1 wk. At the 5-mo visit, mean ± SD infant age was 5.1 ± 1.2 mo. Table 1 shows additional characteristics of the study participants with complete data at birth and at 5 mo.

Correlations between anthropometric indicators

Supplemental Table 1 displays raw Spearman correlations between the derived indicators, sum of skinfolds, FM, %FM, FFM, and length z score.

Multivariate analyses

Table 2 shows associations of the derived indicators, sum of skinfolds, and length z score with FM and FFM at birth and at 5 mo, and for change in anthropometric measures between the 2 time points. At birth, all 3 derived indicators (WFAZ, WFLZ, BMIZ) and the sum of skinfolds were associated with both aspects of body composition, and all of the indicators were more strongly correlated with FFM than with FM. For example, each 1-U increment in WFAZ corresponded with 0.342 kg FFM (95% CI: 0.331, 0.351 kg FFM) compared with 0.121 kg FM (95% CI: 0.114, 0.128 kg FM) ($P < 0.0001$, pairwise difference). We observed similar trends but of smaller magnitude for WFLZ, BMIZ, and sum of skinfolds. By 5 mo of age, WFLZ, BMIZ, and sum of skinfolds were more strongly related to FM than with FFM, with a similar but nonsignificant association for WFAZ. When we examined change from birth to 5 mo, all 3 derived indicators were better proxies of ΔFM than of ΔFFM. Length z score exhibited stronger associations with FFM than with FM at both time points and for change during follow-up.

Table 3 shows associations of the derived z score indicators with body composition at birth, within categories of birth size. At birth, WFAZ was a better surrogate for FFM than FM among infants: each unit of WFAZ corresponded with 0.247 kg FFM (95% CI: 0.201, 0.293 kg FFM) compared with 0.052 kg FM (95% CI: 0.025, 0.079 kg FM) ($P < 0.0001$, pairwise difference). This was also true for WFAZ and BMIZ among AGA infants. However, for LGA newborns, WFLZ, BMIZ, and sum of skinfolds were all more strongly related to FM than to FFM. Across the 3 birth size categories, length z score demonstrated consistently stronger associations with FFM than with FM.

Table 4 shows associations of the derived indicators with body composition at 5 mo, within categories of birth size. At this age, the derived indicators and sum of skinfolds were more highly associated with FM than with FFM across birth size categories, with the most consistent associations observed for AGA and LGA infants. Length z score was more strongly associated with FFM than with FM among infants who were SGA [0.464 kg FFM (95% CI: 0.324, 0.604 kg FFM) and 0.126 kg FM (95% CI: 0.023, 0.229 kg FM); $P = 0.0002$, pairwise difference] and AGA [0.164 kg FFM (95% CI: 0.117, 0.212 kg FFM) and 0.064 kg FM (95% CI: 0.022, 0.105 kg FM); $P = 0.0007$, pairwise difference]. No significant differences were found in body composition with respect to length z score for LGA infants ($P = 0.51$, pairwise difference).

Table 5 shows associations among change in the anthropometric indicators from birth to 5 mo, within categories of birth size. ΔWFLZ and, to a lesser extent, ΔBMIZ were associated with ΔFM but not ΔFFM among SGA infants. Among AGA infants, all 3 derived z score indicators and sum of skinfolds were better proxies of ΔFM than of ΔFFM. For LGA infants, ΔWFAZ and change in the sum of skinfolds were the only indicators differentially associated with body composition, and both were more highly associated with ΔFM. As with our cross-sectional findings at 5 mo of age, Δlength z score was more strongly related to ΔFFM across the birth size categories, although we note that the associations for AGA and LGA infants only approach significance.

In addition to comparing the strength of associations among change in each of the derived indicators with ΔFM and ΔFFM

TABLE 2
Associations [βs (95% CIs)] of each derived anthropometric indicator with fat mass and fat-free mass at birth, at 5 mo, and with change during follow-up[1]

	Fat mass (kg)	Fat-free mass (kg)	*P* value[2]
At birth (n = 1027)			
WFAZ	0.121 (0.114, 0.128)	0.342 (0.331, 0.351)	<0.0001
WFLZ	0.078 (0.069, 0.087)	0.115 (0.904, 0.135)	0.0002
BMIZ	0.111 (0.103, 0.118)	0.250 (0.233, 0.267)	<0.0001
Sum of skinfolds	0.029 (0.027, 0.031)	0.041 (0.036, 0.047)	<0.0001
Length z score	0.063 (0.055, 0.070)	0.235 (0.222, 0.247)	<0.0001
At 5 mo (n = 706)			
WFAZ	0.384 (0.354, 0.413)	0.337 (0.292, 0.382)	0.12
WFLZ	0.302 (0.275, 0.328)	0.135 (0.092, 0.177)	<0.0001
BMIZ	0.339 (0.313, 0.366)	0.182 (0.138, 0.225)	<0.0001
Sum of skinfolds	0.031 (0.027, 0.035)	0.009 (0.003, 0.015)	<0.0001
Length z score	0.091 (0.056, 0.126)	0.224 (0.183, 0.266)	<0.0001
Change from birth to 5 mo (n = 706)			
WFAZ	0.326 (0.294, 0.358)	0.277 (0.234, 0.320)	0.09
WFLZ	0.244 (0.216, 0.272)	0.141 (0.104, 0.179)	<0.0001
BMIZ	0.250 (0.223, 0.276)	0.176 (0.140, 0.213)	0.002
Sum of skinfolds	0.028 (0.025, 0.032)	0.010 (0.005, 0.015)	<0.0001
Length z score	0.085 (0.047, 0.122)	0.166 (0.123, 0.210)	0.003

[1] Estimates were derived from separate multivariate models where the independent variable was the residual of the derived anthropometric indicator of interest regressed on maternal race/ethnicity, with fat mass and fat-free mass as the outcomes. For sums of skinfolds, the residuals were obtained from a model that also included age and sex as covariates. BMIZ, BMI-for-age z score; WFAZ, weight-for-age z score; WFLZ, weight-for-length z score.
[2] Calculated through the use of the Hotelling-Lawley trace test.

through the use of separate models, we sought to directly compare them using a single multivariate model in order to identify which was the best proxy for adiposity accrual. The multivariate analysis of variance for an overall difference in the association of Δ%FM with change in the derived indicators was statistically significant ($P < 0.0001$, Hotelling-Lawley trace test). Thus, we further examined pairwise differences of Δ%FM with change in the z score indicators and found the strongest

TABLE 3
Associations [βs (95% CIs)] of each derived anthropometric indicator with fat mass and fat-free mass at birth, stratified by birth size[1]

	Fat mass, kg	Fat-free mass, kg	*P* value[2]
SGA infants (n = 136)			
WFAZ	0.052 (0.025, 0.079)	0.247 (0.201, 0.293)	<0.0001
WFLZ	0.022 (0.001, 0.043)	0.037 (0.001, 0.074)	0.53
BMIZ	0.034 (0.015, 0.054)	0.073 (0.030, 0.116)	0.15
Sum of skinfolds	0.016 (0.012, 0.022)	0.009 (−0.004, 0.023)	0.34
Length z score	0.009 (−0.008, 0.027)	0.122 (0.090, 0.153)	<0.0001
AGA infants (n = 856)			
WFAZ	0.124 (0.113, 0.135)	0.335 (0.319, 0.350)	<0.0001
WFLZ	0.057 (0.048, 0.067)	0.055 (0.035, 0.074)	0.79
BMIZ	0.095 (0.085, 0.105)	0.177 (0.157, 0.197)	<0.0001
Sum of skinfolds	0.024 (0.022, 0.027)	0.022 (0.017, 0.027)	0.42
Length z score	0.039 (0.030, 0.049)	0.175 (0.160, 0.191)	<0.0001
LGA infants (n = 35)			
WFAZ	0.367 (0.134, 0601)	0.152 (−0.136, 0.440)	0.39
WFLZ	0.093 (0.046, 0.140)	−0.090 (−0.144, −0.035)	0.0002
BMIZ	0.163 (0.094, 0.232)	−0.125 (−0.213, −0.037)	0.0002
Sum of skinfolds	0.025 (0.015, 0.035)	−0.019 (−0.032, −0.006)	<0.0001
Length z score	−0.094 (−0.162, −0.026)	0.139 (0.071, 0.206)	0.0004

[1] Estimates were derived from separate multivariate models where the independent variable was the residual of the derived anthropometric indicator of interest regressed on maternal race/ethnicity, with fat mass and fat-free mass as the outcomes. For sums of skinfolds, the residuals were obtained from a model that also included age and sex as covariates. AGA, appropriate for gestational age; BMIZ, BMI-for-age z score; LGA, large for gestational age; SGA, small for gestational age; WFAZ, weight-for-age z score; WFLZ, weight-for-length z score.
[2] Calculated through the use of the Hotelling-Lawley trace test.

TABLE 4
Associations [βs (95% CIs)] of each derived anthropometric indicator with fat mass and fat-free mass at 5 mo, stratified by birth size[1]

	Fat mass, kg	Fat-free mass, kg	*P* value[2]
SGA infants (n = 96)			
WFAZ	0.304 (0.221, 0.387)	0.440 (0.301, 0.560)	0.14
WFLZ	0.285 (0.198, 0.372)	0.101 (−0.065, 0.267)	0.04
BMIZ	0.328 (0.247, 0.409)	0.249 (0.089, 0.409)	0.39
Sum of skinfolds	0.022 (0.012, 0.033)	0.003 (−0.016, 0.021)	0.05
Length z score	0.126 (0.023, 0.229)	0.464 (0.324, 0.604)	0.0002
AGA infants (n = 593)			
WFAZ	0.417 (0.383, 0.451)	0.301 (0.250, 0.353)	0.0007
WFLZ	0.296 (0.268, 0.324)	0.129 (0.086, 0.172)	<0.0001
BMIZ	0.332 (0.304, 0.361)	0.161 (0.116, 0.205)	<0.0001
Sum of skinfolds	0.033 (0.029, 0.037)	0.010 (0.004, 0.016)	<0.0001
Length z score	0.064 (0.022, 0.105)	0.164 (0.117, 0.212)	0.0007
LGA infants (n = 17)			
WFAZ	0.395 (0.109, 0.682)	0.194 (−0.145, 0.532)	0.46
WFLZ	0.522 (0.201, 0.843)	−0.112 (−0.532, 0.308)	0.04
BMIZ	0.498 (0.191, 0.805)	−0.109 (−0.410, 0.292)	0.04
Sum of skinfolds	0.013 (−0.022, 0.047)	0.025 (−0.006, 0.056)	0.65
Length z score	0.117 (−0.141, 0.375)	0.250 (0.028, 0.473)	0.51

[1] Estimates were derived from separate multivariate models where the independent variable was the residual of the derived anthropometric indicator of interest regressed on maternal race/ethnicity, with fat mass and fat-free mass as the outcomes. For sums of skinfolds, the residuals were obtained from a model that also included age and sex as covariates. AGA, appropriate for gestational age; BMIZ, BMI-for-age z score; LGA, large for gestational age; SGA, small for gestational age; WFAZ, weight-for-age z score; WFLZ, weight-for-length z score.
[2] Calculated through the use of the Hotelling-Lawley trace test.

associations with ΔBMIZ: each 1-U increment in Δ%FM corresponded with 0.110 U BMIZ (95% CI: 0.099, 0.122 U BMIZ), compared with 0.091 U WFAZ (95% CI: 0.082, 0.101 U WFAZ) ($P < 0.0001$, pairwise difference) and 0.097 U WFLZ (95% CI: 0.085, 0.110 U WFLZ) ($P < 0.0001$, pairwise difference). We observed similar patterns of association among AGA and LGA infants, but not in the SGA group (**Supplemental Table 2**).

TABLE 5
Associations [βs (95% CIs)] of change in derived anthropometric indicators with changes in fat mass and fat-free mass between birth and 5 mo, stratified by birth size[1]

	ΔFat mass, kg	ΔFat-free mass, kg	*P* value[2]
SGA infants (n = 96)			
ΔWFAZ	0.325 (0.246, 0.405)	0.366 (0.225, 0.506)	0.64
ΔWFLZ	0.263 (0.171, 0.356)	0.065 (−0.094, 0.224)	0.03
ΔBMIZ	0.316 (0.242, 0.390)	0.176 (0.030, 0.323)	0.09
ΔSkinfold sum	0.022 (0.012, 0.032)	0.007 (−0.010, 0.024)	0.10
ΔLength z score	0.128 (0.029, 0.227)	0.368 (0.231, 0.505)	0.004
AGA infants (n = 593)			
ΔWFAZ	0.374 (0.339, 0.409)	0.273 (0.224, 0.322)	0.002
ΔWFLZ	0.252 (0.222, 0.281)	0.141 (0.101, 0.180)	<0.0001
ΔBMIZ	0.279 (0.250, 0.308)	0.174 (0.134, 0.214)	<0.0001
ΔSum of skinfolds	0.031 (0.026, 0.035)	0.009 (0.003, 0.014)	<0.0001
ΔLength z score	0.083 (0.041, 0.124)	0.133 (0.085, 0.180)	0.09
LGA infants (n = 17)			
ΔWFAZ	0.521 (0.292, 0.750)	0.048 (−0.228, 0.324)	0.04
ΔWFLZ	0.292 (−0.025, 0.608)	0.144 (−0.112, 0.400)	0.53
ΔBMIZ	0.471 (0.143, 0.800)	0.062 (−0.253, 0.376)	0.13
ΔSum of skinfolds	0.030 (0.002, 0.059)	0.004 (−0.023, 0.030)	0.22
ΔLength z score	0.398 (0.143, 0.653)	0.006 (−0.248, 0.260)	0.06

[1] Estimates were derived from separate multivariate models where the independent variable was the residual of the derived anthropometric indicator of interest regressed on maternal race/ethnicity, with fat mass and fat-free mass as the outcomes. For sums of skinfolds, the residuals were obtained from a model that also included age and sex as covariates. AGA, appropriate for gestational age; BMIZ, BMI-for-age z score; LGA, large for gestational age; SGA, small for gestational age; WFAZ, weight-for-age z score; WFLZ, weight-for-length z score; Δ, change.
[2] Calculated through the use of the Hotelling-Lawley trace test.

DISCUSSION

Despite a large amount of the literature linking newborn and infant weight and length to long-term health outcomes [e.g., cardiovascular disease (32), diabetes (33–35), and obesity (3)], the extent to which these derived indicators correspond with FM as opposed to FFM during infancy remains unknown. In this study of >1000 infants in a multiethnic prebirth cohort, we examined the extent to which 3 common weight- and length-derived indicators of adiposity—WFAZ, WFLZ, and BMIZ—correlate with FM and FFM (also referred to as "lean mass") at birth and 5 mo. At birth, all 3 derived indicators were more strongly associated with lean mass than FM. However, by 5 mo of age, the derived indicators were more highly associated with of FM; WFLZ and BMIZ emerged as more discriminating proxies of body composition than WFAZ. Change in all 3 z score indicators from birth to 5 mo was more strongly related to gains in adiposity than in lean mass. A direct comparison of the relation between Δ%FM and change in the z score indicators through use of a multivariate ANOVA showed that ΔBMIZ was most strongly associated with adiposity accrual, with Δ%FM accounting for 21% and 13% more variability in ΔWFAZ and ΔWFLZ, respectively.

Associations between derived indicators and ADP-measured body composition at birth

Our finding that the weight- and length-derived anthropometric indicators were more strongly associated with FFM than FM at birth corroborates results from a study of 120 neonates in Tennessee (15). In that investigation, Koo et al. (15) found that weight and length, as well as various combinations of the 2, were consistently better proxies for lean mass than FM, as measured by dual-energy X-ray absorptiometry. When the investigators stratified the analysis by birth size, they found that the association was driven primarily by SGA and AGA infants (15), which aligns with results of the present analysis.

Of note, when we compared the magnitude of association of the 3 derived indicators with FM at birth, we observed a markedly larger magnitude of association for WFAZ than for WFLZ and BMIZ, whereas by 5 mo of age, the effect sizes were comparable across the derived indicators. This is in line with the findings of Ramel et al. (16), who reported that weight alone, compared with weight/length, weight/length^2, and weight/length^3, was the best surrogate marker for percentage body fat among preterm infants, as measured with ADP. A potential explanation for this is that inaccurate or inconsistent length assessment (36), due to the difficulties of working with newborn infants, could contribute to nonsystematic measurement error, thus detracting from its value in anthropometric indexes (37). Another explanation is that weight alone is sufficient to explain variance in body composition in newborns, given that FM is sensitive to the gestational metabolic milieu (38), whereas fetal length accretion may be less susceptible to intrauterine conditions, particularly in developed countries where environmental constraints and prevalence of maternal undernourishment are low (39).

Associations between derived indicators and ADP-measured body composition at 5 mo

At 5 mo, length was included in the derived indexes and seemed to be an important contributor to the estimation of adiposity, as evidenced by our finding that WFLZ and BMIZ were not only more strongly associated with FM than lean mass, but also that both indexes were superior to WFAZ in terms of distinguishing between the 2 components of body composition, particularly among AGA infants. This could be due to improved accuracy in assessing length in older, more cooperative infants, and to greater interindividual variability in linear growth over time, making it an increasingly important variable to account for at older ages.

Associations between change in derived indicators and ADP-measured body composition

Change in all 3 derived indicators from birth to 5 mo were more highly associated with gains in FM than in lean mass. Although the magnitude of association was largest for WFAZ, its ability to discriminate between FM and lean mass was only marginally significant; this is likely because weight gain in growing infants and children is nonspecific, as it captures increases in adiposity and the accrual of lean muscle and bone mass (12–14). When we directly compared how change in %FM, a measure of relative FM that is complementary to percentage lean mass, correlated with change in all 3 indicators at the same time, we found that change in %FM was most strongly associated with change in BMIZ, particularly among AGA and LGA infants. These findings suggest that, as with older children (40, 41), prospective change in BMIZ is an ideal surrogate indicator for adiposity accrual during the first 5 mo of life.

Associations of the sum of skinfolds and length z score with body composition

As was the case with the derived indicators, sum of skinfolds was more strongly associated with lean than FM at birth among all infants. Interestingly, when we stratified by birth size, sum of the skinfolds did not distinguish between FM and lean mass among SGA and AGA infants but was associated with FM among LGA infants. One explanation for this finding could be that subcutaneous FM varies more in LGA infants, enhancing the capacity of skinfold thicknesses to detect adiposity. At 5 mo, and for change in anthropometry during follow-up, we observed stronger associations of the sum of skinfolds with FM than with lean mass, particularly among AGA infants. Taken together, these results suggest that skinfold thicknesses are a suitable proxy for adiposity, particularly among healthy, non–growth-restricted infants, when gold standard methods of body-composition assessment are not available. Length z score was consistently more strongly associated with FFM than with FM, both cross-sectionally and during follow-up. This was expected given that length is directly correlated with bone mass, which constitutes a major component of lean body mass in infants (9).

Strengths and limitations

This study has several strengths. Previous studies relating weight- and length-derived indexes to directly measured adiposity have taken place in relatively small ($n < 250$) (15–17) and predominantly white populations (16, 17). Healthy Start comprises a large, multiethnic population of >1000 mother-child pairs, which improves our ability to generalize our findings. In addition, we were able to examine associations of the

derived indicators with body composition at >1 time during infancy, which is critical given that the first few postnatal months are characterized by rapid changes in body composition (12–14). Limitations of this study include the fact that the analysis was restricted to singletons born at term; thus, results may not be applicable to cases of multiple gestation or preterm infants, although we note that a study conducted among preterm neonates found similar results (16).

In summary, our findings suggest that although weight- and length-based anthropometric indexes are suitable proxies of adiposity in older infants 5 mo of age, they poorly reflect adiposity in newborns and are, in fact, more strongly correlated with lean mass at birth. These results are likely related to the fact that infants undergo a drastic increase in FM during the first 6 mo of life (13), and thus, FM may account for greater variability in the derived indicators at 5 mo than at birth. In addition, we found that, when assessing adiposity gain, change in BMIZ is the best proxy during the first 5 mo of life. Additional studies are warranted to confirm our findings, which could have ramifications for clinical assessment of infant growth and identification of infants at future risk of obesity [e.g., see the study by Taveras et al. (4)], and to relate directly measured adiposity to long-term health outcomes.

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