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Original article

Skinfold-based-equations to assess longitudinal body composition in children from birth to age 5 years

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SUMMARY

Background & aims: In order to identify children at risk for excess adiposity, it is important to determine body composition longitudinally throughout childhood. However, most frequently used techniques in research are expensive and time-consuming and, therefore, not feasible for use in general clinical practice. Skinfold measurements can be used as proxy for adiposity, but current anthropometry-based-equations have random and systematic errors, especially when used longitudinally in pre-pubertal children. We developed and validated skinfold-based-equations to estimate total fat mass (FM) longitudinally in children aged 0–5 years.

Methods: This study was embedded in the Sophia Pluto study, a prospective birth cohort. In 998 healthy term-born children, we longitudinally measured anthropometrics, including skinfolds and determined FM using Air Displacement Plethysmography (ADP) by PEA POD and Dual energy X-ray Absorptiometry (DXA) from birth to age 5 years. Of each child one random measurement was used in the determination cohort, others for validation. Linear regression was used to determine the best fitting FM-prediction model based on anthropometric measurements using ADP and DXA as reference methods. For validation, we used calibration plots to determine predictive value and agreement between measured and predicted FM.

Results: Three skinfold-based-equations were developed for adjoined age ranges (0-6 months, 6-24 months and 2-5 years), based on FM-trajectories. Validation of these prediction equations showed significant correlations between measured and predicted FM (R: 0.921, 0.779 and 0.893, respectively) and good agreement with small mean prediction errors of 1, 24 and -96 g, respectively.

Conclusions: We developed and validated reliable skinfold-based-equations which may be used longitudinally from birth to age 5 years in general practice and large epidemiological studies.

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1. Introduction

Childhood obesity is a global public health threat, with an alarming rise in incidence [1]. Obesity at young age has short-term morbidity, such as musculoskeletal problems and low self-esteem, as well as long-term morbidity, such as cardiovascular disease, insulin resistance and type 2 diabetes. Without intervention, children with overweight or obesity have a high risk of remaining

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overweight or obese as adults [1]. It is, therefore, important to determine body composition longitudinally throughout childhood to early identify children at risk for developing excess adiposity. Techniques that are frequently used in research to determine body composition in young children are Air Displacement Plethysmography (ADP) and Dual energy X-ray Absorptiometry (DXA) [2,3]. However, these techniques are both expensive and time consuming and are, therefore, not feasible for use in general clinical practice.

Various anthropometric measurements are used in general practice as a proxy for adiposity. Body Mass Index (BMI) is mostly used, but BMI is poorly associated with true body composition and BMI SD-scores have low specificity to identify changes in fat mass percentage (FM%) [4,5]. Skinfold measurements are known to

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correlate better with fat mass (FM) compared to BMI [6,7]. They are based on the hypotheses that skinfold thicknesses are representative of the total amount of subcutaneous adipose tissue and that the subcutaneous adipose tissue has a known relationship with total body fat mass [8]. Skinfold measurements are useful as stand-alone measurements to identify children with extreme low or high fat mass [7,9]. Skinfolds have also been used to estimate body fat using anthropometry-based-equations. However, these equations are often developed in infants or older children and adolescents [10-12]. Existing equations are described as being biased and having random and systematic errors when used in pre-pubertal children and are, therefore, not reliable to predict body composition longitudinally in young children [13–15]. This is presumably caused by the multiple changes in body composition throughout infancy and childhood [16-18]. Potentially, the use of multiple adjoined prediction equations for different age categories could reduce proportional bias and systematic errors. This could make anthropometry-based equations more reliable for the prediction of body composition longitudinally in both infancy and childhood. Recently, an American research group developed 3 separate anthropometry-based equations, for ages 3 days and 15 and 54 weeks [19]. However, these equations have not been validated yet and equations for older children are not yet available.

Based on the longitudinal data of our large cohort of healthy children, we developed and validated skinfold-based-equations to estimate fat mass in children aged 0–5 years, for use in general clinical practice when DXA or ADP is not available. We hypothesized that mean total FM estimated by using these equations will not be significantly different from mean FM determined by ADP and DXA in infants and young children, and that proportional bias is reduced due to the use of multiple prediction equations for adjoined age ranges from birth to age 5 years.

2. Material and methods

2.1. Subjects

This study was embedded in the Sophia Pluto study, a large prospective birth cohort study in healthy term-born infants, aiming to provide detailed data on body composition trajectories from early life to childhood [20,21]. Infants were recruited from several maternity wards in the Rotterdam area, The Netherlands. All participants met the following inclusion criteria: born term (\geq 37 weeks of gestation), with an uncomplicated neonatal period. Exclusion criteria were severe asphyxia (defined as an Apgar-score below 3 after 5 min), sepsis or the need for respiratory ventilation, and congenital or postnatal disease, intrauterine infection, genetic syndromes and maternal disease or medication use that could interfere with fetal or child's growth, including maternal corticosteroids and diabetes mellitus. The Medical Ethics Committee of Erasmus Medical Centre approved the study and written informed consent was given by all parents or caregivers with parental authority.

2.2. Data collection and measurements

In 998 children, study visits were scheduled at age 0, 1, 3, 6, 9, 12 and 18 months and annually from 2 to 5 years. Birth data were taken from hospital and midwife records. Ethnicity was reported by parents.

2.3. Anthropometrics

Trained staff carried out the measurements according to standard procedures. Weight was measured to the nearest 5 g by an

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electronic infant scale (Seca 717, Hamburg, Germany) until 2 years and to the nearest 100 g by a flat scale (Seca 876) until 5 years. Length was measured in supine position to the nearest 0.1 cm by an infantometer (Seca 416) until 2 years and in upright position by a stadiometer (Seca 213) until 5 years. Head, waist and hip circumference were measured to the nearest 0.1 cm by a non-stretchable circumference measuring tape (Seca 201). Skinfolds were measured by well-trained personnel, to the nearest mm with a skinfold caliper (Slimguide C-120, Creative Health) during every visit on 4 sites: biceps, triceps, subscapular and suprailliacal, all at the left side of the child. The intra-observer intra-class correlation coefficient (ICC) and inter-observer ICC were determined previously as 0.88 and 0.76, respectively [22]. Total skinfolds were calculated as the sum of all 4 skinfolds.

2.4. Body composition

Body composition was measured with ADP by PEA POD, Infant Body Composition System (COSMED, Italy) during the visits at 0, 1, 3 and 6 months of age and by DXA scan (GE Prodigy Advance R000279) with encore 14.1 software during the visits from 6 months until the age of 5 years. During the DXA scan, children only wore a diaper or underwear and were swaddled in a cotton blanket. To prevent unsuccessful DXA scan due to movement artifacts, children were swaddled in a vacuum cushion until the age of 2 years (465 75,100, Schmidt, Germany), which had similar FM results at age 6 months compared to ADP [16]. During the study period, the same machines were used and were calibrated daily, according to the user's manual.

2.5. Statistical analysis

SD-scores for birth length and birth weight were calculated and corrected for gestational age and sex. SD-scores for length, weight and weight-for-length were calculated at every visit. SD-scores were calculated based on Dutch references, using Growth Analyser software (http://www.growthanalyser.org) [23,24]. Baseline characteristics and body composition measurements are expressed as mean (SD). Not normally distributed values are expressed as median [interquartile range]. Differences between boys and girls were determined with an independent student's t-test. Spearman's correlations were used to calculate correlation coefficients of skinfold measurements and FM measurements. Statistical tests were performed with SPSS statistical package version 25.0 (SPSS Inc. Chicago, Illinois). Results were regarded statistically significant if the p-value was <0.05.

2.5.1. Skinfold-based-equations

To decrease proportional and systemic errors, 3 skinfold-basedequations were developed for adjoined age ranges. The age ranges were chosen based on the fat mass trajectories in young children and the used reference methods [16,25]. The first prediction equation was developed for children aged 0–6 months, using ADP by PEA POD as the reference method. The second was developed for children aged 6 months–2 years, with DXA with vacuum cushion as reference method. And the last, for children aged 2–5 years, using DXA as reference method. In total, almost 5200 measurements were conducted. For each equation, 1 random measurement of each child was used to develop the skinfold-based-equation ('determination cohort'), the other measurement(s) were used for the internal validation of the prediction equations ('validation cohort').

Skinfold-based equations were developed using multiple linear regression analyses, determining the best fitting prediction model. We used 'FM' as the dependent variable. Potential predictors were: skinfold measurements, sex, age, ethnicity, weight, length, waist-

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and hip circumference and interaction terms with age. Using backward elimination, non-significant predictors were removed from the model. To prevent overfitting, regression coefficients were adjusted by shrinkage, using the Copas shrinkage formula [26].

To validate the skinfold-based-equations, FM was predicted in the validation cohort. A calibration plot and linear regression analyses were used to determine predictive value and agreement between predicted and measured FM. Skinfold-based equations were developed and validated using SPSS statistical package version 25.0 (SPSS Inc. Chicago, Illinois). Results were regarded statistically significant if the p-value was <0.05.

3. Results

Child characteristics are presented in Table 1. The total cohort consisted of 998 children, of which 53.9% was male and 59.3% Caucasian. Characteristics of the determination and validation cohorts are presented in supplementary Table 1.

3.1. Skinfold-based-equations

3.1.1. Age 0–6 months

Between the age of 0–6 months, total skinfold measurement was correlated with total fat mass (FM) (R = 0.672, p < 0.001) measured by Air Displacement Plethysmography (ADP). Besides total skinfolds, sex, length and weight were significant predictors for total FM (Table 2). The skinfold-based-equation for total FM in children aged 0–6 months was determined as:

FM (kg) = 0.576 + 0.118 * Sex (0 = male/1 = female) + 0.010 *Total skinfolds (mm) + 0.474 * Weight (kg) - 0.040 * Length (cm).

This prediction model explained 84.9% of the variance in total FM of infants aged 0-6 months.

3.1.2. Age 6-24 months

Between the age of 6-24 months, total skinfold measurement was correlated with total FM (R = 0.486, p < 0.001) measured by Dual energy X-ray absorptiometry (DXA). Besides the total skinfolds, age, sex, length and weight were significant predictors for total FM (Table 2). The skinfold-based-equation for FM in children aged 6-24 months was determined as:

 $\label{eq:FM} \begin{array}{l} \mbox{(kg)} = 2.143 + 0.188 * \mbox{Sex} \ (0 = male/1 = female) + 0.017 * \\ \mbox{Total skinfolds} \ (mm) - 0.034 * \mbox{Age} \ (months) + 0.457 * \mbox{Weight} \ (kg) \\ - \ 0.062 * \mbox{Length} \ (cm). \end{array}$

This predication model explained 65.5% of the variance in total FM of children aged 6–24 months.

Table 1Child characteristics.

	Boys	Girls	p-value
N (%)	538 (53.9%)	460 (46.1%)	
Ethnicity N (%)			0.882
Caucasian	325 (60.3%)	267 (58.0%)	
Black	39 (7.2%)	36 (7.8%)	
Asian	7 (1.3%)	8 (1.7%)	
Latin-American	1 (0.2%)	1 (0.2%)	
Other & mixed	108 (20.0%)	102 (22.2%)	
Missing	59 (10.9%)	46 (10.0%)	
Gestational age (weeks)	39.65 (1.29)	39.64 (1.22)	0.835
Birth weight SDS	0.31 (0.99)	0.15 (1.13)	0.018
Birth length SDS ^a	-0.47 (1.37)	-0.51 (1.33)	0.737
Total visits per child [IQR]	7 [3–9]	6 [3-8]	0.408

Data expressed as mean (SD), except for total measurements, which is expressed as median [interquartile range]. Significant p-values are boldfaced.

Abbreviations: N = number of subjects, SDS = standard deviation score.

^a 329 boys and 265 girls.

3.1.3. Age 2-5 years

Between the age of 2 and 5 years, total skinfold measurement was correlated with total FM (R = 0.541, p < 0.001) measured by DXA. Besides the total skinfolds, age, sex, length and weight were significant predictors for total FM (Table 2). The skinfold-based-equation for children aged 2–5 years was determined as:

 $\label{eq:FM} \begin{array}{l} \mbox{(kg)} = 4.127 + 0.359 * \mbox{Sex} \ (0 = male/1 = female) + 0.028 * \\ \mbox{Total skinfolds} \ (mm) - 0.013 * \mbox{Age} \ (months) + 0.525 * \mbox{Weight} \ (kg) \\ - 0.083 * \mbox{Length} \ (cm). \end{array}$

This prediction model explained 76.8% of the variance in total FM in children aged 2–5 years.

3.2. Validation of skinfold-based-equations

3.2.1. Age 0–6 months

In the infants between age 0–6 months of the validation cohort, mean total FM measured by ADP and predicted with the skinfold-based-equation were both 1.22 kg. The mean prediction error, calculated as measured FM minus predicted FM, was 0.001 kg (SD: 0.24) (Table 3). There was a significant correlation between the measured and predicted FM (kg), with R: 0.921 (p < 0.001). The calibration plot is presented in Fig. 1. Its slope was not different from 1 (β : 0.997, with 95% confidence interval [0.976–1.019]), indicating good agreement between the measured FM and predicted total FM.

3.2.2. Age 6-24 months

In children aged 6–24 months of the validation cohort, mean total FM measured by DXA was 2.05 kg. Mean total FM predicted with the skinfold-based-equations was 2.03 kg (Fig. 1). The mean prediction error was 0.024 kg (SD: 0.37), meaning that the mean FM measured by DXA was 24 g higher than the mean predicted FM (Table 3). There was a significant correlation between the measured and predicted FM, with R: 0.779 (p < 0.001). The calibration plot had a slope that was slightly different from 1 (β : 0.964, with 95% confidence interval [0.932–0.997]) (Fig. 1), indicating that this skinfold-based-equation is likely to underestimate FM in children with very low FM and overestimate in children with very high FM.

3.2.3. Age 2-5 years

In children aged 2–5 years of the validation cohort, mean total FM measured by DXA was 4.94 kg. Mean total FM predicted with the skinfold-based-equations was 5.03 kg (Fig. 1). The mean prediction error was –0.096 kg (SD: 0.58), meaning that the mean FM measured by DXA was 96 g lower compared to the mean predicted FM (Table 3). There was a significant correlation between the measured and predicted total FM (kg), with R: 0.893 (p < 0.001). The calibration plot had a slope that was not different from 1 (β : 0.989, with 95% confidence interval [0.941–1.038]), indicating good agreement between the measured and predicted total FM (Fig. 1).

4. Discussion

To our knowledge, we are the first who developed and validated skinfold-based-equations to predict total fat mass (FM) longitudinally from birth to 5 years of age in a large cohort of healthy children. The validation of these equations showed significant correlations between predicted and measured FM with good agreement and small mean prediction errors, calculated as measured FM minus predicted FM, of 1, 24 and –96 g, for adjoined age ranges 0–6 months, 6–24 months and 2–5 years, respectively.

ADP and DXA are often used in research to determine body composition in infancy and childhood. However, these methods are expensive and time consuming, and, therefore, not feasible for use in general clinical practice [2]. So, in the past, anthropometric

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Table 2

Skinfold-based-equation	s to estimate	FM (kg) in	children aged	0-5 years.
				,

		Total skinfolds	Age	Sex	Length	Weight	Constant	R ²
Age 0–6 months	Β±SE β	0.010 ± 0.001 0.122*		0.118 ± 0.010 0.097 *	-0.040 ± 0.003 -0.394*	0.474 ± 0.012 1.213*	0.576 ± 0.115	0.849
Age 6–24 months	Β±SE β	0.017 ± 0.002 0.197*	-0.034 ± 0.006 -0.354^{*}	0.189 ± 0.030 0.158*	-0.062 ± 0.007 -0.792*	0.459 ± 0.019 1.549*	2.143 ± 0.378	0.655
Age 2—5 years	$\frac{B \pm SE}{\beta}$	0.028 ± 0.005 0.183*	-0.013 ± 0.006 -0.110°	0.361 ± 0.070 0.143*	-0.084 ± 0.013 -0.524*	0.528 ± 0.026 1.240*	4.122 ± 0.862	0.768

 $B\pm SE = Unstandardized$ coefficient B and Standard Error. $\beta = standardized$ coefficient Beta. *p < 0.001, $\hat{p} = 0.033$.

Table 3

Predicted vs measured fat mass percentage in validation cohort.

	Measured FM (kg)	Predicted FM (kg)	Prediction error (kg)	p-value	R
Age 0–6 months N = 1461	1.22 (0.61)	1.22 (0.56)	0.001 (0.24)	0.911	0.921 (p < 0.001)
Age 6–24 months N = 2159	2.05 (0.59)	2.03 (0.48)	0.024 (0.37)	0.002	0.779 (p < 0.001)
Age 2–5 years N = 411	4.94 (1.28)	5.03 (1.16)	-0.096(0.58)	<0.001	0.893 (p < 0.001)

Data expressed as mean (SD). Prediction error is calculated as measured FM minus predicted FM. P-values for the differences between measured and predicted FM are presented, which are boldfaced when significant. R = Pearson's correlation coefficient for measured and predicted FM (kg). N = number of measurements.



Fig. 1. Calibration plots. Calibration plots for measured and predicted FM% by 3 skinfold-based equations. A. Equation age 0–6 months B. Equation age 6–24 months. C. Equation age 2–5 years. The red dashed line represents the 45°-line.

equations have been developed, of which the equations of Slaughter et al. [10], Aris et al. [11] and Catalano et al. [12] are mostly used in clinical research and general practice. However, the Slaughter equation has been developed in 1988 in children and adults aged 8–29 years [10]. The Aris and Catalano equations have both been developed in 1–3 day old infants using only 1 skinfold measurement [11,12]. These equations have been validated against ADP and hydrodensitometry, but all have considerable random and systematic errors especially when used in children in other age categories and are, therefore, not reliable during the first years of life [13,15]. Recently, we developed anthropometry-based prediction equations for FM and fat free mass in infants aged 5-16 weeks, which were externally validated in children aged 3-6 months. These equations were more accurate compared to the aforementioned prediction equations [15]. Although smaller, a proportional bias remained, which made these equations less accurate for older children and longitudinal use. We now developed and validated skinfold-based-equations, that may be used to predict total FM longitudinally throughout the first 5 years of life in general practice and large epidemical studies.

During infancy and early childhood, it is known that body composition and the distribution of body fat undergo multiple changes. Total fat mass is known to increase with age, but the velocity of the increase is not constant over time. This velocity is highest from birth until 6 months of age. Between age 6 and 24 months total fat mass remains more or less stable, and again increases after the age of 2 years [16–18,25]. We, therefore,

developed and validated 3 separate skinfold-based-equation for adjoined age ranges (0–6 months, 6–24 months and 2–5 years).

With the available tools it is not possible to use one single method longitudinally to determine body composition from birth into childhood [27,28]. Furthermore, total fat mass measurements differ between available techniques and even between different machines, modes or software of the same technique [29-31]. Therefore, reference values for fat mass, to identify infants and young children at risk for developing excess adiposity, were lacking until recently. Our research group published reference values based on 3500 ADP and DXA measurements of healthy term-born children from age 0-2 years. We found that body composition measured by ADP using PEA POD and DXA with vacuum cushion were comparable in children aged 6 months and that DXA scanning, with a vacuum cushion to prevent movement artifacts, provides accurate measurements until the age of 2 years [16]. For older children, we published reference values based on 600 DXA measurements of healthy children aged 2-5 years [25]. Our skinfoldbased-equations were determined using the same equipment as reference methods. They can, therefore, be used in combination with our previously published reference values, to monitor fat mass and identify infants and young children developing excess adiposity [16.25].

Our skinfold-based equations showed good agreement with measured total fat mass. Only in the model for children aged 6–24 months, the slope was slightly lower than 1, indicating that the skinfold-based equations are likely to underestimate FM in children

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with very low FM and overestimate in children with very high FM. Since FM increases with age, the difference between measured and predicted FM will increase with age. By developing 3 equations for adjoined age categories, we partly removed this bias, and assume that differences between measured and predicted FM will remain small. We, therefore, consider the equations to be reliable for clinical use, when used in the assigned age category.

We found skinfolds, age, sex, weight and length to be significant predictors for total FM. This is in line with literature [11,17]. Waistand hip circumference were no significant predictors for FM. Waistand hip circumference were reported to correlate with abdominal fat mass and total fat mass [32,33], but our findings show waistand hip circumference are not reliable proxy's for total FM in young children until age 5 years. In our multi-ethnic cohort, with 40.7% being non-Caucasian, ethnicity was also not a significant predictor for total FM. Others found ethnicity to be an predictor for fat mass in infants aged 1–3 days [34], but our data did not confirm these findings.

The strength of this study is the large number of longitudinal skinfold and fat mas measurements in a cohort of healthy termborn children. We acknowledge the use of internal validation on a random sample of our cohort as a limitation. Internal validation could lead to overestimation of the performance of the prediction model, especially when small sample sizes are used. However, we used a very large number of measurements for the determination of the models and we corrected for overfitting to minimize overestimation. Although our multi-ethnic is representative for the Dutch population, we acknowledge a relative underrepresentation of the Asian and Latin population. As the validation was done on healthy, term-born children, the performance in chronically ill, and preterm-born children cannot be guaranteed. Validation on specific patient-groups is, therefore, needed in the future.

In conclusion, we determined and validated reliable 3 skinfoldbased-equations for adjoined age ranges, which may be used longitudinally in healthy children from birth to age 5 years, in general practice and large epidemiological studies to identify those with increased or increasing adiposity.

Author contributions

AHK was in charge of designing the study. IvB, DD, KdF and AHK were in charge of the cohort, design, and collecting of the data. MdR consulted on the statistical plan. IvB did the statistical analysis. Drafting the manuscript was primarily done by IvB and AHK. All authors were involved in writing the manuscript and had final approval of the submitted version.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2023.04.024.

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