

Original Research Article

Body composition reference charts for infants from birth to 24 months: Multicenter Infant Body Composition Reference Study

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A B S T R A C T

Background: Body composition assessment in the first 2 y of life provides important insights into child nutrition and health. The application and interpretation of body composition data in infants and young children have been challenged by a lack of global reference data.

Objectives: We aimed to develop body composition reference charts of infants aged 0–6 mo based on air displacement plethysmography (ADP) and those aged 3–24 mo based on total body water (TBW) by deuterium dilution (DD).

Methods: Body composition was assessed by ADP in infants aged 0–6 mo from Australia, India, and South Africa. TBW using DD was assessed for infants aged 3–24 mo from Brazil, Pakistan, South Africa, and Sri Lanka. Reference charts and centiles were constructed for body composition using the lambda- μ -sigma method.

Results: Sex-specific reference charts were produced for FM index (FMI), FFM index (FFMI), and percent FM (%FM) for infants aged 0–6 mo ($n = 470$ infants; 1899 observations) and 3–24 mo ($n = 1026$ infants; 3690 observations). When compared with other available references, there were observable differences but similar patterns in the trajectories of FMI, FFMI, and %FM.

Conclusions: These reference charts will strengthen the interpretation and understanding of body composition in infants across the first 24 mo of life.

Keywords: body composition, infants, air displacement plethysmography, deuterium dilution, reference charts, fat-free mass index, fat mass index

Introduction

The double burden of malnutrition presents a significant global health concern, especially in low- and middle-income countries where high levels of undernutrition remain in addition to increasing obesity

levels. The first years of life are recognized as a priority in establishing strong nutrition foundations to ensure optimal growth and functional development, as well as long-term health. Policies and programs to improve feeding practices and food quality in early life are essential for preventing malnutrition across the life course. Infant and young child

Abbreviations used: ADP, air displacement plethysmography; DD, deuterium dilution; D₂O, deuterium oxide; EDF, equivalent degrees of freedom; FFMI, FFM index; FMI, FM index; INTERGROWTH-21st, International Fetal and Newborn Growth Consortium for the 21st Century; MGRS, Multicentre Growth Reference Study; MIBCRS, Multi-center Infant Body Composition Reference Study; TBW, total body water.

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feeding interventions must be informed by accurate, informative, and relevant data.

To promote effective early-life interventions and understand the associations between early-life nutrition and later health, it is important to capture the nutritional status of infants through the collection of body composition data [1]. Although length and weight are core components of early childhood global nutrition surveillance, these measurements (and derivatives, such as BMI) do not provide information on FM and FFM. Body composition has important implications for energy metabolism and long-term health. The literature has highlighted the need for the assessment of body composition in infants [1,2] and assessment techniques have become more accessible; however, the lack of available reference body composition data has been a key barrier to the implementation of these techniques in public health or clinical settings.

Body composition can be challenging to assess in infants and young children, although several techniques are available, which have been shown to be feasible and accurate in children aged <2 y [3–6]. The “PEA POD” uses air displacement plethysmography (ADP) to assess body composition from birth up to 6 mo of age, and is a simple, noninvasive, and quick technique that can be used in public health and clinical settings. Deuterium dilution (DD) can be used to accurately determine total body water (TBW) in the field, which makes it a feasible technique with wide applicability for assessing the body composition of infants. To ensure that body composition data from these techniques are valuable for public health guidance as well as clinical evaluation, reference data are needed.

Limited body composition reference data have been published for infants, covering different age ranges, using different techniques and building on the classic body composition model of Fomon et al. [7]. Wells et al. [8] extracted data from multiple United Kingdom studies to generate body composition reference charts for children aged 6 w–5 y based on the DD technique whereas Butte et al. [9] used a multicomponent model to produce reference data from North American infants over the first 2 y of life, and recently, body composition reference charts were published in the Netherlands using ADP and dual energy x-ray absorptiometry in infants aged 1–24 mo [10]. In 0–6-mo-old infants, reference charts are available for ADP from Ethiopia [11] and Canada [12], and pooled data from several high-income country studies were published by Norris et al. [13]. To provide useful tools for the global community to interpret body composition, there is a need for infant body composition reference data that are developed from multicountry studies with aligned protocols. The objective of our study was to create international body composition reference curves for the first 24 mo of life of children.

Methods

The Multicenter Infant Body Composition Reference Study (MIBCRS) was an observational, longitudinal, prospective, multinational study that followed infants from birth to 24 mo of age in lower-middle (India, Pakistan, and Sri Lanka), upper-middle (Brazil and South Africa), and high-income (Australia) countries according to World Bank classifications. Data collection for the study started in 2013 and was fully completed by December 2019 across all the countries. The study complied with the International Ethical Guidelines for Biomedical Research Involving Human Subjects [14], and received ethical approval from national and local ethical review committees. Written informed consent was obtained from the mothers of all children enrolled in the study.

Infants were enrolled at birth at the Launceston General Hospital in Tasmania (Australia); at the 5 hospitals with maternity ward in Pelotas (Brazil); at St John’s Medical College Hospital, Bengaluru (India); at Aga Khan University Hospital in Karachi (Pakistan); Chris Hani Baragwanath Academic Hospital in Johannesburg (South Africa); and at the University Unit of the De Soysa Hospital for Women in Colombo (Sri Lanka). Mother–infant dyads were approached and screened by trained interviewers at all sites. The inclusion criteria aligned with the WHO Multicentre Growth Reference Study (MGRS) eligibility criteria at the newborn screening to ensure that no health, environmental, or economic constraints on growth, including mother intending to breastfeed up to 6 mo, single birth, between 37 and 42 wk of gestation, absence of significant morbidity of the mother and infant, nonsmoking mother aged ≥ 18 y, and meeting country-specific criteria of middle socioeconomic status (based on education or income levels) [15]. Infants with significant morbidity, such as cardiorespiratory illnesses and congenital abnormalities, which might affect infant growth, and mothers living with HIV/AIDS were excluded. Maternal demography, obstetric history, and education were recorded using questionnaires based on MGRS and International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) studies [15].

Standardized protocols for anthropometry were developed based on the INTERGROWTH-21st protocol [16] and an expert trainer (LIC) conducted training at each site to ensure harmonization. Newborns were weighed and measured no later than 24 h after birth and at each follow-up visit. From 3 mo onward, the maximum recommended delay of measurements was 10% of the child’s age. Weight and length were measured for each participant on the same day as the body composition assessment. Infant weight was measured naked, using a pediatric electronic scale (SECA 376), accurate to the nearest 5 g up to 7.5 kg and to the nearest 10 g up to 20 kg. The length was measured using a Harpenden stadiometer (300–1100 mm, accurate to 1 mm; Holtain Ltd) in all countries, except India and Sri Lanka, where the SECA 417 infantometer was used. Measurements were taken independently by 2 trained anthropometrists. The maximum allowed differences were 50 g for weight and 7 mm for length for all ages. If the difference between a pair of measurements was larger than the maximum allowed differences, then each anthropometrist repeated that measurement (measurements could be repeated twice). Weight and length data were converted to *z*-scores according to the WHO 2006 Child Growth Standards [17].

In Australia, India, and South Africa, infants were recruited at birth, and their body composition was assessed by ADP (PEA POD, Software version 3.5.0, 201, COSMED) within 3 d of birth, at 2 wk, and at 1, 2, 3, 4, and 6 mo employing standard procedures [18]. The equipment was calibrated daily, with a hollow cylinder of known mass and volume, and had a measurement precision of 0.07% across the 3 sites. The total body density, calculated as the ratio of weight (kg) and the measured body volume (L), was used to calculate the proportions of FM and FFM using assumed densities (0.9007 and 1.063 kg/L for FM and FFM, respectively). The FM and FFM were expressed in kg, as a percentage of body weight (percent FM [%FM] and percent FFM [%FFM]). FM and FFM were reported as an index related to length (FM index [FMI in kg/m²] FFM index [FFMI in kg/m²]) as previously described [19] and used in other reference charts [8,11] after the investigation in the 3–24 mo group showed that an exponent of 1.9 eliminated the correlation of these indices with height.

In Brazil, Pakistan, South Africa, and Sri Lanka, infants were recruited at birth, and TBW was assessed using the DD technique at 3, 6, 9, 12, 18, and 24 mo of age. From 3 to 9 mo, all infants received 1 g

of deuterium oxide (D₂O; 99.8 atom % ²H) sterility tested. At 12, 18, and 24 mo, the dose was increased to 1.5 g. The D₂O was administered to the child by using a 3-mL dosing syringe. The syringe was filled with the required amount of D₂O and was weighed before and after administration to determine the weight of D₂O consumed. Saliva was sampled before D₂O administration and 3 h after the administration of the dose. The baseline saliva sample was collected at least 15 min after the last feed to ensure that no waste milk or other food was present in the child's mouth. Saliva samples were collected with cotton swabs. If any of the D₂O was regurgitated, the protocol was interrupted and the mother was invited to return in 7 d. The enrichment of D₂O in saliva was measured either by isotope ratio MS [20] or by FITR [21] using an Agilent 4500 Series spectrometer. The quality of measurements was ensured by site visits, interlaboratory comparisons, and quality checking of the analyzed data by the same team member across all sites. TBW was calculated using the weight of D₂O consumed, the enrichment of the deuterium in the dose, and the enrichment of deuterium in the saliva, with a small correction (4.1%) for nonaqueous exchange of deuterium [22]. FFM was estimated by dividing by an age-related constant for the hydration of FFM [23], and FM was calculated as the difference between body weight and FFM. These parameters were expressed in kg (FM and FFM), %FM, %FFM, FMI, and FFMI.

Statistics

Descriptive statistics were produced after stratifying according to sex. We produced sex-specific growth charts for each of the 5 outcomes (FM, FFM, FMI, FFMI, and %FM), based on ADP for 0–6 mo and based on DD for 3–24 mo. The lambda–mu–sigma method was used to estimate centiles in the Generalized Additive Model for Location, Scale, and Shape package in R version 4.0.5 [24]. Briefly, this approach models variation in size across age as a function of 3 curves: 1) the L curve describes the Box–Cox power needed to remove skewness, 2) the M curve describes the median, and 3) the S curve describes the CV. These curves are fitted using penalized likelihood as cubic splines, with the number of equivalent degrees of freedom (EDF) determining the curve complexity. Models were built by choosing the EDF for M, then S, and then L, with the aim of making EDF for M > EDF for S > EDF for L. Determination of the number of degrees of freedom (and thus complexity) of the L, M, and S curves was guided by model fit statistics (e.g., Bayesian Information Criterion), visual inspection of the centiles, and standard model diagnostics (e.g., worm plots of residuals) [25]. Body composition curves were produced depicting the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th centiles. We also produced figures superimposing the 10th, 50th, and 90th centiles of our charts on those from the publications of Wells et al. [8] for DD. Finally, we converted the published body composition data of Fomon et al. [7] and Butte et al. [9] to z-scores according to our new 3–24-mo DD charts and plotted the results for visual inspection. Centile estimation was performed using the Generalized Additive Model for Location, Scale, and Shape package in R version 4.0.5, and all other analyses were performed in Stata SE version 15.1.

Results

A description of our study sample is shown in Table 1. Body composition was assessed using ADP in 470 infants from 0 to 6 mo of age, with 1899 observations from 3 countries (Australia: *n* = 586; India: *n* = 574; and South Africa: *n* = 739) (Supplemental Figure 1). Body composition was assessed using DD in 1026 infants from 3 to 24

TABLE 1
Description of study samples

		Males	Females
ADP			
Observations			
Total	<i>N</i>	905	994
0 mo	<i>n</i> (%)	220 (24.3)	224 (22.5)
0.5 mo	<i>n</i> (%)	56 (6.2)	62 (6.2)
1 mo	<i>n</i> (%)	149 (16.5)	157 (15.8)
2 mo	<i>n</i> (%)	130 (14.4)	143 (14.4)
3 mo	<i>n</i> (%)	149 (16.5)	167 (16.8)
4 mo	<i>n</i> (%)	95 (10.5)	116 (11.7)
6 mo	<i>n</i> (%)	106 (11.7)	125 (12.6)
Country			
Australia	<i>n</i> (%)	284 (31.4)	302 (30.4)
India	<i>n</i> (%)	286 (31.6)	288 (29.0)
South Africa	<i>n</i> (%)	335 (37.0)	404 (40.6)
Weight z score	Mean (SD)	−0.50 (0.88)	−0.43 (0.99)
Length z score	Mean (SD)	−0.60 (1.01)	−0.51 (1.06)
Weight-for-length z score	Mean (SD)	−0.04 (1.24)	−0.02 (1.25)
DD			
Observations			
Total	<i>N</i>	1869	1821
3 mo	<i>n</i> (%)	371 (19.9)	337 (18.5)
6 mo	<i>n</i> (%)	330 (17.7)	322 (17.7)
9 mo	<i>n</i> (%)	303 (16.2)	324 (17.8)
12 mo	<i>n</i> (%)	321 (17.2)	301 (16.5)
15 mo	<i>n</i> (%)	58 (3.1)	52 (2.9)
18 mo	<i>n</i> (%)	234 (12.5)	237 (13.0)
24 mo	<i>n</i> (%)	252 (13.5)	248 (13.6)
Country			
Brazil	<i>n</i> (%)	586 (31.4)	621 (34.1)
Pakistan	<i>n</i> (%)	395 (21.1)	393 (21.6)
South Africa	<i>n</i> (%)	600 (32.1)	550 (30.2)
Sri Lanka	<i>n</i> (%)	288 (15.4)	257 (14.1)
Weight z score	Mean (SD)	−0.26 (1.11)	−0.12 (1.07)
Length z score	Mean (SD)	−0.48 (1.15)	−0.35 (1.14)
Weight-for-length z score	Mean (SD)	0.08 (1.18)	0.17 (1.10)

ADP, air displacement plethysmography; DD, deuterium dilution.

mo of age, with 3690 observations from 4 countries (Brazil: *n* = 1207; Pakistan: *n* = 788; South Africa: *n* = 1150; and Sri Lanka: *n* = 545) (Supplemental Figure 2).

Observations with weight, length, and/or weight-for-length z score of ≤ -5 or $\geq +5$ were removed during data cleaning. Relative to the WHO reference data, both sexes had less weight and height, but the weight-for-length z-scores were similar. The percentage of exclusively breastfed infants in the 0–6-mo group was 62.3% at 3 mo and 13.6% at 6 mo, and in the 3–24 mo group, 52.7% were exclusively breastfed at 3 mo and 19.7% at 6 mo.

ADP-based FMI, FFMI, and %FM for infants aged 0–6 mo are shown in Figure 1, and FM and FFM are presented in Supplemental Figure 3. LMS data are available in Supplemental Tables 1 and 2. The median FM for men and women was 1.9 kg, whereas the FFM was higher in men at 5.6 kg compared with 5.1 kg for women at 6 mo of age. FMI increased rapidly in the first 3 mo in both sexes, with men having an FMI of 4.2 kg/m² and women having that of 4.5 kg/m² at 6 mo of age. FFMI also increased from birth to 6 mo of age in both sexes, where it increased from 11.7 kg/m² to 12.6 kg/m² in men and from 11.4 kg/m² to 12.1 kg/m² in women.

DD-based FMI, FFMI, and %FM for infants aged 3–24 mo are shown in Figure 2, and FM and FFM are available in Supplemental Figure 4. LMS data are available in Supplemental Tables 3 and 4. FM, FMI, and %FM were higher in women than men across all ages, with a similar pattern in both sexes. %FM in men and women increased from

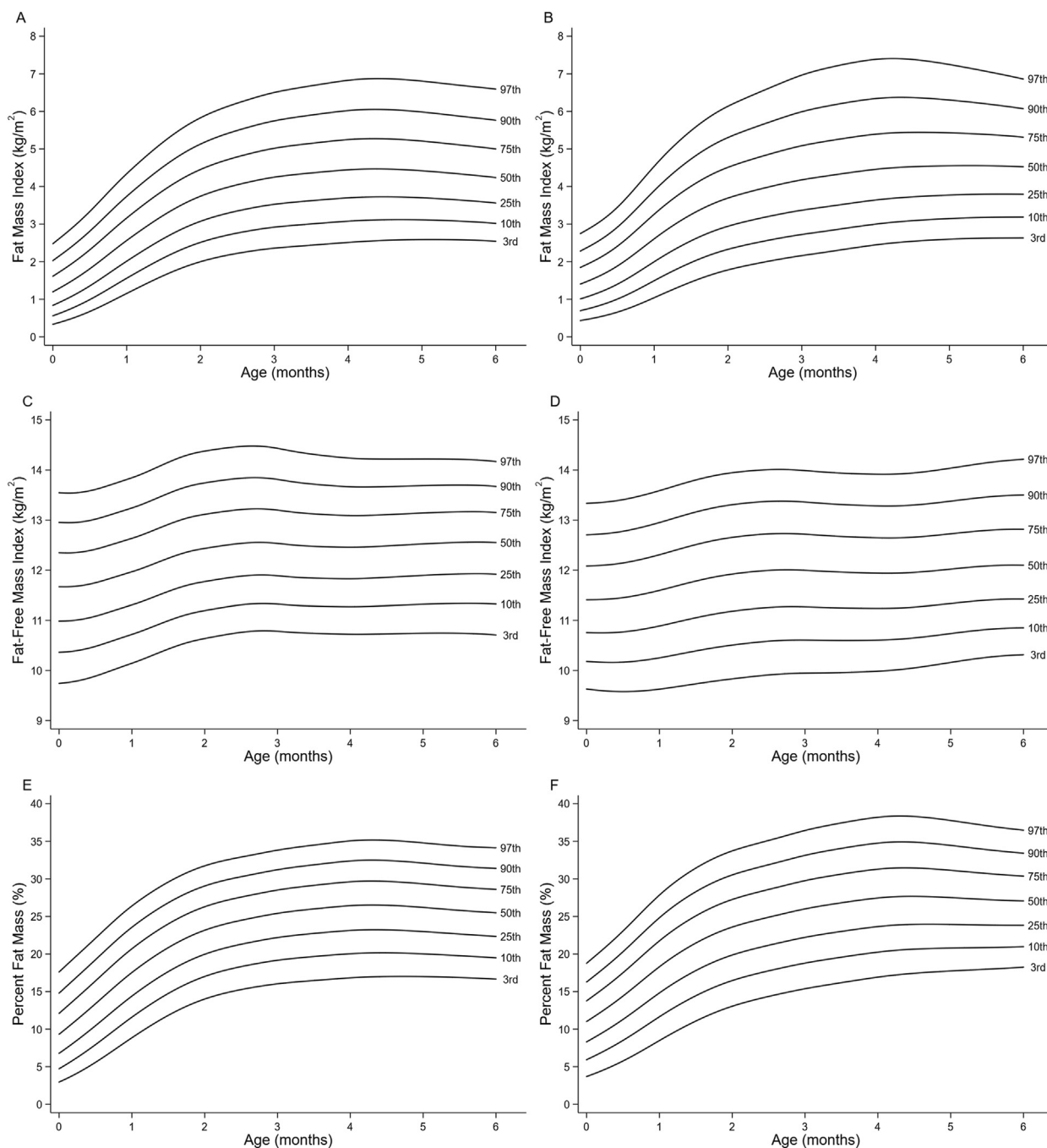


FIGURE 1. Centiles for 0–6 mo from ADP for (A) FMI in men, (B) FMI in women, (C) FFMI in men, (D) FFMI in women, (E) %FM in men, and (F) %FM in women. Men: $n = 231$ individuals, $n = 905$ observations; Women: $n = 239$ individuals, $n = 994$ observations. ADP, air displacement plethysmography; FMI, FM index, FFMI, FFM index; %FM, percent FM.

3 to 6 mo of age, plateaued between 6 and 9 mo of age, after which it gradually decreased until 24 mo of age, where the %FM at 24 mo (men: 20.8% and women: 22.6%) approximated that at 3 mo of age (men: 20.0% and women: 22.7%). FMI peaked at 9 mo of age in both men (3.9 kg/m^2) and women (4.1 kg/m^2), after which it gradually decreased until 24 mo of age (men: 3.2 kg/m^2 and women: 3.6 kg/m^2). FFM increased by 5.3 kg in men and 4.4 kg in women over the 3–24 mo period, whereas FFMI slightly declined from 3 to 24 mo in both men ($13.3\text{--}12.7 \text{ kg/m}^2$) and women ($12.6\text{--}12.1 \text{ kg/m}^2$).

Figure 3 shows the FMI and FFMI centiles 3–24 mo compared with those of Wells et al. [8]. The FMI was lower in our population than

those of Wells et al. [8] for both men and women across all ages but followed the same curve. FFMI of our population was higher than those of Wells et al. [8], and although their data plateaued around 12 mo, our data declined from 9 to 24 mo. Figure 4 plots data from Fomon et al. [7] and Butte et al. [9] as z-scores relative to our data for 3–24 mo. For FMI, the data of Fomon et al. [7] showed similar age trends, whereas the data of Butte et al. [9] showed higher FMI at all ages. For FFMI, although Fomon et al. [7] showed similar FFMI to our reference data until 12 mo, it was ~ 0.67 SDS higher at 24 mo, whereas Butte et al. [9] reported substantially lower FFMI values until 9 mo, with an FFMI of ~ -0.67 SD lower at 24 mo.

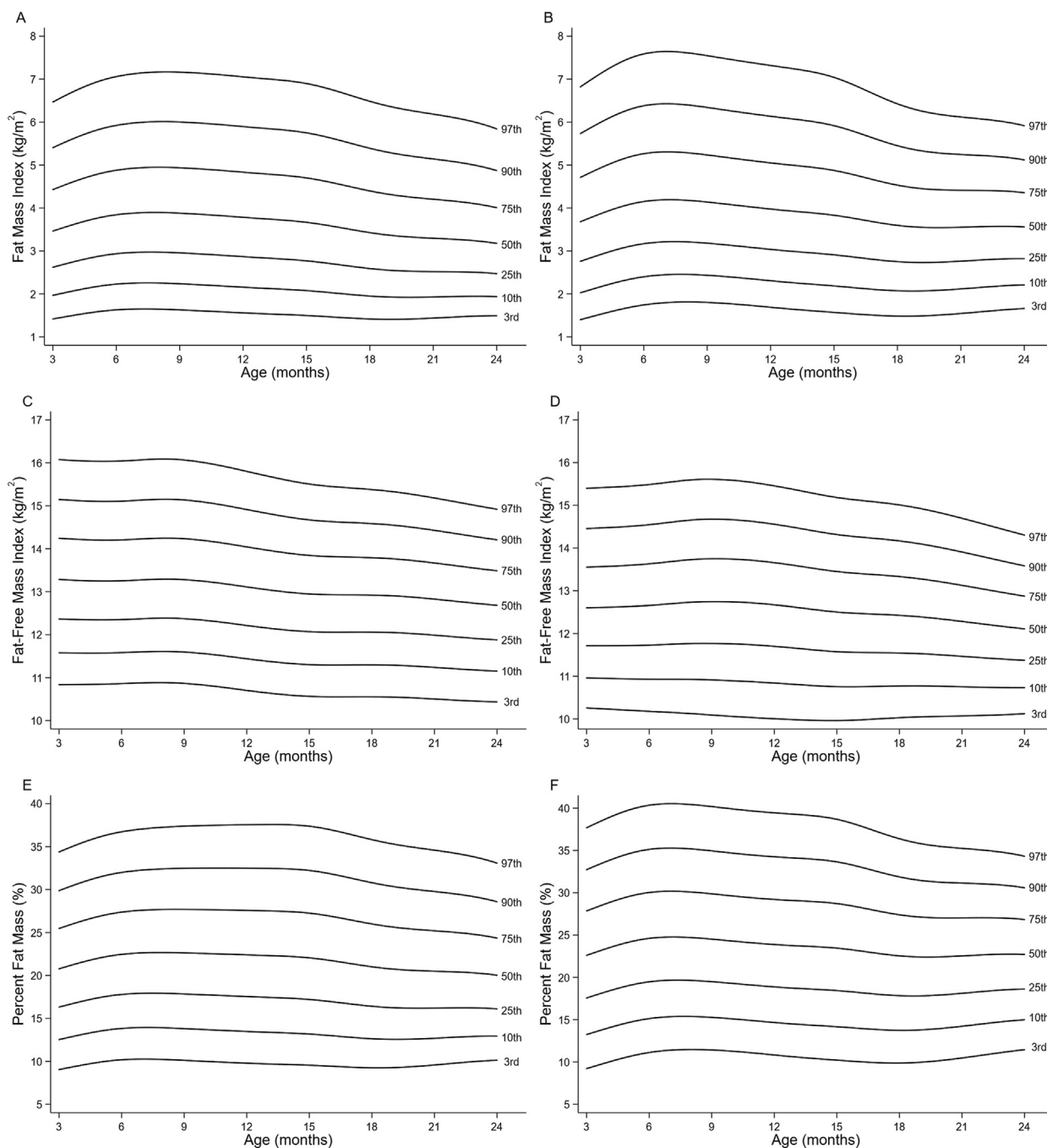


FIGURE 2. Centiles for 3–24 mo from DD for (A) FMI in men, (B) FMI in women, (C) FFMI in men, (D) FFMI in women, (E) %FM in men, and (F) %FM in women. Men: $n = 535$ individuals, $n = 1869$ observations. Women: $n = 491$ individuals, $n = 1821$ observations. DD, deuterium dilution; FMI, FM index, FFMI, FFM index; %FM, percent FM.

Discussion

We present body composition reference curves between birth and 24 mo, which will allow the body composition to be evaluated over the first 2 y of life. We have combined longitudinal data from 4 regions (Africa, Asia, Oceania, and South America) and collected data matching the MGRS eligibility criteria [15] and harmonized protocols across all countries. The longitudinal data collected on healthy infants with >5500 measurements represent the most diverse collection available of body composition data across the first 24 mo. Now with the reference data available, clinicians and researchers have the tools to

evaluate and interpret body composition measurements to inform and evaluate interventions to combat the double burden of malnutrition and setup healthier childhood trajectories.

The DD and ADP technique-specific references have the benefit over data collected using anthropometry or skinfold thicknesses, in being able to differentiate FM and FFM and provide useful information on the components of body mass. With ADP being suitable for measuring infants weighing up to 8 kg and DD being easy to perform in field and clinic settings across all ages, the combination of these 2 techniques provides a means to assess body composition in the first 2 y of life. Body composition techniques are based on

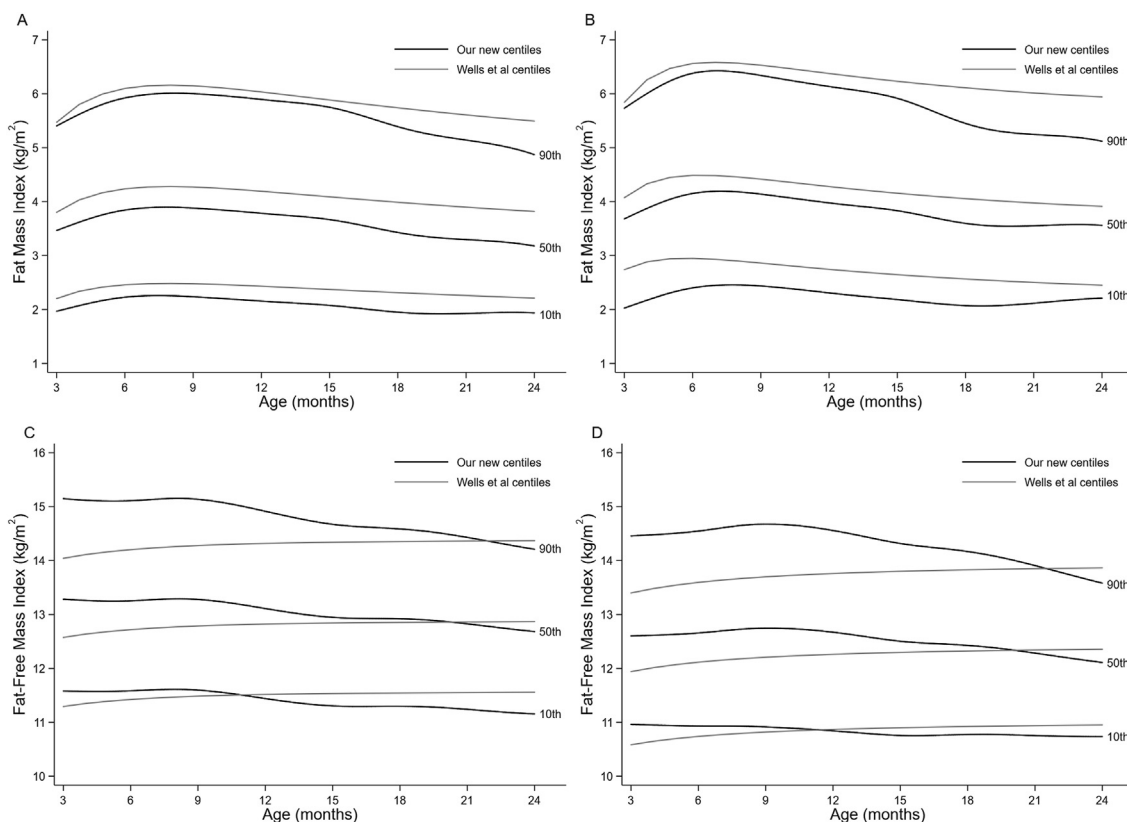


FIGURE 3. Body composition centiles for 3–24 mo compared with those reported by Wells et al. [8] for (A) FMI in men, (B) FMI in women, (C) FFMI in men, and (D) FFMI in women. *n* = 211 men and 252 women. FMI, FM index; FFMI, FFM index.

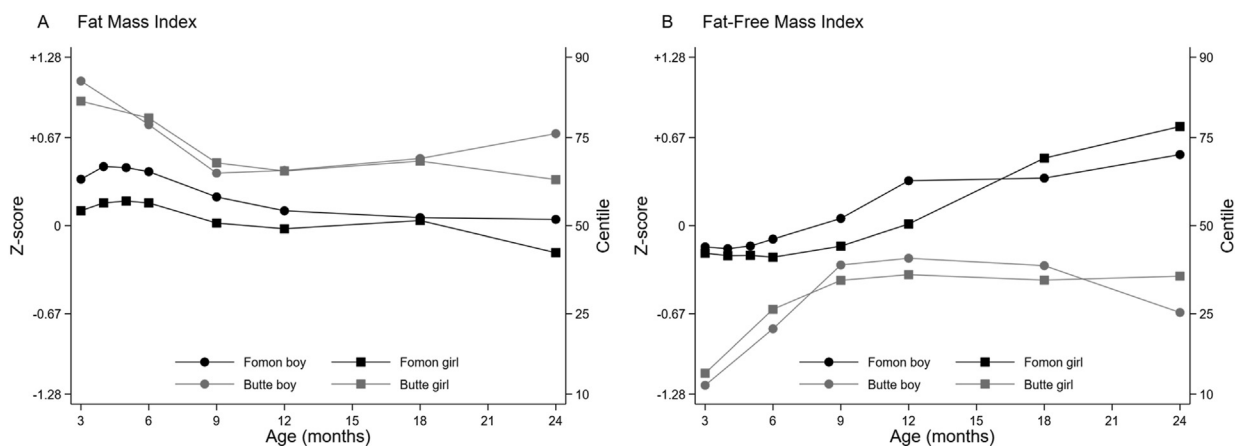


FIGURE 4. Published data of Fomon et al. [7] and Butte et al. [9] for (A) FMI and (B) FFMI converted to z-scores using our new DD references (mean published values). DD, deuterium dilution; FMI, FM index; FFMI, FFM index.

assumptions and have limitations in infants [2,26–28]. It is recommended that the 2 sets of charts based on ADP and DD should not be used interchangeably for children between 3 and 6 mo of age, and the technique-specific chart should be used for longitudinal assessment in each child.

Consistent with previous studies [29,30], our charts confirm differences between female and male infants, with females having higher FMI and lower FFMI than males. Sex differences have been primarily attributed to endogenous testosterone production in men [29], whereas there have been no sex differences shown for growth-regulating factors in human milk [31].

The comparison of these charts with published references confirms the variability in infant body composition. When examining the 3–24 mo charts compared with other reference data [7–9], there were observable differences, particularly in FFMI, that varied across the age ranges. Factors contributing to the variation in the body composition data between the studies may be differences in study design, recruitment criteria, and assessment techniques. The reference data from Fomon et al. [7] are estimates based on very little data from various combined sources before the 1980s. Butte et al. [9] assessed longitudinal TBW, total body potassium, and bone mineral content in 76 healthy infants to calculate body composition using a multicomponent

model, while the infant reference data from Wells et al. [8] were based on several studies assessing TBW. Although these studies and our study assessed TBW, the methodology varied, which may have contributed to variability; Wells et al. [8] used the back extrapolation method, Butte et al. [9] used both this method and the plateau method, and our study used the plateau method. Differences between the reference data may also be because of secular trends, with the data from the current study collected 2 decades after the data of Wells et al. [8] and Butte et al. [9], as well as the ethnic and environment diversity in our data compared with these smaller single country studies conducted in the United States or United Kingdom [7–9].

The strength of these new international reference charts lies in the large number of longitudinal observations, data reflecting ethnic variability and geographic regions, the stringent inclusion criteria, and harmonized protocols. However, we recognize several limitations of our study. Only 3 countries were able to participate in the 0–6-mo data collection of ADP, which limits the available data for the ADP charts. As with all longitudinal studies, challenges existed with attrition (absolute loss to follow-up and at cross-sectional assessments points); however, all attempts were made to minimize missing data, but challenges of early life meant that many infants did not complete all measurement time points. Although the mothers and infants recruited to the study were selected according to the MGRS criteria to be healthy children living under conditions that favored the achievement of full genetic potential, these charts are not standards because all 6 major geographic regions are not represented, the study site selection was based on factors other than epidemiologic data, and the stringent quality monitoring required in developing standards could not be supported for the body composition assessments.

In conclusion, we have developed sex-specific reference charts for infant body composition from birth to 24 mo of age based on ADP and DD techniques. These charts provide the tools to assess body composition in both public health and clinical settings, and will enhance early-life growth monitoring. Further work with the charts should investigate the use of body composition data as predictors for later health outcomes, the relationship between standard anthropometric growth charts and these body composition charts, and the feasibility and applicability of the charts in various settings.

Conflicts of Interest

AVK is an Editor for The American Journal of Clinical Nutrition and played no role in the Journal's evaluation of the manuscript. All other authors declare no competing interests.

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Author Contributions

The authors' responsibilities were as follows – AJMA, ISS, APH, SA, VPW, RK, NL, CSC, NB, CS, SN: designed the research; ISS, APH, SA, VPW, RK, NL, CSC, TA, PD, SN: conducted the research; WJ, LN: performed the statistical analyses; AJMA, WJ: wrote the drafts of the paper; AJMA: has primary responsibility for the final

content; and all authors contributed to the study and have read and approved the final manuscript.

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Data Availability

The data described in the manuscript, code book, and analytic code will be made publicly and freely available without restriction at OSF (<https://doi.org/10.17605/OSF.IO/EUXR2>).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajcnut.2023.02.012>.

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