New charts for the assessment of body composition, according to air-displacement plethysmography, at birth and across the first 6 mo of life

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Background: Air-displacement plethysmography (ADP) is a good candidate for monitoring body composition in newborns and young infants, but reference centile curves are lacking that allow for assessment at birth and across the first 6 mo of life.

Objectives: Using pooled data from 4 studies, we aimed to produce new charts for assessment according to gestational age at birth (30 + 1 to 41 + 6 wk) and postnatal age at measurement (1–27 wk).

Methods: The sample comprised 222 preterm infants born in the United States who were measured at birth; 1029 term infants born in Ireland who were measured at birth; and 149 term infants born in the United States who were measured at birth; 1029 term infants born in Ireland who were measured at birth; and 149 term infants born in the United States who were measured at birth; and 149 term infants born in Italy; and 149 term infants born in the United States (1, 2).

Results: For each sex and measure (e.g., fat mass), the new charts comprised 2 panels. The first showed centiles according to gestational age, allowing term infants to be assessed at birth and preterm infants to be monitored until they reached term. The second showed centiles according to postnatal age, allowing all infants to be monitored to age 27 wk. The LMS values underlying the charts were presented, enabling researchers and clinicians to convert measurements to centiles and z-scores.

Conclusions: The new charts provide a single tool for the assessment of body composition, according to ADP, in infants across the first 6 mo of life and will help enhance early-life nutritional management.

Keywords: infant, body composition, air-displacement plethysmography, reference charts, centiles

Introduction

Assessment of infant growth is a core component of nutritional management programs worldwide, and is typically based on measurements of weight and height. Such measures are, however, only crude indicators of nutritional status; body composition assessment allows a more detailed investigation of an infant’s current health and the effects of clinical conditions and treatments (1, 2).

Air-displacement plethysmography (ADP) is a viable candidate for monitoring the nutritional status of infants, and the development of the “PEA POD” (3) has made it possible to measure body composition quickly, accurately, and reliably in current health and the effects of clinical conditions and treatments (1, 2).

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Supplemental Figures 1–8 and Supplemental Tables 1–10 are available from the “Supplementary data” link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/ajcn/.

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Abbreviations used: ADP, air-displacement plethysmography; AGA, appropriate for gestational age; DXA, dual-energy X-ray absorptiometry; EDF, Equivalent degrees of freedom; LMS, lambda-mu-sigma; PBF, percentage body fat.

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infants as young as 0–6 mo (4–6), including in preterm infants (7). ADP is superior to other body composition assessment methods, e.g., bioelectrical impedance analysis and dual-energy X-ray absorptiometry (DXA), which either have limited accuracy (bioelectrical impedance analysis) (8) or are reliant on exposing the infant to small doses of radiation (DXA), which, without pediatric programming, could be up to 3 times higher than for adults (9). These characteristics, along with its simplicity [ADP does not require a still infant and takes <5 min (10)], have resulted in an accumulation of ADP-derived body composition data in early infancy.

With the objective of assessing the normality or otherwise of these ADP data, a number of ADP references have been developed for use at birth and early infancy (11–16). However, the existing ADP references are piecemeal, characterized by their differences in coverage, methodology, and sample sizes (constraining the ability to conduct more complex analyses), which limits their practical utility. However, pooling the data used in the construction of the existing body composition references would provide sufficient data to produce a more comprehensive set of sex-specific centiles that cover a wider range of gestational and postnatal ages. The aim of our study therefore was to produce a set of gestational age and postnatal age references for fat mass, fat-free mass, and percentage body fat (PBF) for use at birth and in the first 6 mo of life using pooled data across studies in high-income countries. There are few reference data based on infants from low and middle-income countries. However, a set of sex-specific centiles that cover a wider range of gestational and postnatal ages. The aim of our study therefore was to produce a set of gestational age and postnatal age references for fat mass, fat-free mass, and percentage body fat (PBF) for use at birth and in the first 6 mo of life using pooled data across studies in high-income countries.

In order to make the 4 samples more comparable, without imposing strict inclusion criteria for the present study and thereby drastically reducing the sample sizes, we restricted analyses to infants whose birth weights were between the 3rd and 97th percentiles according to the INTERGROWTH-21st standard (23). The charts, therefore, depict body composition based on a total of 1457 infants (Demerath et al $n = 222$; Fields et al $n = 149$; Roggero et al $n = 57$; Hawkes et al $n = 1029$) whose birth weights did not indicate suboptimal fetal growth (Supplemental Figure 1).

For each of the included cohorts, ethical approval was obtained from each of the relevant committees prior to the commencement of the respective studies. For more details, refer to the individual studies (11, 12, 14, 15).

**Data**

In each study, infant sex, birth weight, and gestational age at birth (assessed via ultrasound or date of last menstrual period) were recorded. Fat mass, fat-free mass, and percentage body fat were assessed using ADP (PEA POD infant body composition system, COSMED) using standard procedures (11, 12, 14, 15). Measurements were taken at birth in all studies, and for the present study were restricted to those occurring within 72 h of delivery. Further, the Fields et al. and Roggero et al. studies included postnatal measurements at 1 and 2 wk of age, and at 1, 2, 3, 4, 5, and 6 mo of age; and the Hawkes et al. study included a postnatal assessment at age 2 mo.

The primary outcomes were fat mass, fat-free mass, and percentage body fat charts according to gestational age. Accordingly, we used cross-sectional birth data from all 4 studies ($n = 623$ males; $n = 616$ females). For the postnatal age charts, we used longitudinal data from the Roggero et al. and Fields et al. studies ($n = 95$ males with 542 observations; $n = 105$ females with 592 observations), resulting in a total of 1134 observations (median per person = 7; range = 1–8). No birth data were included in these charts as our objective was to create separate charts for the gestational and postnatal periods, with an intervening period of 1 wk. This is in line with published guidelines (24), and its purpose is to avoid the misinterpretation of measurements taken in the first few days of life as a result of the weight loss commonly observed in this period (25, 26). Postnatal data from the Hawkes et al. study were not included as, unlike the longitudinal studies of Fields et al. and Roggero et al. they are only collected at
a single time point. Finally, for the postconceptional age charts (secondary outcome, representing gestational age at birth plus postnatal age at measurement), we pooled all birth and postnatal data from all 4 studies (n = 733 males; n = 720 females), resulting in a total of 3104 observations (median per person = 2; range = 1–8) (Supplemental Figure 1).

**Statistical analysis**

**Descriptive statistics.**

Descriptive statistics for sex, gestational age at birth, and birth weight were produced according to each study. Birth weight-for-gestational age \( z \)-scores were computed according to the INTERGROWTH-21\(^{st} \) charts in order to ascertain how the samples in the present paper compare against an international standard. Low birth weight was defined as \(<2.5 \text{ kg.} \)

**Centile estimation.**

For each chart, the lambda-mu-sigma (LMS) method (27) was used to estimate centiles. 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 coefficient of variation. These curves are fitted as restricted cubic splines, with the number of equivalent degrees of freedom (EDF) determining the complexity of the curve. In line with recommendations, models were built by choosing the EDF for M, then S, then L, with the aim of making the EDF for M > the EDF for S > the EDF for L. Determining the EDF (and thus complexity) of the L, M, and S curves was guided by improvements in the Bayesian information criterion. Adjusting the M curves for study, to capture all known and unknown differences between the 4 samples, did not improve the model fit, thus all models do not include this adjustment. For the postconceptional charts, the outcomes were transformed (\( \ln(\text{outcome}) + 10 \)) to aid convergence. Standard model diagnostics (e.g., detrended \( q-q \) plots of residuals ("worm plots") (28) for assessing the normality of residuals over specific age periods were used to assess the fit of the final models (29). Differences between the expected and observed percentage of participants with values below given centiles were also investigated.

Daily LMS values were obtained (provided in Supplemental Tables 1–6) and used to construct sex-specific charts depicting the 3rd, 10th, 25th, 50th, 75th, 90th, and 97th centiles. For both sexes, the gestational age charts span 30 + 1 to 41 + 6 wk and the postnatal charts span 1–27 wk. Each of the 3 outcomes (fat mass, fat-free mass, and percentage body fat) are presented in a separate figure with 4 panels, with 1) gestational age panels on the left and postnatal age panels on the right and 2) male panels on the top and female panels on the bottom. Postconceptional age charts (spanning 30 + 3 to 67 + 3 wk) for each outcome were also developed, again with male panels on the top and female panels on the bottom.

**Comparison to INTERGROWTH 21\(^{st} \) standards.**

To determine the degree to which these charts represent more optimal growth, we compared the proposed charts to the recently published INTERGROWTH-21\(^{st} \) body composition standards (13). Specifically, we calculated the absolute (grams) and percentage [(INTERGROWTH-21\(^{st} \) centile value – proposed centile value)/proposed centile value] \( \times 100 \) differences between the fat mass and fat-free mass values at the 10th, 50th, and 90th centiles of our charts and those of the INTERGROWTH-21\(^{st} \) Project. This was done at 38, 39, 40 and 41 completed weeks of gestation, as this was the period of overlap between the 2 charts.

Centile estimation was performed using the GAMLSS (Generalized Additive Models for Location Scale and Shape) package in R v.3.2.3. The production of the final plots and the subsequent comparison to INTERGROWTH-21\(^{st} \) were done in StataSE version 15.

**Results**

**Sample description**

Sample descriptive statistics are reported in **Table 1**. The mean birth weight was \( \sim 1 \text{ kg} \) lower in the Demerath et al. study than in the other studies, reflecting the preterm status of the Demerath et al. sample. When standardized against the INTERGROWTH-21\(^{st} \) standards, however, the mean birth weight-for-gestational age \( z \)-scores in each of the 4 studies were within approximately half a centile band from the 50th centile (i.e., between \(-0.38 \) and \(+0.38 \) \( z \) scores).

**Gestational age and postnatal age charts**

**Figures 1–3** show the charts for fat mass, fat-free mass, and percentage body fat. Underlying model fits were deemed to be good according to the detrended \( q-q \) plots (Supplemental Figures 2–4) and the differences between the expected and observed percentage of participants below given centiles (Supplemental Table 7). Each chart includes 2 panels for each sex. The first (left) panel shows centiles according to gestational age, which allow term infants to be assessed at birth and preterm infants to be monitored until they reach term. The second (right) panel shows centiles according to postnatal age, which allow all infants to be monitored to age 27 wk.

Fat-free mass exhibited a more linear relationship with gestational age than did fat mass and percentage body fat. In the postnatal age charts, fat mass gain slowed after \( \sim 12 \) wk of age, which resulted in a flattening of the PBF curves after this point.

**Comparison to INTERGROWTH 21\(^{st} \) standards.**

For fat-free mass, values at the 10th, 50th and 90th centiles in both males and females were within 4% of those estimated by the INTERGROWTH-21\(^{st} \) Project. For example, differences in grams at the 50th centile between 38 and 41 wk ranged from 64 to 85 g in males and from 46 to 72 g in females (Supplemental Table 8). For fat mass, although the differences in grams between the respective centile values were smaller than those observed for fat-free mass (e.g., maximum difference \( 48 \) g), they represent larger proportional differences, as the size of the fat mass compartment is smaller than that of the fat-free mass (i.e., the denominator is smaller) (Supplemental Table 9).
TABLE 1 Description of study samples

<table>
<thead>
<tr>
<th></th>
<th>Demerath et al. (12)</th>
<th>Fields et al. (15)</th>
<th>Rogerro et al. (14)</th>
<th>Hawkes et al. (11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 222</td>
<td>n = 149</td>
<td>n = 57</td>
<td>n = 1029</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>114 (51)</td>
<td>76 (51)</td>
<td>23 (40)</td>
<td>522 (51)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>108 (49)</td>
<td>73 (49)</td>
<td>34 (60)</td>
<td>507 (49)</td>
</tr>
<tr>
<td>Gestational age, mean ± SD</td>
<td>33.8 ± 1.9</td>
<td>39.4 ± 1.1</td>
<td>39.2 ± 1.3</td>
<td>40.0 ± 1.3</td>
</tr>
<tr>
<td>30 + 0, 32 + 6, n (%)</td>
<td>77 (35)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>33 + 0, 37 + 6, n (%)</td>
<td>145 (65)</td>
<td>8 (5)</td>
<td>6 (11)</td>
<td>66 (6)</td>
</tr>
<tr>
<td>38 + 0, 41 + 6, n (%)</td>
<td>0 (0)</td>
<td>141 (95)</td>
<td>51 (89)</td>
<td>963 (94)</td>
</tr>
<tr>
<td>Birth weight, mean ± SD</td>
<td>2.2 ± 0.5</td>
<td>3.4 ± 0.3</td>
<td>3.1 ± 0.4</td>
<td>3.4 ± 0.4</td>
</tr>
<tr>
<td>Birth weight-for-gestational age</td>
<td>0.1 ± 0.7</td>
<td>0.4 ± 0.8</td>
<td>-0.1 ± 0.8</td>
<td>0.3 ± 0.8</td>
</tr>
<tr>
<td>z score(^1), mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low birth weight (&lt;2500 g), n (%)</td>
<td>168 (76)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>9 (0.9)</td>
</tr>
</tbody>
</table>

\(^{1}\)z scores according to INTERGROWTH 21st birth size for gestational age standards (23).

Postconceptional age charts

Charts according to postconceptional age are shown in Supplemental Figures 5–7. Model diagnostics are shown in Supplemental Figure 8, and the differences between the expected and observed percentage of participants below given centiles are provided in Supplemental Table 10.

The changes in median fat mass by postconceptional age were gradual before 40 wk, increasing thereafter. For fat-free mass, a linear pattern was observed until ∼50 wk, with slower changes in median fat-free mass after this. PBF showed a more curvilinear pattern with postconceptional age, such that gradual increases were observed before 40 wk, which then increased to ∼55 wk in males and 60 wk in females, and reached a plateau thereafter.

FIGURE 1 Fat mass centile curves according to gestational age at birth (30 + 1 to 41 + 6 wk; males: n = 623, females: n = 616) and postnatal age at measurement (1–27 wk; males: n = 95, females: n = 105).
FIGURE 2  Fat-free mass centile curves according to gestational age at birth (30 + 1 to 41 + 6 wk; males: \( n = 623 \), females: \( n = 616 \)) and postnatal age at measurement (1–27 wk; males: \( n = 95 \), females: \( n = 105 \)).

LMS values for \( z \) score calculation

Daily LMS values for each of the charts are presented in Supplementary Tables 1–6. With these values, sex- and age-adjusted \( z \) scores (and therefore centiles) can be calculated using the following formula:

\[
z = \left( \frac{x}{\mu} \right)^{\lambda} - 1 \tag{I}
\]

where \( x \) is the body composition measurement.

These LMS values therefore allow researchers and clinicians to assess infant body composition according to the new charts presented in this paper.

Discussion

With developments in technology, infant body composition assessment is becoming a more common component of pediatric growth monitoring both clinically and in research programs. ADP is a good candidate for such assessment because it provides an accurate, quick, and safe assessment of body composition. In order to assess the normality or otherwise of an infant’s body composition, one needs to compare his or her measurements (e.g., fat mass, fat-free mass, and percentage fat) against a comparative or reference population. In the present paper, we have pooled data from 4 studies in order to create a comprehensive set of body composition charts, based on >1000 infants, for use at birth and in the first 6 mo of life. The gestational age component of the charts, which range from 30 + 1 to 41 + 6 wk, allow term infants to be assessed at birth and preterm infants to be monitored until they reach term. Subsequently, the postnatal age component of the charts allows all infants to be monitored throughout the first 6 mo of life. We have also produced a set of postconceptional charts, spanning 30 + 3 to 67 + 3 postconceptional weeks, which enable the monitoring of body composition in preterm infants and are similar to those used in the United States for preterm weight and length monitoring (18). The LMS values underlying all 3 sets of charts are presented, enabling researchers and clinicians to convert measurements to \( z \) scores and thus centiles.

Our charts are based on data from 4 studies, which led to a large sample size compared with previous charts (13, 30, 31). Although the included studies had distinct inclusion and exclusion criteria, each study attempted to select a sample...
representative of a healthy population. For example, the sample of preterm infants (12) used in the gestational age references were medically stable, singleton AGA births, and measured within 72 h of birth in order to minimize any postnatal growth restriction that normally follows preterm birth. These inclusion criteria sought to reflect the recommendations of the American Academy of Pediatrics, which state that preterm infants should grow similarly to healthy in utero infants (32). Similarly, the 2 studies which provided data predominantly for the postnatal references (14, 15) both employed inclusion criteria similar to those of the WHO Multicentre Growth Reference Study [e.g., singleton birth, full-term infants (gestational age 37–<42 wk) with a birth weight >2.5 kg, born to nonsmoking mothers, who were then exclusively breastfed). Accordingly, we omitted the data from the Hawkes et al. study for the construction of the postnatal charts as exclusive breastfeeding was not part of the inclusion criteria of that study. As such, although we are unable to label our charts as standards, we believe that the combination of the detailed inclusion criteria across studies, the removal of infants with birth weights in the extremes of the distribution (<3rd and >97th centiles), and the observed similarities between birth weight and the proposed centile values with those of the INTERGROWTH-21st standards means that these proposed charts likely represent a more optimal pattern of growth than that described by a reference. For example, the mean birth weight z scores in our sample were within 0.38 of those of INTERGROWTH-21st, representing approximately half of a centile band on a standard growth chart. Furthermore, comparison of our centile values to the INTERGROWTH-21st standards revealed remarkable similarities for fat-free mass, with the 10th, 50th, and 90th centile values differing by ≤4% between our charts and their charts, although the differences were greater for fat mass.

In terms of strengths, a major advantage of the proposed charts is the large sample size used to construct them (n > 1000). This has not only enabled us to increase the periods of measurement, but has also afforded us greater power to model the more complex pattern of body composition change over time. In comparison, the INTERGROWTH-21st standards were based on 247 infants, and such a small sample size may have reduced the ability to model nonlinear relationships, particularly at the extremes of the gestational age and body composition distributions. This may be evidenced by their monotonically increasing straight
line “curves”, which do not match with the more complex fat mass centiles presented in the current paper. This may therefore have contributed to the observed differences between the values obtained in our charts and those of the INTERGROWTH-21st standards. Another key strength of these newly created charts is that, by providing the daily LMS values and statistical code, any ADP-derived estimate of fat mass, fat-free mass, or body fat percentage, obtained either at birth (between 30 + 1 and 41 + 6 wk) or postnatally (in the first 6 mo of life), can be easily converted to a $z$ score or percentile, therefore providing an evaluation of their body composition relative to a large sample of AGA infants. This information not only enables an evaluation of the body composition of the infant during the crucial early months of life, but can also be used by researchers interested in identifying the extent to which deviations from normal body composition in early life are associated with adverse distal outcomes. Finally, as our charts span the gestational and postnatal periods, researchers will benefit from comparing their data with the same sample across the whole period, instead of having to use 2 separate references (constructed using separate sample), which alters the interpretation of comparisons. The increasing use of ADP for infant body composition assessment, owing to its ease of use, safety, and ability to provide valid and reliable estimates (3–5, 7, 8, 33), means that these charts will serve as a highly relevant and popular resource in both clinical and research settings.

In terms of limitations, we would ideally have split our sample into 2 for the internal validation of the centiles, with 1 half representing the construction sample and the other half representing the validation sample. However, even with our large sample size, this was not possible. Future work will seek to validate these centiles in a number of populations and across different body composition methodologies. Another limitation is that, as we did not link the charts to any clinical outcomes, we are unable to recommend cutoffs representing increased risk. Further work should also investigate the clinical utility of the charts and the degree to which they represent a more optimal pattern of growth [i.e., the extent to which $z$ scores/cutoffs representing suboptimal body composition (e.g., <10th centile or >90th centile) based on these values are associated with adverse neurodevelopmental and metabolic outcomes in the future]. As all of the studies in the present paper were based in high-income countries, our charts may not accurately reflect body composition in low or middle-income settings.

Although we believe the inclusion criteria of the studies likely reduced the differences in body composition between settings, future work is required to validate these charts in different populations, as ethnic differences in infant fat and fat-free mass have been observed (16, 34). Finally, these charts are based on cross-sectional data, or have been analyzed as if they were cross-sectional. Although it is common to use cross-sectional charts such as these to analyze individual growth (i.e., change in $z$ scores over time), with the assumption being that upward or downward centile crossing is indicative of growth above or below the average, a more appropriate (but less practical) assessment of an individual’s change in body composition would be based on charts developed using a longitudinal sample measured at predefined measurement occasions.

In conclusion, we have developed a set of ADP body composition charts according to gestational, postnatal, and postconceptional age. These new charts provide a single tool for the assessment of body composition in infants at birth and across the first 6 mo of life, and will help enhance early-life growth monitoring and nutritional management.

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References