Fetal programming of body composition: relation between birth weight and body composition measured with dual-energy X-ray absorptiometry and anthropometric methods in older Englishmen

Osama A Kensara, Steve A Wootton, David I Phillips, Mayke Patel, Alan A Jackson, Marinos Elia, and the Hertfordshire Study Group

ABSTRACT
Background: Reduced fetal growth is associated with differences in body composition in adult life that may predispose to cardiovascular disease and diabetes. Most published data are based on simple anthropometric measures, which incompletely describe body composition.

Objective: The objective was to assess body composition and fat distribution by using dual-energy X-ray absorptiometry (DXA).

Design: This was a case-control study of 64–72-y-old white men (n = 32) with a low (x: 2.76 kg) or high (x: 4.23 kg) birth weight.

Results: Compared with the high-birth-weight group, after adjustment for weight and height, the low-birth-weight group had a higher percentage body fat (29.31% compared with 25.33%; P = 0.029) and fat mass (P = 0.039) but a lower fat-free soft tissue (56.32 compared with 59.22 kg; P = 0.024), muscle mass (27.25 compared with 29.22 kg; P = 0.022), and muscle-to-fat ratio. Low birth weight was also associated with a higher trunk-to-limb fat ratio after control for total fat mass (1.42 compared with 1.16; P = 0.005) or percentage body fat (P = 0.041). The same body mass index predicted a greater percentage body fat (P = 0.019) in the low- than in the high-birthweight group, and the same ratio of trunk-to-limb skinfold thickness (or waist-to-hip ratio) predicted a higher trunk-to-limb fat ratio (P < 0.01).

Conclusion: Lifelong differences in adult body composition and fat distribution between the low- and high-birth-weight groups are consistent with programming in early life. The use of BMI to predict percentage body fat and the use of the trunk-to-limb skinfold thickness ratio (and waist-to-hip ratio) to predict the trunk-to-limb fat ratio measured by DXA can be misleading when low- and high-birth-weight groups are compared.


KEY WORDS Body composition, birth weight, fat, lean mass, muscle programming, body mass index, dual-energy X-ray absorptiometry, waist-to-hip ratio, fat distribution, skinfold thickness

INTRODUCTION
Low birth weight is associated with increased morbidity and mortality in later life from cardiovascular disease, type 2 diabetes, and the metabolic syndrome (1). Because body fat and percentage body fat have been causally linked to the development of insulin resistance and cardiovascular disease, several studies have evaluated the extent to which birth weight is associated with adiposity and body composition in adult life. However, few reference body-composition techniques (hydrodensitometry and scanning techniques) have been used for this purpose (2–5), and the sample sizes have sometimes been small (5). In most studies, simple surrogate measures of body composition have been used, such as skinfold thicknesses and BMI (in kg/m²), which depend on both adipose and lean tissue mass. Although some reports indicate no relation between birth weight and adult BMI (3, 4, 6, 7), many others indicate a positive relation between the 2 (2, 7–12). A recent review concluded that, despite the lack of information on potential confounding factors, the positive association seemed robust (13). However, these observations present a conundrum, because a high BMI is generally associated with increased risk of cardiovascular disease, but a high BMI in subjects with a high birth weight has been shown to be associated with reduced risk (11, 14). One explanation for this conundrum is that the reduced risk in adults with a high birth weight is mediated by factors that can override any adverse effects of gross body composition, such as excess adiposity. A second, and very different, explanation is that—compared with individuals with a low birth weight—persons with a high birth weight have relatively less body fat (and a lower ratio of fat to lean tissue, which includes insulin-sensitive muscular tissue), even after adjustment for BMI or weight plus height. If this were true, it would seriously question the value of BMI for comparing body composition in this situation. At the same time it would shed fresh light on the link between birth weight and outcomes in later life, allowing a re-examination of previous studies that may have used BMI inappropriately. Such a situation is analogous to ethnic differences in body composition. In comparison with whites (adults and children), Asians have been found to have 2–6% more percentage body fat after adjustment for BMI (15–18), and neonates have been found to have a greater subscapular skinfold thickness after adjustment for the ponderal index (19).

1 From the Institute of Human Nutrition, University of Southampton, Southampton General Hospital, Southampton, United Kingdom (OAK, SAW, AAJ, and ME), and the MRC Epidemiology Resource Centre, University of Southampton, Southampton, United Kingdom (DIP and MP).
2 Supported in part by NIH grant RO1 HD 41107-01 (to DIP), by core funds from the Institute of Human Nutrition and Epidemiology Resource Centre, and a grant from Umm Al Qura University, Saudi Arabia, which supported OAK during his studies at the University of Southampton.
3 Address reprint requests to M Elia, Institute of Human Nutrition, University of Southampton, Southampton General Hospital, Tremona Road, Southampton SO16 6YD, United Kingdom. E-mail: elia@soton.ac.uk.
Received March 23, 2005.
Accepted for publication July 8, 2005.
Birth weight is related to percentage fat, which in turn is related to subcutaneous fat (over entire body segments). Furthermore, if abdominal adiposity (8) have frequently been used for this purpose, but the results have been used to address this issue. In contrast, the waist-to-hip ratio (20) is influenced by skeletal shape and muscular development, and, in some individuals, by intestinal gas and fecal mass. In addition, in subjects with a low BMI, it has been suggested that waist circumference reflects the variation in abdominal lean tissue as much as it reflects variation in abdominal adiposity (8). Skinfold thicknesses reflect only subcutaneous fat at the measurement sites, rather than total fat (internal and subcutaneous fat) over entire body segments. Furthermore, if birth weight is related to percentage fat, which in turn is related to fat distribution, then the use of simple unadjusted (or incorrectly adjusted) anthropometric indexes of fat distribution may produce biased results and potentially incorrect conclusions.

The aims of this study were 2-fold: 1) to test the hypothesis that anthropometric markers of health risk, such as BMI, skinfold thicknesses, and waist-to-hip ratio can be misleading in comparisons of body composition and fat distribution between low- and high-birth-weight groups.

**TABLE 1**
Characteristics of the 32 older men with low or high birth weight (BW)

|                      | All subjects (n = 32) | Low BW (n = 16) | High BW (n = 16) | P*
|----------------------|-----------------------|-----------------|-----------------|------
| Age (y)              | 67.7 ± 0.47           | 67.56 ± 0.60    | 68.00 ± 0.74    | 0.651
| Weight (kg)          | 83.61 ± 1.91          | 79.44 ± 2.15    | 87.78 ± 2.84    | 0.026
| Height (m)           | 1.74 ± 0.013          | 1.70 ± 0.017    | 1.78 ± 0.016    | 0.003
| BMI (kg/m²)          | 27.50 ± 0.54          | 27.14 ± 0.49    | 27.87 ± 0.96    | 0.506
| Fat-free mass (kg)   | 60.33 ± 1.23          | 56.55 ± 1.57    | 64.51 ± 1.32    | 0.001
| Bone mineral content (kg) | 2.76 ± 0.09       | 2.64 ± 0.16     | 2.88 ± 0.08     | 0.181
| Fat-free soft tissue (kg) | 57.77 ± 1.28       | 53.92 ± 1.44    | 61.62 ± 1.29    | < 0.001
| Limb fat-free mass (kg) | 26.48 ± 0.62         | 24.58 ± 0.84    | 28.38 ± 0.62    | < 0.001
| Limb fat-free soft tissue (kg) | 24.89 ± 0.58        | 23.07 ± 0.77    | 26.72 ± 0.60    | < 0.001
| Muscle mass (kg)     | 28.23 ± 0.63          | 26.06 ± 0.88    | 30.41 ± 0.69    | 0.001
| Fat mass in whole body (kg) | 23.10 ± 1.09         | 22.88 ± 1.06    | 23.27 ± 1.94    | 0.861
| Fat mass (% of body weight) | 27.32 ± 0.95        | 28.71 ± 1.03    | 25.93 ± 1.55    | 0.147
| Fat mass in trunk (kg) | 12.50 ± 0.63          | 12.73 ± 0.69    | 12.27 ± 1.07    | 0.724
| Fat mass in limbs (kg) | 9.75 ± 0.40           | 9.14 ± 0.45     | 10.35 ± 0.64    | 0.132
| Fat mass in nonlimbs (kg) | 13.54 ± 0.64         | 13.74 ± 0.70    | 13.34 ± 1.10    | 0.757
| Fat mass in abdomen (kg) | 2.73 ± 0.14           | 2.67 ± 0.16     | 2.80 ± 0.23     | 0.651
| Nonlimb:limb fat mass | 1.40 ± 0.05           | 1.52 ± 0.06     | 1.28 ± 0.06     | 0.010
| Trunk:limb fat mass  | 1.29 ± 0.05           | 1.41 ± 0.06     | 1.17 ± 0.07     | 0.011
| Abdomen:limb fat mass | 0.28 ± 0.01           | 0.29 ± 0.01     | 0.26 ± 0.01     | 0.158
| Muscle:fat ratio     | 1.35 ± 0.11           | 1.19 ± 0.07     | 1.50 ± 0.17     | 0.124
| Skinfold thickness   |                      |                 |                 |      
| SS                   | 17.74 ± 0.91          | 18.28 ± 1.10    | 17.21 ± 1.48    | 0.567
| SI                   | 18.19 ± 0.77          | 18.21 ± 1.06    | 18.17 ± 1.15    | 0.980
| B                    | 6.53 ± 0.44           | 6.46 ± 0.41     | 6.61 ± 0.79     | 0.868
| T                    | 11.49 ± 0.61          | 12.11 ± 0.71    | 10.88 ± 0.99    | 0.323
| Waist circumference (cm) | 102.6 ± 1.70         | 101.5 ± 1.44    | 103.6 ± 3.11    | 0.509
| Hip circumference (cm) | 108.1 ± 0.83          | 106.7 ± 0.75    | 109.4 ± 1.43    | 0.099
| Skinfold thickness   |                      |                 |                 |      
| SS + SI + B + T      | 1.96 ± 0.06           | 2.00 ± 0.08     | 2.08 ± 0.13     | 0.596
| SS/B                 | 2.75 ± 0.13           | 2.88 ± 0.12     | 2.89 ± 0.25     | 0.973
| SS/T                 | 1.63 ± 0.12           | 1.59 ± 0.56     | 1.71 ± 0.71     | 0.613
| SI/B                 | 2.86 ± 0.19           | 2.91 ± 0.19     | 3.23 ± 0.37     | 0.461
| SI/T                 | 1.64 ± 0.11           | 1.54 ± 0.08     | 1.86 ± 0.20     | 0.153
| Waist-to-hip circumference ratio | 0.95 ± 0.01 | 0.95 ± 0.01 | 0.95 ± 0.02 | 0.897

1 All values are x ± SE. The body-composition results were obtained with the use of dual-energy X-ray absorptiometry. SS, subscapular; SI, suprailiac; B, biceps; T, triceps.
2 Reflects differences between the low- and high-birth-weight groups (ANOVA).

Fat distribution also predicts risk of cardiovascular disease and type 2 diabetes, independently of fat mass (FM) and percentage body fat. It is possible that early life programming of body composition affects fat distribution between body segments, but reference scanning body-composition techniques do not appear to have been used to address this issue. In contrast, the waist-to-hip circumference ratio or ratio of trunk to limb skinfold thickness (7) have frequently been used for this purpose, but the results have been variable, at least partly because of the limitations associated with the use of these techniques. For example, the waist-to-hip ratio (20) is influenced by skeletal shape and muscular development, and, in some individuals, by intestinal gas and fecal mass. In addition, in subjects with a low BMI, it has been suggested that waist circumference reflects the variation in abdominal lean tissue as much as it reflects variation in abdominal adiposity (8). Skinfold thicknesses reflect only subcutaneous fat at the measurement sites, rather than total fat (internal and subcutaneous fat) over entire body segments. Furthermore, if birth weight is related to percentage fat, which in turn is related to fat distribution, then the use of simple unadjusted (or incorrectly adjusted) anthropometric indexes of fat distribution may produce biased results and potentially incorrect conclusions.

The aims of this study were 2-fold: 1) to assess whether birth weight is related to the mass and proportion of tissues (lean fat, muscle fat), percentage body fat, and its distribution across body segments in older adults, as measured by dual-energy X-ray absorptiometry (DXA), and 2) to test the hypothesis that anthropometric markers of health risk, such as BMI, skinfold thicknesses, and waist-to-hip ratio can be misleading in comparisons of body composition and fat distribution between low- and high-birth-weight groups.

**SUBJECTS AND METHODS**

**Subjects**

Thirty-two healthy adult white men aged 64–72 y were recruited and invited to the Wellcome Trust Clinical Research Facility, Southampton General Hospital (Table 1), to undergo...
assessments of anthropometric and body-composition characteristics. All subjects were born in Hertfordshire, where detailed birth records were routinely kept. The subjects were chosen randomly from among those below the 25th centile of birth weight [<3.18 kg (7 lb); n = 16] or above the 75th centile [3.86 kg (8.5 lb); n = 16] of birth weight. Only 55% of those who were contacted by letter (after permission was granted by their general practitioners) agreed to have a home visit and participate in the body-composition studies. Written informed consent was obtained from each subject, and ethical approval for the study was obtained from local research committees. This study was part of a larger study that included other measurements of energy metabolism and fuel selection (data not reported in this article), which for practical reasons limited the sample size. All the required measurements were obtained from each subject participating in the study. Weight was measured to the nearest 0.1 kg with a Seca 708 electronic weighing scale, and height was measured to the nearest 0.1 cm with a Seca electronic stadiometer (Seca Ltd, Medical Scales and Measurement Systems, Birmingham, United Kingdom). Information on socioeconomic status (both currently and at the time of birth), smoking status, alcohol consumption, and physical activity (Table 2) was obtained by using questionnaires that were administered to the subjects on the study day. The study was conducted according to the South-West Hampshire Local Ethics Committee.

**Methods**

Body composition was measured by using DXA Hologic Delphi (Vertec Scientific Ltd, Reading, United Kingdom), which

---

**Table 2**

Socioeconomic status and physical activity in 32 older men with either low or high birth weight (BW)

<table>
<thead>
<tr>
<th></th>
<th>All subjects (n = 32)</th>
<th>Low BW (n = 16)</th>
<th>High BW (n = 16)</th>
<th>p²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Smoking status</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>40.65</td>
<td>50.00</td>
<td>31.30</td>
<td>0.543</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>53.15</td>
<td>43.80</td>
<td>62.50</td>
<td></td>
</tr>
<tr>
<td>Current smoker</td>
<td>6.25</td>
<td>6.30</td>
<td>6.30</td>
<td></td>
</tr>
<tr>
<td><strong>Alcohol intake</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (&lt;10 units/wk)</td>
<td>50.00</td>
<td>56.25</td>
<td>43.75</td>
<td>0.723</td>
</tr>
<tr>
<td>Moderate (11–21 units/wk)</td>
<td>18.75</td>
<td>8.75</td>
<td>18.75</td>
<td></td>
</tr>
<tr>
<td>High (&gt;21 units/wk)</td>
<td>31.25</td>
<td>25.00</td>
<td>37.50</td>
<td></td>
</tr>
<tr>
<td><strong>Current social class</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-IIINM²</td>
<td>46.65</td>
<td>40.00</td>
<td>53.30</td>
<td>0.464</td>
</tr>
<tr>
<td>IIIM-V</td>
<td>53.35</td>
<td>60.00</td>
<td>46.70</td>
<td></td>
</tr>
<tr>
<td><strong>Father’s social class</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-IIINM</td>
<td>25.63</td>
<td>20.00</td>
<td>31.25</td>
<td>0.924</td>
</tr>
<tr>
<td>IIIM-V</td>
<td>74.37</td>
<td>80.00</td>
<td>68.75</td>
<td></td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Degree of walking problem</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No limiting abnormality</td>
<td>93.75</td>
<td>93.75</td>
<td>93.75</td>
<td>1.000</td>
</tr>
<tr>
<td>Abnormal gait or walking problem</td>
<td>6.25</td>
<td>6.25</td>
<td>6.25</td>
<td></td>
</tr>
<tr>
<td>Walking outdoors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤15 min</td>
<td>43.75</td>
<td>56.25</td>
<td>31.25</td>
<td>0.183</td>
</tr>
<tr>
<td>1–4 h</td>
<td>50.00</td>
<td>43.75</td>
<td>56.25</td>
<td></td>
</tr>
<tr>
<td>&gt;4 h</td>
<td>6.25</td>
<td>0.00</td>
<td>12.50</td>
<td></td>
</tr>
<tr>
<td>Walking speed</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slow</td>
<td>25.00</td>
<td>31.25</td>
<td>18.75</td>
<td>0.675</td>
</tr>
<tr>
<td>Normal</td>
<td>43.75</td>
<td>37.50</td>
<td>50.00</td>
<td></td>
</tr>
<tr>
<td>Fairly brisk or fast</td>
<td>31.25</td>
<td>31.25</td>
<td>31.25</td>
<td></td>
</tr>
<tr>
<td>Housework</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;4 h/week</td>
<td>81.25</td>
<td>81.25</td>
<td>81.25</td>
<td>0.549</td>
</tr>
<tr>
<td>5–8 h/week</td>
<td>15.63</td>
<td>12.50</td>
<td>18.75</td>
<td></td>
</tr>
<tr>
<td>&gt;8 h/week</td>
<td>3.12</td>
<td>6.25</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Stair climbing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occasionally</td>
<td>15.63</td>
<td>18.75</td>
<td>12.50</td>
<td>0.524</td>
</tr>
<tr>
<td>Once or several times per week</td>
<td>3.13</td>
<td>0.00</td>
<td>6.25</td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>3.13</td>
<td>6.25</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Several times per day</td>
<td>78.13</td>
<td>75.00</td>
<td>81.25</td>
<td></td>
</tr>
<tr>
<td>Carry load</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occasionally</td>
<td>15.63</td>
<td>8.75</td>
<td>12.50</td>
<td>0.173</td>
</tr>
<tr>
<td>Once or several times per week</td>
<td>31.25</td>
<td>31.25</td>
<td>31.25</td>
<td></td>
</tr>
<tr>
<td>Daily</td>
<td>28.13</td>
<td>2.50</td>
<td>43.75</td>
<td></td>
</tr>
<tr>
<td>Several times per day</td>
<td>25.00</td>
<td>37.50</td>
<td>12.50</td>
<td></td>
</tr>
</tbody>
</table>

¹ Chi-square test.  
² Professional, managerial, and skilled-nonmanual.  
³ Skilled-manual, partly skilled, and unskilled.
processed data using software version 12.2 to obtain information on fat-free soft tissue (FFST) mass, bone mineral content (BMC), and the percentage of these components in the whole body and in specific body segments. It was also assessed by using the BOD POD S/T air-displacement plethysmography unit (Life Measurement Inc, Cranlea & Co, Birmingham, United Kingdom).

Whole body weight (in kg), obtained from the sum of the weights of body segments reported by DXA, was highly correlated \((r = 0.997)\) with measured weight. Waist and hip circumferences were measured according to standard procedures \((21)\). Skinfold thicknesses (biceps, triceps, subscapular, and suprailiac) were measured according to the method of Durnin and Womersley \((22)\) and were used to calculate percentage body fat. Midupper arm circumference was measured midway between the acromion and olecranon, and, together with triceps-skinfold thickness, was used to calculate arm muscle area \((23)\):

Midupper arm muscle area \(= \frac{1}{4} \pi \times \text{triceps skinfold thickness}^2 \) 

\[ (1) \]

All anthropometric measurements were made by a single observer.

Whole-body muscle mass was estimated by using the equation of Kim et al \((24)\), which was established by relating DXA measurements of appendicular (limb) FFST with whole-body measurements of muscle mass obtained by using magnetic resonance imaging in healthy adults. The equation for men is as follows:

\[
\text{Total body skeletal mass (kg)} = 1.13 \times \text{limb FFST (kg)} - 0.02 \times \text{age (y)} + 1.58 \tag{2}
\]

Fat distribution was estimated as the nonlimb-to-limb FM ratio, trunk-to-limb FM ratio, and abdominal-to-limb FM ratio. The FMs in the trunk and limbs were those reported by the DXA machine, whereas the abdominal FM had to be established. First, the region of interest was identified as the area between the superior border of the iliac crest to the inferior border of the fourth lumbar vertebra \((25)\). The region of interest was identified manually to the nearest pixel \((1.3035 \text{ cm})\) and then its composition was established by using the software program version 12.2 of Hologic Delphi. The bitrochanteric breadth was estimated with the use of a photoenlarged paper copy of the scans by using the known diameter of the scanned area as the reference distance.

The inter- and intraobserver CVs for body fat and fat-free mass (FFM) (as a percentage of body weight) for repeated measurements in the same subjects is \(\approx 1\%\) for DXA and air-displacement plethysmography \((\approx 3\%–4\%\) of actual FFM, \(\approx 1.4\%\) of actual FFST). For BMI, the CV is \(<1\%\) (interobserver and intraobserver CVs). For DXA the CVs (as a percentage of actual tissue or body component) were as follows: \(\approx 2\%–3\%\) for fat in the trunk and in the limbs, \(\approx 2.0\%\) for the trunk-to-limb fat ratio, \(\approx 0.9\%\) for bone mineral, \(\approx 1\%\) for FFST, and \(1.5\%\) of estimated skeletal muscle mass, and \(0.9\%\) for bone mineral content. The intraobserver CVs for measurements with the same scan were \(1.35\%\) for the bitrochanteric breadth (manual procedure) and \(3.5\%\) for abdominal FM. The intraobserver variation for skinfold thicknesses \((\approx 5\%–10\%)\) \((23, 26, 27)\) yield CVs for skinfold ratios of \(3\%–10\%\) \((\approx 3.5\%–7.0\%\) for the ratio of subscapular + suprailiac/biceps + triceps) when calculated with the use of propagation of errors \((28)\) and correlation coefficients between numerator and denominator obtained in our study \((r = 0.40–0.77)\). Interobserver variations were generally greater \((26, 27, 29)\). The CVs for midarm circumference and for waist-to-hip ratio were \(\leq 2\%\).

### Statistical analysis

One-way analysis of variance was used to compare the mean differences in weight, height, FFST, FM, muscle mass, and the ratios of nonlimb to limb, trunk to limb, and abdomen to limb FFST between the low- and high-birth-weight groups. Analysis of covariance was also used to explore the effect of birth weight (low- and high-birth-weight groups as fixed factors) on body composition and fat distribution, with and without adjustment for covariates such as body mass index (BMI) and weight plus height. Chi-square tests were used to assess categorical data, such as socioeconomic status. Total observed variance was taken to be the sum of biological variance, variance due to observer error, and variance due to instrument error, which was assumed to be negligible \((26)\). The statistical analyses were carried out by using the STATISTICAL PACKAGE FOR THE SOCIAL SCIENCES (version 12.0; SPSS Inc, Chicago, IL). Continuous data are expressed as means ± SEs.

### RESULTS

#### Subject characteristics

The mean birth weights of the low- and high-birth-weight groups were \(2.76 \pm 0.058\) and \(4.23 \pm 0.077\) kg \((6.08 \pm 0.13\) and \(9.30 \pm 0.17\) lb), respectively. There was no significant difference between the groups with respect to gestational age \((39 \pm 5.0\) and \(40 \pm 0.3\) wk), smoking status, alcohol consumption, socioeconomic status at birth and at the time of the study, and physical activity (Table 2). Although subjects in the low-birth-weight group were significantly shorter \((8.0\) cm) and lighter \((8.3\) kg) as adults than were the subjects in the high-birth-weight group, their BMIs were not significantly different (Table 1).

#### Body composition and fat distribution measured by DXA

Compared with the high-birth-weight group, the low-birth-weight group was found to have significantly less FFST \((\approx 8\) kg), less FFST \((\approx 7\) kg) in the whole body (Table 1) and in the limbs (limb FFST, \(\approx 3.8\) kg; limb FFST, \(\approx 3.6\) kg), and less muscle in the whole body \((\approx 4.4\) kg), but not significantly less FM. Because these differences could be due to the smaller adult size (weight and height) of the low-birth-weight group, the data were reexamined after control for weight plus height (Table 3) (weight + height\(^2\) or weight + 1/height\(^2\) gave identical or almost identical results and significance values; data not shown). However, both FFM and FFST remained significantly lower in the low-birthweight subjects than in the high-birth-weight subjects, by \(\approx 3\) kg (muscle mass by \(\approx 2\) kg), whereas FM was significantly lower by \(\approx 3\) kg, corresponding to \(\approx 4\%\) of body weight (Table 3). The effect of other potential variables, such as socioeconomic status, physical activity, and smoking status (Table 2) were also examined, by adding them as covariates (no more than one at a time) in the model, but because they were evenly matched between groups and had no significant effect, they were removed from the model for simplicity. The same applied to the other analyses reported below.

The gross body-composition differences between the low- and high-birth-weight groups obtained by DXA were confirmed with
Fat mass distribution, measured by dual-energy X-ray absorptiometry, in the low- and high-birth-weight (BW) groups

<table>
<thead>
<tr>
<th></th>
<th>Low BW</th>
<th>High BW</th>
<th>p²</th>
<th>Adjusted for weight and height</th>
<th>Low BW</th>
<th>High BW</th>
<th>p²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (m) (n = 16)</td>
<td>1.70 ± 0.016</td>
<td>1.78 ± 0.016</td>
<td>0.002</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Weight (kg) (n = 16)</td>
<td>80.41 ± 1.55</td>
<td>86.82 ± 1.55</td>
<td>0.007</td>
<td>59.12 ± 0.86</td>
<td>61.95 ± 0.86</td>
<td>0.039</td>
<td></td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>56.90 ± 1.27</td>
<td>64.16 ± 1.27</td>
<td>&lt; 0.001</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Fat-free soft tissue (kg)</td>
<td>54.26 ± 1.19</td>
<td>61.28 ± 1.19</td>
<td>&lt; 0.001</td>
<td>56.32 ± 0.80</td>
<td>59.22 ± 0.80</td>
<td>0.024</td>
<td></td>
</tr>
<tr>
<td>Muscle mass (kg)</td>
<td>26.19 ± 0.68</td>
<td>30.38 ± 0.68</td>
<td>0.001</td>
<td>27.25 ± 0.53</td>
<td>29.22 ± 0.53</td>
<td>0.022</td>
<td></td>
</tr>
<tr>
<td>Bone mineral content (kg)</td>
<td>2.65 ± 0.13</td>
<td>2.87 ± 0.13</td>
<td>0.220</td>
<td>2.80 ± 0.12</td>
<td>2.72 ± 0.12</td>
<td>0.658</td>
<td></td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>23.49 ± 0.93</td>
<td>22.66 ± 0.93</td>
<td>0.536</td>
<td>24.49 ± 0.86</td>
<td>21.67 ± 0.86</td>
<td>0.039</td>
<td></td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>29.12 ± 1.02</td>
<td>25.52 ± 1.02</td>
<td>0.019</td>
<td>29.31 ± 1.13</td>
<td>25.33 ± 1.13</td>
<td>0.029</td>
<td></td>
</tr>
<tr>
<td>Trunk fat mass</td>
<td>1.53 ± 0.06</td>
<td>1.27 ± 0.06</td>
<td>0.008</td>
<td>1.54 ± 0.07</td>
<td>1.27 ± 0.07</td>
<td>0.018</td>
<td></td>
</tr>
<tr>
<td>Limb fat mass</td>
<td>1.42 ± 0.06</td>
<td>1.16 ± 0.06</td>
<td>0.007</td>
<td>1.42 ± 0.07</td>
<td>1.16 ± 0.07</td>
<td>0.015</td>
<td></td>
</tr>
<tr>
<td>Nonlimb:limb fat mass</td>
<td>0.293 ± 0.011</td>
<td>0.266 ± 0.011</td>
<td>0.097</td>
<td>0.289 ± 0.013</td>
<td>0.270 ± 0.013</td>
<td>0.314</td>
<td></td>
</tr>
<tr>
<td>Muscle:fat</td>
<td>1.15 ± 0.11</td>
<td>1.54 ± 0.11</td>
<td>0.025</td>
<td>1.11 ± 0.12</td>
<td>1.57 ± 0.12</td>
<td>0.022</td>
<td></td>
</tr>
</tbody>
</table>

1 All values are x ± SE. Dual-energy X-ray absorptiometry was used for all measurements except height.
2 Analysis of covariance.

Anthropometric adjustments and predictions of body composition and fat distribution measured by DXA

Regression analysis showed that BMI predicted 35% of the variance in percentage body fat (% fat = -1.606 ± 1.052 BMI; r² = 0.35), which increased significantly to 47% when birth weight category was added to the model (% fat = -1.838 ± 1.126 BMI - 3.596 B; r² = 0.47), where B = 0 for the low-birth-weight group and 1 for the high-birth-weight group. Significant differences in percentage body fat were observed between the low- and high-birth-weight groups, both before and after (29.98 ± 1.14% and 24.66 ± 1.14%, respectively; P = 0.003) control for weight,
weight + height (29.31% and 25.33%, respectively; Table 3), and BMI (29.31% and 25.33%, respectively; Table 3).

Percentage body fat, estimated from skinfold thicknesses in all subjects (27.3 ± 0.62%; n = 32), was not significantly different from measurements obtained by DXA (27.3 ± 0.95%; n = 32) or air-displacement plethysmography (27.9 ± 1.38%). Although skinfold thicknesses predicted a lower percentage body fat in the low- than in the high-birth-weight group, the difference was not significant, either before or after adjustment for BMI or weight plus height. More than 90% of the variability in all skinfold-thickness ratios and waist-to-hip circumference was estimated to be due to biological variability and <10% to measurement error. The mean ratios of trunk (subscapular + suprailiac) to limb skinfold thicknesses (biceps + triceps) were not different between the low- and high-birth-weight groups (80–100% of the values obtained in the high-birth-weight group, both before (Table 1) and after adjustment for BMI and weight plus height (data not shown). This was also shown by analysis of covariance, in which the skinfold-thickness ratio was used as a covariate. This analysis showed that any given trunk-to-limb skinfold-thickness ratio was associated with a significantly greater ratio of whole trunk to whole limb fat obtained by DXA in the low- than in the high-birth-weight group (Table 5), even when further adjustments were made for BMI (Table 5). The same was found to apply to the waist-to-hip ratio (Table 5).

The midupper arm cross-sectional areas tended to be smaller in the low- than in the high-birth-weight group both before (47.1 ± 2.18 and 53.8 ± 2.59 cm², respectively; P = 0.057) and after (42.2 ± 2.63 and 53.8 ± 2.63 cm², respectively; P = 0.109) adjustment for height or for height plus weight (47.7 ± 2.65 and 53.0 ± 2.65 cm², respectively; P = 0.175), but the differences were not statistically significant. The bitrochanteric breadth, which was close to the level of the hip circumference measurement, was found to be significantly lower in the low- than in the high-birth-weight group, both before (30.49 ± 0.37 and 32.60 ± 0.39 cm, respectively; P = 0.001) and after (31.01 ± 0.34 and 32.09 ± 0.34 cm, respectively; P = 0.044) adjustment for height or for weight plus height (31.00 ± 0.35 and 32.09 ± 0.35 cm, respectively; P = 0.05). Whole-body bone mineral content did not differ significantly between the low- and the high-birth-weight groups before or after adjustment for BMI, weight, height, or weight plus height (Table 3).

### DISCUSSION

This study raises 3 issues about gross body composition in older men, in relation to their birth weight, which are relevant to mortality and morbidity from cardiovascular disease and diabetes in later life. First, this study not only confirmed that low birth weight is associated with lower adult weight, height, and FFM, but it also found that the low birth weight is associated with less appendicular and whole-body FFST and less muscle. This observation is in keeping with programming during early life of adult weight and height and mass of various lean tissues. Second, it suggests that differences in tissue proportions and fat distribution measured by DXA persist even after adjustments for body size (weight + height) or adiposity (FM and percentage body fat), which implies subtle effects on body composition. Third, it suggests that biased and potentially misleading information can be obtained when traditional anthropometric measures are used to compare body composition and fat distribution (over body segments) between low- and high-birth-weight groups. These last 2 issues are considered separately in more detail below.

### Body composition and fat distribution measured by DXA

The low-birth-weight group was found to have a greater amount (≈5 kg) and proportion (≈4%, after control for weight plus height) of fat, a more central fat distribution (after control for the amount of or percentage of body fat), and a lower muscle mass and muscle to fat ratio (after control for weight, or weight plus height, or BMI), all of which contribute to an increased risk of cardiovascular disease and diabetes. Although the ratio of abdominal to limb FM was greater in the low than in the high-birth-weight group, the differences were not significant, possibly because of anatomical variation and the inability to define upper and lower boundaries of the region of interest by <1.305 cm (1 pixel, or ≈15% of the distance between the boundaries). It is unlikely that significant differences in fat and lean tissue masses between the groups were due to methodologic problems associated with DXA because of the concordance of results with those obtained by air-displacement plethysmography, which is based on very different principles for measuring body composition.

The observed association of birth weight with body composition (lean and FM) in older adults is consistent with the results of
another DXA study in England, which suggested that body composition is programmed (2). Although this study did not report on muscle mass, fat distribution, or muscle-fat ratios, it reported a weak but significant association between whole-body bone mineral content and birth weight category (after adjustment for height and sex), which was not observed in our study. Two other studies have suggested that muscle mass is reduced in low-birth-weight individuals. One of these studies, which was based on a timed overnight urine collection for creatinine excretion (30), considered weight and not height in the comparison; the other study, which was based on anthropometric measures of the thigh adjusted for weight but not height (8). The results of the present study, which are based on DXA estimates of muscle mass, suggest differences between the low- and high-birth-weight groups after adjustment for both weight and height. This could help explain another observation (31), which is the reported positive relation between muscular strength and birth weight, after adjustment for weight and height. Unfortunately, no estimates of muscle mass were made in this last study.

**Anthropometric adjustments and predictions of body composition and fat distribution measured by DXA**

**Body fat**

This study suggests that the use of BMI (or weight plus height) to compare body composition between the high- and low-birth-weight groups can be misleading. At the same BMI, or same weight and height, percentage body fat was greater in the low-birth-weight group (=4% of body weight) than in the high-birth-weight group. Therefore, previous studies that have attempted to control for differences in body composition using BMI may have done so inadequately. This could help explain (together with differences in fat distribution, in the muscle-to-fat ratio, or in both) the apparent paradox of a lower risk of cardiovascular disease and diabetes in high-birth-weight individuals with the same and even greater BMI than in low-birth-weight individuals (11, 14). An analogous situation concerns ethnic differences in body composition. At the same adult BMI, Asians often have 2–6% more body weight as fat than do whites (15–18), who generally have a lower risk of cardiovascular disease and diabetes than do Asians. A study that compared anthropometric estimates of body composition in neonates born in England (mean birth weight: 3.49 kg) and India (mean birth weight: 2.70 kg; 2.76 kg in the low-birth-weight group in the present study) suggests that ethnic differences are present early in life (19). The extent to which these ethnic differences are due to genetic or environmental factors operating in early life is uncertain. The failure of skinfold thicknesses to demonstrate significant differences between the low- and high-birth-weight group (after adjustment for weight and height). This could help explain another observation (31), which is the reported positive relation between muscular strength and birth weight, after adjustment for weight and height. Unfortunately, no estimates of muscle mass were made in this last study.

**Fat distribution**

Although DXA measurements showed significant differences between the low- and the high-birth-weight groups in the distribution of body fat between central and peripheral body segments, no significant differences were obtained when the ratio of waist-to-hip circumferences (see below) or trunk-to-limb skinfold thicknesses were used. This last observation may have been due in part to the poorer precision and accuracy of skinfold-thickness measurements obtained at single subcutaneous sites compared with the reference DXA measurements of total fat, both internal and subcutaneous fat, over entire body segments. However, data from this study challenge previous assumptions about the use of skinfold-thickness ratios (or waist-to-hip ratio) for comparing fat distribution between body segments in low- and high-birth-weight groups in an unbiased manner. The same skinfold-thickness ratios (or the same waist-to-hip ratios) and same BMIs were found to be associated with greater trunk and limb fat distribution measured by DXA (ie, anthropometric indexes of fat distribution may have underestimated the central fat distribution in the low-birth-weight group compared with the high-birth-weight group). For skinfold-thickness ratios, this may have been because of differences between the low- and high-birth-weight groups in the distribution of fat between internal and external fat and between different parts of the same body segment. For the waist-to-hip circumference ratio, it is possible that different musculoskeletal to fat proportions produce the same circumferences. The significantly greater birochanteric breadth observed in the high- than in the low-birth-weight group, after adjustment for height or weight plus height, is consistent with this proposal.

Previous attempts to assess fat distribution on the basis of the waist-to-hip ratio or the ratio of trunk to limb skinfold thicknesses have produced inconsistent results, with some studies reporting significantly more central fat distribution in individuals with low birth weight (32–36) and others reporting no such relations (37–40). One of the reasons for the lack of consistency is that different skinfold-thickness ratios (subscapular to triceps (32–35, 40), subscapular + suprailiac to triceps + thigh (35), and subscapular + midaxillary to triceps + medial calf (34) or different circumference ratios [eg, waist to hip (36–40) or waist-to-thigh (8)] have been used for this purpose. Another reason is that some studies have adjusted for weight and not height (36, 40), others have adjusted for height and not weight (8), whereas most studies have adjusted for BMI (32, 33, 35, 38, 39), which controls for neither weight or height (Table 2), and a few studies adjusted for none of these (41–43).

**Muscle and muscle-to-fat ratio**

The use of midupper arm muscle area as a surrogate measure of muscle mass suggested less muscle in the low- than high-birth-weight group before and after anthropometric adjustments. These differences were not statistically significant, in contrast with the measurements obtained with DXA, which were significantly different. These significant differences were possibly due to the larger technical error associated with the anthropometric measurements, which in reality arise from 2 independent measurements (arm circumference and triceps skinfold thickness). However, the trends observed in this study are consistent with the results of another study (8), which found that birth weight was related to the cross-sectional area of thigh + bone (after adjustment for height and race), assessed by anthropometric methods in applicants for military service in the United States (age: 17–22 y; mean BMI: 23.2).

The present study had several limitations. The number of subjects was small, and it is perhaps surprising that significant results were obtained. However, the study included only subjects with high or low birth weights, excluding subjects with intermediate birth weight, which probably increased the chances of identifying any differences in body composition. It can be hypothesized that intermediate values occur in the “middle” group, but this needs to be established. The different birth weight–disease relations that have
been reported, including U-shaped birth weight–adult BMI relations (10), suggest that investigations across all birth weight categories, not just low and high birth weight categories, should be carried out. In our investigation, only men within a narrow age range (64–72 y) were studied, in an attempt to reduce the confounding effects of sex and age, but this limits generalizations to other age groups. However, this approach precludes extrapolation to women and individuals in a different age range. Another limitation was that muscle mass was not measured directly but was estimated through measurements of FFST in the limbs. Finally, because all of the subjects involved in this study were white, there is a need to examine these relations in subjects with different ethnic backgrounds.

All authors helped plan the study or analyzed and discussed the results. OAK undertook most of the practical work. None of the authors had a conflict of interest.

REFERENCES


