Rapid growth among term children whose birth weight was appropriate for gestational age has a longer lasting effect on body fat percentage than on body mass index

Nadina Karaolis-Danckert, Anette E Buyken, Katja Bolzenius, Carolina Perim de Faria, Michael J Lentze, and Anja Kroke

ABSTRACT

Background: It is not clear whether and how rapid growth in infancy, a risk factor for later obesity, differentially affects growth and body-composition development throughout childhood in term children with an appropriate-for-gestational age (AGA) birth weight.

Objective: The aim was to examine the effect of rapid growth in infancy on body mass index SD score (BMI SDS) and body fat percentage (%BF) trajectories until age 7 y.

Design: This analysis included 206 (50.5% female) AGA term participants of the Dortmund Nutritional and Anthropometric Longitudinally Designed Study. Repeated anthropometric measurements were obtained between 0.5 and 7 y of age.

Results: Fifty-nine of the 206 children (28.6%) displayed rapid growth (an increase in SDS for weight of >0.67 between birth and age 2 y). From 6 mo of age, their growth trajectories diverged from normal growers, and by age 7 y they had a higher BMI, more fat mass, and a higher risk of overweight (odds ratio: 6.2; 95% CI: 2.4, 16.5; P = 0.0002). Multilevel model analyses showed that the differences in BMI were achieved within the first 2 y of life [β (±SE) SDS: 1.22 ± 0.13], after which they persisted at this level until the age of 7 y, whereas differences in %BF, which were also already discernible by age 2 y (1.52 ± 0.34%), became progressively larger over the next 5 y (adjusted difference: 0.23 ± 0.11%/y; P = 0.03).

Conclusions: Rapid growth in infancy and early childhood results in an increased BMI and %BF throughout childhood and an increased risk of overweight at age 7 y among AGA children. Rapid growth in AGA children has a more pronounced effect on %BF than on BMI.

KEY WORDS Rapid growth, cohort study, children, body fat percentage, trajectories, appropriate for gestational age

INTRODUCTION

Catch-up growth, as it was classically defined by Prader, described the "nutritional recovery following a period of growth restriction after the latter is removed" (1). This recovery mechanism in childhood appears to reduce both morbidity and mortality for growth-retarded malnourished children in developing countries (2). Paradoxically, other research has suggested that a related phenomenon, rapid growth in infancy, is not only a potential risk factor for obesity (3), but also for a range of other morbidities, including cardiovascular disease (4), high blood pressure (5), and cancer (6). These studies illustrated that children whose low birth weight (LBW), small size for gestational age (SGA), or both reflected poor intrauterine growth were at particularly high risk and have subsequently stimulated a debate that claims it is not small size at birth that is important but change in body size, which then modifies the relation between birth weight and adult obesity and disease (7–10).

Most children born in developed countries, the same countries which are currently part of the obesity epidemic, are not SGA but appropriate for gestational age (AGA). Other studies investigating growth in infancy and early childhood have suggested that some full-term children also display rapid growth and consequently have a higher risk for obesity in later childhood and young adulthood than do those who did not grow rapidly (3, 11–13). However, these studies have not always exclusively considered term AGA children, whose growth and body-composition development differ considerably from term SGA children or children who are large for gestational age (LGA) (14, 15). More importantly, no other study to date has sufficient prospectively collected longitudinal data to identify how rapid growth in infancy affects growth trajectories throughout childhood and whether this influence differs between body mass index (BMI) and body fatness. A selective effect of rapid growth on fat mass would be of particular interest because it is this component of body composition that has the clearest link to disease risk (16). We therefore aimed to investigate the consequence of rapid growth in AGA children for BMI and body fat percentage (%BF) trajectories throughout infancy and early childhood and for anthropometric measurements at age 7 y using data from the Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study.

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2 The DONALD Study is funded by the Ministry of Science and Research of North Rhine Westphalia, Germany.
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SUBJECTS AND METHODS

Study population

The DONALD Study is an ongoing, open cohort study conducted by the Research Institute of Child Nutrition in Dortmund, Germany. This study was previously described in detail (17). Briefly, since recruitment began in 1985, detailed information concerning diet, growth, development, and metabolism between infancy and adulthood has been collected for >1100 children. Every year, an average of 40–50 infants are newly recruited and first examined at the age of 3 mo. Each child returns for 3 more visits in the first year, 2 in the second, and then once annually until early adulthood. The study was approved by the Scientific Committee of the Research Institute of Child Nutrition, and all examinations are performed with parental consent.

The ages of the children who were initially recruited into the DONALD Study were quite variable, ie, information on the first few years of life was not always available. In addition, many children have not yet reached 7 y of age. Therefore, the total number of children for whom a minimum of measurements at 0.5, 2, and 7 y were available is 297. This number was reduced to those term (37–42 wk gestation) singletons with a birth weight >2500 g (n = 288) and again to those whose birth weight and length were appropriate-for-gestational-age (n = 229), ie, all birth weights and lengths were between the 10th and 90th percentiles of the German sex-specific birth weight-for-gestational-age curves (18, 19). Finally, all children had to have complete information on breastfeeding and maternal characteristics (BMI and education status; n = 206). The subcohort analyzed here therefore includes 206 AGA term singletons (50.5% female). The mean number of measurements per child was 9.9 (range: 6–10).

Anthropometric measurements

At each visit, the children are measured by trained and regularly monitored nurses according to standard procedures. The children are dressed in underwear only and are barefoot. Recumbent length is measured in children <2 y of age to the nearest 0.1 cm by using a Harpenden (UK) stadiometer. From the age of 2 onwards, standing height is measured to the nearest 0.1 cm by using a digital stadiometer. Weight is measured to the nearest 0.1 kg with an electronic scale. Skinfold thicknesses are measured from the age of 6 mo onwards on the right side of the body at the biceps, triceps, subscapular, and suprailiac sites to the nearest 0.1 mm by using a Holtain caliper. Midupper arm circumference (MUAC) is recorded to the nearest 0.1 cm by using a metal measuring tape.

Parents are interviewed, weighed, and measured by the Study nurses on their child’s admission to the study. Information on birth weight, length, and head circumference at birth as well as gestational age and maternal weight gain during pregnancy are abstracted from the “Mutterpass,” a standardized document given to all pregnant women in Germany.

Calculations

Sex- and age-independent SD scores (SDS) were calculated with the use of the German reference curves for weight, height, and body mass index (BMI; in kg/m²) (20) and with the Tanner and Whitehouse reference data for subscapular and triceps skinfold-thickness measurements (21). To remove general deviations of our sample from the reference data, the variables above were then internally standardized. Percentage body fat was calculated by using the equations of Deurenberg (22). Overweight at age 7 y was defined according to the International Obesity Task Force BMI cutoffs for children, which correspond to an adult BMI of 25 (23). MUAC was used to calculate the following indexes: total midupper arm area = MUAC²/(4 × π), arm muscle area = [MUAC – (triceps × π)]²/(4 × π), and arm fat area = total midupper arm area – arm muscle area (24).

Rapid growth was defined as an increase in weight SDS >0.67 kg between birth and 24 mo, as recommended by Monteiro and Victora (1). A change in weight SDS between the ages of 0 and 24 mo was chosen because it was shown to be the best predictor of BMI at age 7 y (25). We chose age 7 y as our endpoint because it is an age at which BMI in childhood correlates well with BMI in adulthood (26, 27).

Statistical analysis

Unadjusted associations between the independent variables and rapid growth were tested by using chi square, Student’s t test, or Wilcoxon’s rank-sum test as appropriate. There were equal numbers of boys and girls in the 2 growth groups (chi square = 0.004, P = 0.95); therefore, they were pooled together for all statistical analyses. Multivariate logistic regression was used to calculate odds ratios (OR) for the risk of overweight at age 7 y. Linear mixed-effects regression models (PROC MIXED), including both fixed and random effects, were used to construct longitudinal models of BMI SDS and %BF trajectories subsequent to the period of rapid growth, ie, between 2 and 7 y of age, and to investigate the effect of rapid growth on baseline BMI SDS or %BF status at age 2 y and changes over time. The random component of these models accounts for the nested nature of our data (children within families) and the lack of independence that exists between repeated observations on the same person. Basic models included either BMI SDS or %BF measurements between 2 and 7 y inclusive as the dependent continuous variable and rapid growth, time (chronological age and age²), and the interaction between rapid growth and time as the independent fixed effects. For %BF, sex and the interaction between sex and time were also included in the basic model to remove the known effect of sex on differences in %BF. Analyses were then carried out separately for the effect of the following variables and their interaction with time on the basic model: sex, gestational age, breastfeeding status, maternal weight status and educational status, and either BMI SDS at birth or %BF at 6 mo of age. Only those variables that significantly modified the effect of rapid growth in the basic models were included in subsequent multivariate analyses. An advantage of the MIXED procedure is that it does not delete children from the analysis if they are missing data for a particular time point but analyzes all of the data available on the assumption that any missing data are missing at random. Of the 1236 possible BMI SDS and %BF values, only 15 (1.2%) BMI SDS values and 23 (1.9%) %BF values were missing. A P value < 0.05 was considered statistically significant. All statistical analyses were carried out by using SAS version 8.2 (SAS Inc, Cary, NC).

RESULTS

Overall, 28.6% (59 of 206) of the children displayed rapid growth between birth and 24 mo. These children were both significantly lighter, and shorter at birth and were born slightly

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earlier than were the normal growers (Table 1). Rapid growers were also more likely to be first born. No significant differences, however, in the proportion of infants who were fully breastfed for ≥4 mo or their parental anthropometric measures or educational status were observed between the rapid growers and the normal growers.

The observed mean weight SDS, height SDS, and BMI SDS growth trajectories of the children who grew rapidly and those who did not are shown in Figure 1. Although relatively smaller than other children at birth, within 6 mo the BMI SDS trajectories of the rapid growers increased, overtook, and visibly diverged from those of the other children. This process appears to have occurred faster in boys than in girls. Having achieved a mean 0.5–0.6 SDS at 1 y and 1.5 y of age in boys and girls, respectively, the BMI SDS trajectories of the rapid growers reached a plateau along which they tracked until the age of 7 y. In the case of %BF, as illustrated in Figure 2, both rapid and normal growers experienced a decrease in body fat over time. However, this decrease occurred more slowly in those children who grew rapidly, and they appeared to maintain an overall larger %BF than did the other children.

By the age of 7 y, not only were the children who grew rapidly significantly heavier and taller, with a higher BMI SDS and %BF than those children who did not grow rapidly (Table 2), but they were also significantly different in all other anthropometric measurements considered. In addition, a significantly larger proportion of these children were classified as overweight (31% compared with 10%; P = 0.0003).

Next, we investigated whether rapid growth between birth and 24 mo was a risk factor for overweight at age 7 y when other influences were adjusted for. In the unadjusted univariate analysis (Table 3), rapid growth significantly increased a child’s risk of being overweight at age 7 y by almost 4 times. When birth characteristics were adjusted for, the OR for rapid growth increased to 6.5 (Model 1) and this remained relatively unchanged and highly significant even when breastfeeding status (Model 2)

### Table 1

| Birth and parental characteristics of the Dortmund Nutritional and Anthropometric Longitudinally Designed Study children who grew rapidly between the ages of 0 and 24 mo and of those who did not |
|---------------------------------|--------------|--------------|
|                                  | Normal growth (n = 147) | Rapid growth (n = 59) |
| M/F                             | 73/74         | 29/30        |
| Birth characteristics           |               |              |
| Birth weight (g)                | 3605 ± 308 \(^{1}\) | 3246 ± 284 \(^{1}\) |
| Birth length (cm)               | 52 (51, 54) \(^{2}\) | 51 (50, 52) \(^{2}\) |
| Gestational age (wk)            | 40 (39, 41) \(^{2}\) | 39 (38, 40) \(^{2}\) |
| Fully breastfed >4 mo [n (%)]   | 94 (64.0)     | 30 (50.9)    |
| Primiparous [n (%)]             | 76 (52.8)     | 39 (68.4)    |
| Parental characteristics        |               |              |
| Overweight mothers [n (%)]      | 34 (23.1)     | 12 (20.3)    |
| Overweight fathers [n (%)]      | 60 (51.3)     | 25 (51.0)    |
| Smoker in the household [n (%)] | 34 (23.1)     | 17 (28.8)    |
| Mothers >12 y schooling [n (%)] | 99 (67.4)     | 33 (55.9)    |
| Fathers >12 y schooling [n (%)] | 100 (68.5)    | 31 (54.4)    |

\(^{1}\) SD (all such values).

\(^{2}\) P < 0.0001. Student’s t test or Wilcoxon test were used for continuous variables; chi-square test for categorical variables.

\(^{3}\) Median, quartile 1 and quartile 3 in parentheses (all such values).

\(^{4}\) P < 0.05.
and maternal characteristics (Model 3) were adjusted for. Interestingly, in those models that included both rapid growth and BMI at birth, a higher BMI at birth significantly doubled a child’s risk of being overweight at age 7 y (OR: 1.9; 95% CI: 1.2, 3.2; $P = 0.01$), which suggests that in our sample there may be two pathways to becoming overweight at age 7 y: being born relatively small and growing rapidly and being born large and staying large (data not presented in tables).

The parameter estimates from the multilevel models for BMI SDS presented in Table 4 confirm that rapid growth between birth and 24 mo resulted in a significantly larger BMI SDS at age 2 y, even after adjustment for birth (Model 2) and maternal (Model 3) characteristics (a difference of 1.22 SDS compared to normal growers (Model 2) and maternal (Model 3) characteristics, a significant independent effect of rapid growth on %BF at age 2 y remained, such that rapid growers had, on average, 1.52% more BF than did normal growers ($P = 0.006$). Rapid growth also affected the rate of %BF change between ages 2 and 7 y, resulting in an adjusted rate difference of 0.23% per year compared with normal growth ($P = 0.03$).

Considering the effect of anthropometric characteristics in early life, the fully adjusted multilevel models showed that a larger BMI SDS at birth also resulted in a significantly larger BMI SDS at age 2 y [$\beta (\pm SE) = 0.34 \pm 0.05, P < 0.0001$], whereas a greater %BF at 6 mo resulted in a greater %BF at age 2 y [$\beta (\pm SE) = 0.33 \pm 0.05, P < 0.0001$]. However, neither factor significantly influenced the rate of change of either BMI SDS or %BF between 2 and 7 y (data not presented).

### DISCUSSION

To our knowledge, this is the first in-depth study to describe the longitudinal effect of rapid growth on the growth patterns of healthy term children whose birth weight was appropriate-for-gestational-age (AGA) but who nevertheless grow rapidly in early childhood. Over one-fourth (29%) of the AGA children in this cohort grew rapidly between birth and 24 mo. They were relatively lighter and smaller at birth and appeared to diverge in their growth patterns from other children as early as 6 mo of age, so that they were taller, heavier, and fatter throughout childhood. By the age of 7 y, a larger proportion of these children were classified as overweight. Importantly, multilevel model analyses showed that the differences in BMI were achieved within the first 2 y of life, after which they essentially persisted at this level until the age of 7 y, whereas differences in %BF, though already discernible by age 2 y, became progressively larger over the next 5 y. The effect of rapid growth on the risk of overweight at age 7 y and on the growth trajectories of both BMI and %BF persisted after adjustment for important confounders, including birth and maternal characteristics.

The effect of early rapid growth on later overweight and adiposity seen in this cohort expands the findings of a recent review.

### TABLE 3
Multivariate logistic regression analysis of the effect of rapid growth on the risk for overweight at 7 y of age

<table>
<thead>
<tr>
<th>Model</th>
<th>Odds ratio (95% CI)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 0</td>
<td>Normal growth</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Rapid growth</td>
<td>3.9 (1.8, 8.3)</td>
</tr>
<tr>
<td>Model 1</td>
<td>Normal growth</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Rapid growth</td>
<td>6.5 (2.6, 16.4)</td>
</tr>
<tr>
<td>Model 2</td>
<td>Normal growth</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Rapid growth</td>
<td>6.1 (2.4, 15.3)</td>
</tr>
<tr>
<td>Model 3</td>
<td>Normal growth</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Rapid growth</td>
<td>6.2 (2.4, 16.5)</td>
</tr>
</tbody>
</table>

1 $n = 206$ children. Model 0 was the unadjusted model. Model 1 was adjusted for sex and birth characteristics, including BMI at birth and gestational age group (37–38 wk, 39–40 wk, or 41–42 wk). Model 2 was adjusted for all variables in model 1 and for breastfeeding for 4 mo (yes or no). Model 3 was adjusted for all variables in model 2 and for maternal characteristics, including maternal weight status (overweight or normal weight) and maternal education (more than or less than 12 y).
Baseline BMI SDS and %BF development. Other studies that have considered rapid growth in “term” children and its consequence for outcomes at single points in time have shown that children who grew rapidly were generally taller, heavier, and fatter at ages 5 y (3), 9 y (11), and 20 y (13) with a more centralized fat distribution. However, these studies did not exclusively consider children whose birth weight was AGA (3, 11, 13) and, in some cases, those who did not was high because of the repeated anthropometric measurements; however, the relatively small size of our sample may explain why we could not detect differences between the growth patterns of those who grew rapidly and those who did not was high because of the repeated anthropometric measurements; however, the relatively small size of our sample may explain why we could not detect differences between rapid growth and baseline BMI SDS at age 2 y (intercept) and BMI SDS slope between 2 and 7 y of age.

### TABLE 4
Linear mixed models of the association between rapid growth and baseline BMI SD score (SDS) at age 2 y (intercept) and BMI SDS slope between 2 and 7 y of age

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate ± SE</th>
<th>P</th>
<th>Estimate ± SE</th>
<th>P</th>
<th>Estimate ± SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline BMI SDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>−0.25 ± 0.08</td>
<td>0.001</td>
<td>−0.32 ± 0.09</td>
<td>0.003</td>
<td>−0.12 ± 0.13</td>
<td>0.3</td>
</tr>
<tr>
<td>Rapid growth</td>
<td>0.89 ± 0.14</td>
<td>0.001</td>
<td>1.22 ± 0.13</td>
<td>0.003</td>
<td>1.22 ± 0.13</td>
<td>0.002</td>
</tr>
<tr>
<td>Rate of change</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>0.01 ± 0.01</td>
<td>0.4</td>
<td>0.03 ± 0.02</td>
<td>0.07</td>
<td>0.08 ± 0.02</td>
<td>0.002</td>
</tr>
<tr>
<td>Age × rapid growth</td>
<td>−0.03 ± 0.02</td>
<td>0.2</td>
<td>−0.05 ± 0.03</td>
<td>0.07</td>
<td>−0.05 ± 0.03</td>
<td>0.07</td>
</tr>
</tbody>
</table>

1 n = 206.
2 Adjusted for sex, sex × time, and gestational age group.
3 Adjusted for sex, sex × time, %BF at 6 mo, %BF at 6 mo × time, and gestational age group.
4 Adjusted for sex, sex × time, %BF at 6 mo, %BF at 6 mo × time, gestational age group, maternal overweight × time, and years of schooling × time.

(1) and of an investigation of 25 putative risk factors for childhood obesity (28). We could confirm that not only is this independent association visible in term AGA children who would not be expected to compensate for their small size, but also that rapid growth in infancy differentially affects the trajectories of BMI SDS and %BF development. Other studies that have considered rapid growth in “term” children and its consequence for outcomes at single points in time have shown that children who grew rapidly were generally taller, heavier, and fatter at ages 5 y (3), 9 y (12), 17 y (11), and 20 y (13) with a more centralized fat distribution. However, these studies did not exclusively consider children whose birth weight was AGA (3, 11, 13) and, in some cases, included both preterm babies (<37 wk), LBW babies (<2500 g), or both (11, 12). The growth of preterm and LBW children is known to differ from those born at term, but recent studies have also shown that even within term children both SGA and LGA children differ from AGA children in terms of their growth and fatness (14, 15).

Although BMI, a proxy for adiposity, is a commonly used outcome in studies on obesity risk, its inability to differentiate between lean and fat mass, especially in children, has often been criticized (29). In our study, those children who grew rapidly not only had larger BMIs than did the children who grew normally but also had significantly larger skinfold thicknesses, MUACs, and arm fat areas, and not only at age 7 y but also throughout childhood (data not shown). Furthermore, our results suggest that the effect of rapid growth on %BF may be more significant than that on BMI because it may lead to an ever-increasing fat mass. A small, recently published study (30) suggested the occurrence of a similar phenomenon in term SGA children. They, too, gained progressively more abdominal fat and body adiposity after a period of catch-up growth.

Similar to a study conducted by Cameron et al (12), rapid growers did not differ significantly from other children in ways that could suggest why they grew rapidly. Ong et al (3) found that rapid growers had taller fathers, were more often from primiparous pregnancies, and their mothers were more likely to smoke during pregnancy, all of which suggest growth restraint. In our study, rapid growers were also more often from primiparous pregnancies but were similar to normal growers in terms of full breastfeeding status and in the anthropometric and socioeconomic characteristics of their parents. Our power to detect differences between the growth patterns of those who grew rapidly and those who did not was high because of the repeated anthropometric measurements; however, the relatively small size of our sample may explain why we could not detect differences between

### TABLE 5
Linear mixed models of the association between rapid growth and baseline percentage of body fat (%BF) at age 2 y (intercept) and %BF slope between 2 and 7 y of age

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate ± SE</th>
<th>P</th>
<th>Estimate ± SE</th>
<th>P</th>
<th>Estimate ± SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline %BF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>20.50 ± 0.31</td>
<td>&lt; 0.0001</td>
<td>12.46 ± 1.33</td>
<td>&lt; 0.0001</td>
<td>12.44 ± 1.33</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Rapid growth</td>
<td>1.23 ± 0.36</td>
<td>0.02</td>
<td>1.55 ± 0.34</td>
<td>0.006</td>
<td>1.52 ± 0.34</td>
<td>0.006</td>
</tr>
<tr>
<td>Rate of change</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>−0.81 ± 0.13</td>
<td>&lt; 0.0001</td>
<td>0.12 ± 0.46</td>
<td>0.8</td>
<td>−0.24 ± 0.45</td>
<td>0.6</td>
</tr>
<tr>
<td>Age × rapid growth</td>
<td>0.20 ± 0.11</td>
<td>0.08</td>
<td>0.23 ± 0.11</td>
<td>0.05</td>
<td>0.23 ± 0.11</td>
<td>0.03</td>
</tr>
</tbody>
</table>

1 n = 206.
2 Adjusted for sex and sex × time.
3 Adjusted for sex, sex × time, %BF at 6 mo, %BF at 6 mo × time, and gestational age group.
4 Adjusted for sex, sex × time, %BF at 6 mo, %BF at 6 mo × time, gestational age group, maternal overweight × time, and years of schooling × time.
5 The multilevel model had two intercepts, one for baseline %BF at age 2 y and another for subsequent linear change in %BF over time. Each represents the mean value of the dependent variable at the baseline time, when all other predictors are 0.
the growth groups in terms of characteristics that had been measured only once, eg, socioeconomic or breastfeeding status.

The longitudinal nature of the DONALD Study requires a high level of dedication on the part of participants. Compared with the general population, the DONALD families are characterized by higher educational attainment and socioeconomic status; thus, they probably do not represent the extremes of behavior or weight status. This homogeneity of the DONALD sample could also explain why we discerned no significant differences between the 2 growth groups in terms of socioeconomic status and parental characteristics. On the other hand, the direction of the association of variables such as full breastfeeding (protective) and maternal overweight status (detrimental) with the risk of overweight at age 7 y and with BMI SDS and %BF growth trajectories seen in the present study was similar to that seen in larger representative cohorts (31, 32). Furthermore, nonrepresentation is less relevant for longitudinal analyses and internal validity. The repeated-measures design of our study and our use of multivariable analysis with information on confounders are both significant advantages over other similar studies.

Once rapid growth was adjusted for, children with a larger BMI at birth displayed an independent increased risk for overweight at age 7 y. This positive association between birth weight and later overweight is well-known (33, 34) and suggests that there are several pathways to becoming overweight, including being born relatively small and growing rapidly and being born large and staying large. Our exclusion of children with birth weights in the top 10% of the distribution (LGA children) may explain why birth weight was not significantly associated with the risk of overweight in the unadjusted models. Interestingly, a recent review concluded that the positive association between birth weight and BMI may not necessarily be the result of increased adiposity but rather a greater degree of lean body mass (34). It remains to be seen if the risks of morbidity are the same regardless of which “pathway” led there. On the other hand, the use of SDS to define rapid growth could also explain the appearance of an effect for BMI at birth after adjustment for rapid growth. Overweight children have to gain, relatively speaking, more weight than do other children to achieve a difference of 0.67 SDS (the definition for rapid growth) because the centiles at the upper ranges of the centile chart are further apart (35). These children are less likely, therefore, to be included in the rapid growth group.

As our study shows, potentially harmful growth patterns are not only restricted to preterm or SGA children but also to some AGA children. When one considers possible public health interventions, however, the apparent benefit of rapid growth in developing countries must be kept in mind. Children who achieve nutritional recovery early in life after a period of restriction experience a reduction in morbidity and mortality (10). The consequences of this reality must be weighed against the association of rapid growth with the risk of obesity and other diseases in later life.

The reasons for rapid growth in this contemporary cohort of healthy, term AGA children are unclear. AGA children would not be expected to grow rapidly to compensate for preterm birth or obvious intrauterine growth deficits, nor could this phenomenon be described as regression to the mean, as the graphs clearly show, but seems rather to be a dramatic overcompensation of growth in children who are relatively small at birth. It remains to be seen whether and how many of these children will maintain their greater weight and height throughout adolescence and adulthood. That this growth pattern may nevertheless be detrimental was suggested by a recent study showing that adrenal androgen concentrations were highest in small infants who gained weight rapidly during early childhood (36). The authors suggested that a higher adrenal androgen secretion could contribute to the links between early rapid growth and adult disease risks by enhancing insulin resistance and central fat deposition. In conclusion, there was a strong, significant, and independent effect of rapid growth between birth and 24 mo of age on both BMI SDS and %BF values at age 2 y in AGA children, and this effect persisted and influenced both BMI SDS and %BF trajectories between 2 and 7 y of age.

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NK-D and CpdF conceived the project and performed initial data analyses. NK-D conducted further analyses and drafted the manuscript. KB provided technical support and statistical expertise. AEB and AK supervised the study. All authors contributed to interpretation of the data and revision of the manuscript. None of the authors have any personal or financial conflicts of interest.

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