Growth Outcomes of Weight Faltering in Infancy in ALSPAC

WHAT'S KNOWN ON THIS SUBJECT:
Studies of clinically derived samples of infants with failure to thrive have reported that children remain shorter and lighter than their peers at school-age. Enhanced weight gain (“catch-up”) in small infants has been linked to subsequent obesity.

WHAT THIS STUDY ADDS:
Infants with early weight faltering caught up in weight by 2 years, but height gain remained disproportionally slow. Those with weight faltering later in infancy remained shorter and lighter throughout childhood. Anthropometric outcomes of both groups were within population norms at 13 years.

OBJECTIVE:
The goal of this study was to investigate growth outcomes in term infants with weight faltering.

METHODS:
Conditional weight gain was calculated on term infants from the Avon Longitudinal Study of Parents and Children. Cases of weight faltering were infants with a conditional weight gain below the fifth centile. Outcome growth measurements included weight and length/height (from 9 months to 13 years), BMI, mid-arm circumference, and waist circumference (at 7, 10, and 13 years).

RESULTS:
Weight data were available on 11 499 infants; 507 had “early” weight faltering (before 8 weeks), and 480 had “late” weight faltering (between 8 weeks and 9 months). The early group showed enhanced weight gain from 8 weeks until 2 years, then gained weight at the same rate as the controls. Gain in height was proportionally slower than gain in weight through childhood. By 13 years, they had BMI, mid-arm circumference, and waist circumference similar to the controls. The late group showed steady weight gain throughout childhood; enhanced weight gain compared with the controls only occurred between 7 and 10 years. Gain in height was proportional to gain in weight. This group remained considerably lighter and shorter than the controls up to the age of 13 years.

CONCLUSIONS:
Children with weight faltering before 8 weeks showed a different pattern of “catch-up” to those with weight faltering later in infancy. By 13 years, the anthropometric profile of the 2 groups was within population norms. Pediatrics 2013;131:e843–e849
Weight gain in infancy has long been recognized as an important determinant of subsequent growth trajectory, and recent attention has focused on rapid weight gain in the second 6 months of life as a precursor of subsequent obesity. Slow weight gain in infancy is often regarded by parents, and by some clinicians, as a sign of underlying ill health, and such infants are expected to be lighter and shorter as children. The evidence for this belief is largely based on clinic-derived samples of infants with failure to thrive. In early studies of failure to thrive, slow-growing infants were found to have poor anthropometric outcomes in later life, to have gained less weight by age 5 years, to be shorter and lighter at age 6 years, and to have lower BMI at age 12 years. Many researchers have identified cases by using a weight for age below a certain centile. However, using a centile-based cutoff for weight will include many healthy, normal small infants. The preferable approach is to use the criteria of weight gain below the fifth centile, adjusted for age, gender, and initial position in the weight distribution to derive a conditional weight gain.

More recent community or population-based cohort studies that define growth faltering on standardized anthropometric criteria of weight gain have challenged the traditional view that slow weight gain is a marker of ill health, or undernutrition. Clinicians working with generally well-nourished populations face a dilemma between identifying slow-growing infants to receive interventions to increase energy input so that they achieve catch-up in weight gain, and being aware of the increasing evidence linking rapid weight gain in infancy with subsequent obesity. We have used the Avon Longitudinal Study of Parents and Children (ALSPAC) to investigate the background factors and the cognitive, psychological, and educational outcomes of children with weight faltering in infancy. In this article, we report their growth outcomes up to the age of 13 years.

**METHODS**

ALSPAC is a United Kingdom–based birth cohort study designed to examine the genetic and environmental determinants of child health and development. The UK Medical Research Council (grant 74882), the Wellcome Trust (grant 076467), and the University of Bristol provide core support for ALSPAC. The study recruited 14 541 pregnant women resident in the former Avon Health Authority area of southwest England with an expected date of delivery between April 1991 and December 1992, resulting in a total birth cohort of 14 062 live births of whom 13 970 were alive at 1 year of age. Avon has a mixture of urban and rural communities with sociodemographic characteristics similar to the rest of the United Kingdom at the 1991 census. Methodologic details of the study have been published, and details of questionnaires and research clinics can be found on the ALSPAC Web site. Ethical approval for the study was obtained from the ALSPAC Law and Ethics Committee and the local research ethics committees.

**Definition of Cases**

Weight data collected by health professionals as part of routine child health surveillance were obtained from the Avon Child Health computer system. Weights were taken at birth, 6 to 8 weeks (range: 1–3 months), and 9 months (range: 6–12 months) and converted to z scores adjusted for gender and age by using the UK 1990 Growth Reference. If data were missing for any of these measures, children were not included in further analyses. Children were also excluded if they had a major congenital abnormality likely to affect growth (eg, cerebral palsy, congenital heart disease, Down syndrome; n = 89), were nonsingleton births (n = 184), or were born preterm (<37 weeks) or postterm (>42 weeks) (n = 871). For this growth study, infants with very extreme weight measurements (≤4 SDS or ≥4 SDS) at birth or 8 weeks were also excluded (n = 35); these were considered likely to be measurement or recording errors. The number of children available for this analysis was thus 11 499.

Growth was measured by calculating differences in z scores between 2 time points and adjusted for regression toward the mean by using Cole’s equation, using regression coefficients derived from within the cohort. The resulting weight gain was conditional on gender, age, and initial weight. Centiles were produced, and as in previous studies investigating weight faltering in ALSPAC, cases were identified as infants with conditional weight gain below the fifth centile within the cohort (z score less than –1.645). All other infants in the cohort with weight gain above the fifth centile at each time interval comprised the control group.

**Outcomes**

Weights and heights measured by health visitors as part of routine preschool surveillance in the community at ages 18 months to 2 years and 3 years 6 months to 4 years were extracted from the Avon Child Health computer system. Weights and heights, mid-arm circumference (MAC), and waist circumference (WC) were measured according to standardized procedures in ALSPAC research clinics at 7, 10, and 13 years. All measures were adjusted for age and gender: weight, height, and BMI were standardized compared with the UK 1990 reference, and MAC and WC were standardized by using the internal means of the ALSPAC cohort as reference. Different numbers of children were available for analysis at each time point depending on whether measurements were performed on them at that time.
Confounders
Maternal educational level, housing tenure, socioeconomic class, and parental heights were obtained by using postal questionnaires completed during the study pregnancy. Mothers and partners were asked to self-report their height; data were available for 10,307 mothers and 7,165 fathers of the children in infancy. Feeding symptoms and difficulties were captured by parent-completed questionnaires. Parents were asked to rate on a scale of 1 to 5 whether their infant demonstrated specific feeding behaviors, which were named but not described in the questionnaire, and no definitions were provided on what constituted a problem. We have used specific questions on feeding from questionnaires completed at 1, 6, and 15 months of age.

Statistical Analysis
The data were analyzed by using Stata (Stata Corp, College Station, TX)21 and SPSS (IBM SPSS Statistics, IBM Corporation, Armonk, NY).22 The effect of early growth on anthropometric outcomes was assessed by running a general linear model.23 Analysis of covariance was used in multivariate analysis to investigate interaction effects. Major confounders included maternal anthropometry, socioeconomic characteristics, and infant-feeding difficulties. Assumption of homogeneity of variances was tested by using Levene’s test,24 and the Pearson product moment correlation coefficient25 was used to assess correlation among variables. To determine whether there was a difference between the expected frequencies and the observed frequencies in ≥1 category, χ² tests were conducted. All tests were performed at a significance level of 0.01. A P value of >0.01 was used for stepwise exclusion of covariates in view of the number of outcome variables investigated and the importance of a conservative approach to analysis. We took the approach of using available data for each outcome because restricting the analysis to only those with complete data for all outcomes would reduce the numbers substantially.

RESULTS
Ascertainment
From the 11,499 children with complete growth measurements in infancy, those with data available at later ages were more likely to come from families of higher socioeconomic class, with a higher maternal educational level, and secure housing tenure (P ≤ .01 for all), compared with those lost to follow-up. However, there were no differences in the proportion of missing data between the 2 weight gain groups and the controls.

Infant Growth
The mean ± SD birth weight of the whole sample was 3,470 ± 475 g. Weight z scores (corrected for gender and gestational age) at birth, 6 to 8 weeks, and 9 months were normally distributed, with a mean just above 0 and an SD of ∼1. Weight gain z scores were also normally distributed, centiles were constructed, and infants below the fifth centile were classified as cases of growth faltering. A total of 507 children showed slow weight gain from birth to 8 weeks (early group) and 480 children from 8 weeks to 9 months (late group). Thirty children (12 boys, 18 girls) were common to both slow weight gain from 8 weeks to 9 months were also normally distributed, centiles were constructed, and infants below the fifth centile were classified as cases of growth faltering. A total of 507 children showed slow weight gain from birth to 8 weeks (early group) and 480 children from 8 weeks to 9 months (late group). Thirty children (12 boys, 18 girls) were common to both slow weight gain groups. The tables show the controls for the early group: the means and confidence interval (CI) for the late control group were similar, with differences <0.07 SDS. The attained weights are shown in Table 1, and the conditional weight gains (weight velocities) are displayed in Table 2. There were no differences in the proportion of low birth weight infants in the 2 groups compared with controls.10

Longitudinal Growth
Early Weight-Faltering Group
Infants with early weight faltering showed an increased weight velocity compared with controls between 8 weeks and 2 years, resulting in their weight returning toward the reference mean for that age (Fig 1). After 2 years, this group gained weight at a similar rate to the controls. From 7 to 13 years, both the early group and the controls gained weight faster than the reference, but at all points those with previous weight faltering remained lighter than control children; at 13 years, the mean weight for the early group was 3.3 kg below the mean for controls but was still above the mean of the UK reference. Children from the control group had mean weights parallel to and above the reference mean at all age points.

The early group was, on average, shorter than controls at all ages, and there were proportionally more children below the 10th centile (Supplemental Appendix 1). Between 8 weeks and 9 months, the early group grew in length at a slower rate than controls; after 9 months, the length/height velocity of the early group was not different from controls (Table 2). The height velocity of the early group was slower than their weight velocity up to 7 years, resulting in these children being disproportionately short compared with their weight, but these differences disappeared after this age, and there was no difference in mean BMI, MAC, or WC between the early group and controls at 13 years (Table 3). For all these outcome measures, in multivariate analysis, weight SDS at 8 weeks explained the differences between the early group and the controls. The models used in the multivariate analyses are presented in Supplemental Appendix 2.
TABLE 1 Mean (99% CI) Measurements and SDS: Weights, Heights, and BMI for Weight-Faltering Groups and Controls

<table>
<thead>
<tr>
<th>Weight Gain Group</th>
<th>Unit</th>
<th>9 mo</th>
<th>2 y</th>
<th>4 y</th>
<th>Subject Age</th>
</tr>
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<tbody>
<tr>
<td>Early</td>
<td>kg</td>
<td>8.51</td>
<td>11.30</td>
<td>15.68</td>
<td>24.61</td>
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<tr>
<td>Weight</td>
<td>SDS</td>
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<td>-0.21</td>
<td>-0.17</td>
<td>-0.14</td>
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<tr>
<td>cm</td>
<td>SDS</td>
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<td>8.26</td>
<td>9.87</td>
<td>12.82</td>
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<tr>
<td>Height</td>
<td>cm</td>
<td>16.94</td>
<td>16.67</td>
<td>16.07</td>
<td>15.96</td>
</tr>
<tr>
<td>Height</td>
<td>w/h²</td>
<td>-0.38</td>
<td>-0.30</td>
<td>-0.46</td>
<td>-0.18</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>451</td>
<td>352</td>
<td>254</td>
<td>195</td>
<td></td>
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<tr>
<td>n</td>
<td>70.86</td>
<td>70.12</td>
<td>70.38</td>
<td>70.04</td>
<td></td>
</tr>
<tr>
<td>Late</td>
<td>kg</td>
<td>7.51</td>
<td>10.22</td>
<td>14.44</td>
<td>22.80</td>
</tr>
<tr>
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<tr>
<td>cm</td>
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<td>80.32</td>
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<td>15.57</td>
<td>15.51</td>
<td>15.19</td>
</tr>
<tr>
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<td>-1.05</td>
<td>-0.48</td>
<td>-0.51</td>
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<tr>
<td>BMI SDS</td>
<td>419</td>
<td>337</td>
<td>395</td>
<td>235</td>
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<td>n</td>
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<td>16.96</td>
<td>16.26</td>
<td>18.25</td>
<td></td>
</tr>
<tr>
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<td>16.42</td>
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<tr>
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<td>0.01</td>
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<td>20</td>
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</tr>
</tbody>
</table>

Control group are the controls for the early growth-faltering group.

Mothers, not fathers, of the early weight-faltering group were on average slightly shorter and lighter than control mothers (mean height: 163.9 cm [95% CI: 163.3–164.5] vs 163.8 cm [95% CI: 163.6–164.1], p = 0.461). However, in the multivariate model, it did not greatly change the effect size. Mothers, but not fathers, of the early weight-faltering group were the controls for the early growth-faltering group.
factors did not attenuate the differences between the late-faltering group and controls (see models in Supplemental Appendix 2).

Both mothers and fathers of the late group were shorter, by \(\sim 2\) cm on average, than the parents of the controls. Mothers' mean height was 162.0 cm (95% CI: 161.2–162.9 \([n = 410]\)) vs 164.1 cm (95% CI: 163.9–164.3 \([n = 8897]\)). Fathers' mean height was 174.5 cm (95% CI: 173.5–175.7 \([n = 270]\)) vs 176.1 cm (95% CI: 175.9–176.3 \([n = 6895]\)). However, when parental height was included in the multivariate model, it did not change the effect size (Supplemental Appendix 2).

### DISCUSSION

The growth outcomes of children with poor weight gain in infancy showed that by age 13 years, they had achieved heights and weights that were close to the reference mean but lower than their peers. The pattern of weight gain in childhood differed depending on when the weight faltering occurred: those with early weight faltering before 8 years of age had a different growth pattern compared to those with late weight faltering. The early group largely reached the reference mean for weight by the age of 2 years, whereas the late group continued to grow slowly until age 13 years, and remained smaller and lighter than the early group.

The mean weights and heights of the boys and girls at 13 years were not statistically different. No gender differences were found in the pattern of weight or height gain in the early- and late-faltering groups, and no differences were apparent in the age of menarche between either of the weight-faltering groups and the controls.

**Comparison of Early and Late Weight-Faltering**

Although the mean weights of both groups of children whose weight faltered in infancy recovered to close to the population reference mean by age 13 years, the pattern of this recovery was quite different. Figure 1 illustrates that the early group largely reached the reference mean for weight by the age of 2 years, whereas the late group continued to grow slowly until age 13 years, and remained smaller and lighter than the early group.
weeks showed early recovery with enhanced weight gain and had almost “caught up” by 2 years, whereas those with later weight faltering between 8 weeks and 9 months gained weight slowly until 7 years, then had a spurt between 7 and 10 years, but remained considerably shorter and lighter than both the normally growing controls and the early weight-faltering group. The differences in anthropometric outcomes between the growth-faltering groups and controls at 13 years was largely explained by their weight gain in infancy, re-enforcing the importance of the first year of life in determining subsequent growth.

Although the infants who faltered in weight gain did eventually recover their weight, their linear growth remained relatively restricted, with ∼20% below the 10th centile at 13 years, showing that slow weight gain in infancy was associated with subsequent shortness consistent with previous studies.5,9,26 As both parents of the late weight-faltering infants were shorter than the parents of control children, it is likely that a proportion of these children were showing growth patterns normal for their genetic potential. The Millennium Cohort Study in the United Kingdom has concluded that both maternal and paternal height and weight exert independent and significant influences on a child’s birth weight and weight gain between birth and 9 months.27

This study used a large representative cohort and avoided the biases inherent in referred samples of children with failure to thrive. The use of conditional weight gain, both to identify children with slow weight gain in the 2 time periods and to measure their subsequent growth trajectories, adjusted for the regression to the mean; this finding would be expected for small infants at the extreme of the distribution. However, the study has some important limitations, especially missing data: although all subjects selected for this project had complete weight data up to 9 months, loss of follow-up took place from 9 months onward, which increased as children got older, so that some of the variables at 13 years were only available for 44% of the original cohort. However, it is reassuring that there were no differences in the proportion of missing data between the weight gain groups and the controls. We used the 1990 UK growth reference because it has data from birth to 18 years derived from British population surveys, whereas the World Health Organization growth standards are only published up to 5 years of age. It must be acknowledged that much of the data that contributed to the 1990 UK reference were collected in the 1970s and 1980s from a British population that was mainly bottle-fed. However, because we are comparing slow-growing groups with controls assessed against the same standards, the conclusions would not be changed if we had used a different standard. A final limitation is that parental heights were self-reported and not based on clinical measurements. Father’s heights were only available in 56% of the late weight-faltering group, and we therefore used maternal height rather than mid-parental height in the final models.

Because ALSPAC is an observational study, with limited information on use of health services, we cannot ascertain which infants showing weight faltering received nutritional or medical interventions. It is likely that many of the infants putting on weight slowly in the first 2 months would have received interventions in primary care, such as management of feeding problems and increasing energy intake by switching to formula and providing supplementary feeds. We have already reported15 that early slow weight gain in ALSPAC infants was associated with feeding symptoms, and we speculate that the infants in the early-faltering group would have been more readily identified at the 8-week check, resulting in early treatment and therefore a more rapid recovery of weight gain. However, it is also possible that the differences in recovery of weight between early and late weight falterers may reflect different underlying causes and mechanisms.

The term catch-up growth can be defined as increased growth velocity (rapid gain in weight or height) during a defined period of time, after a transient period of growth restriction. However, catch-up weight gain is not always beneficial; for example, children who show pronounced catch-up growth

| TABLE 3 Cross-Sectional BMI, MAC, and WC SDS of Weight-Faltering Groups and Controls at 10 and 13 Years |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Weight Gain Group | Anthropometric Measurement SDS | 10 y | 13 y |
| | BMI | WC | BMI | MAC | WC |
| Early | 0.19 (0.00 to 0.37) | −0.16 (−0.32 to −0.008) | 0.21 (0.02 to 0.40) | −0.13 (−0.30 to 0.04) | −0.15 (−0.32 to 0.02) |
| n | 270 | 270 | 228 | 228 | 228 |
| Late | −0.20 (−0.38 to −0.02) | −0.51 (−0.67 to −0.36) | −0.13 (−0.33 to 0.07) | −0.38 (−0.55 to −0.20) | −0.42 (−0.59 to −0.24) |
| n | 276 | 275 | 220 | 219 | 219 |
| Controls | 0.33 (0.29 to 0.36) | 0.007 (−0.03 to 0.04) | 0.33 (0.29 to 0.38) | 0.006 (−0.03 to 0.04) | 0.007 (−0.03 to 0.04) |
| n | 5925 | 5959 | 4887 | 4879 | 4880 |

Control group are the controls for the early growth-faltering group. Data are presented as mean (99%).
in the first 2 years can develop central obesity.\(^8\) The early-faltering group, who showed catch-up by age 2 years, did demonstrate this tendency with weight disproportionate to height during childhood, but by 13 years, their mean BMI was not different from controls. In comparison, the catch-up growth in the late-faltering group was much later in childhood, and these children remained shorter and lighter with a lower mean BMI than their peers, although the findings were within the reference norms at 13 years. Further follow-up of both groups in ALSPAC will be undertaken to trace their growth outcomes during adolescence.

**CONCLUSIONS**

Overall, clinicians and parents alike will find the growth outcomes at 13 years reassuring, in that both early- and late growth-faltering groups recovered to be within normal ranges by this age. The children whose weight faltered in infancy had BMIs within the normal range at 13 years, and any differences between groups at this age can be explained by weight in infancy rather than by other environmental factors.

**ACKNOWLEDGMENTS**

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