Immediate Postnatal Growth Is Associated With Blood Pressure in Young Adulthood
The Barry Caerphilly Growth Study
Yoav Ben-Shlomo, Anne McCarthy, Rachael Hughes, Kate Tilling, David Davies, George Davey Smith

Abstract—There is a consistent inverse association between birth weight and systolic blood pressure; however, few studies have been able to examine the immediate postnatal period. We have examined whether accelerated postnatal growth predicts adult systolic and diastolic blood pressure. We followed up participants from the Barry Caerphilly Growth Study. Blood pressure data were obtained on 679 of the original 951 subjects (73%) aged 25 years. Both multivariable linear regression and spline models were used to examine the association among weight, length, and growth velocities with systolic blood pressure and diastolic blood pressure. Both statistical approaches showed that birth weight was inversely associated with systolic blood pressure. Only the spline models found that immediate (0 to 5 months) weight gain (β coefficient: 1.29 mm Hg; 95% CI: 0.36 to 2.23; P = 0.007) and weight gain between 1 year and 9 months to 5 years (β coefficient: 1.44 mm Hg; 95% CI: 0.31 to 2.57; P = 0.01) were independently associated with systolic blood pressure, whereas only immediate weight gain (β coefficient: 0.74 mm Hg; 95% CI: 0.08 to 1.41; P = 0.03) was associated with diastolic blood pressure. This is the first study to demonstrate that only immediate postnatal growth predicts diastolic blood pressure in term births, whereas it adds further evidence that both birth weight and postnatal growth are associated with systolic blood pressure in support of both the fetal origins and growth acceleration hypotheses. (Hypertension. 2008;52:638-644.)

Key Words: blood pressure ▪ birth weight ▪ cohort study ▪ growth and development ▪ public health

It has been argued that the origin of many adult chronic diseases lies in the early intrauterine experience of the fetus, which programs anatomic, physiological, and endocrine pathways leading to cardiovascular and other diseases. However, fetal growth is just 1 period of development, and influences acting across other phases of the life course may be of similar importance. Evidence cited supporting the fetal origins of adult disease comes from the consistent inverse association between birth weight and blood pressure seen in both developed and developing world populations. The clinical importance of this association remains controversial with suggestions that the magnitude has been overestimated because of publication bias, may be because of genetic effects, and may have resulted from the inappropriate adjustment for adult body size. The strengthening of the birth weight association by adjustment for later size has been interpreted as providing evidence that postnatal “catch-up” growth or centile crossing, rather than prenatal development, is the more critical event, and evidence from the long-term follow-up of randomized trials of breast and formula milk has led to the “growth acceleration hypothesis”; more rapid catch-up growth, particular in the immediate postnatal infancy period and related to nutritional supplementation, rather than poor uterine development, per se, is the key component of the early life blood pressure association.

However, although there are >50 studies comparing birth weight with later blood pressure, there are few that have information on growth in childhood and later blood pressure and none, to our knowledge, that have very detailed measures of postnatal and early childhood growth with adult measures of blood pressure. We have examined the fetal origins and growth acceleration hypotheses by examining whether different growth patterns in early life are associated with adult blood pressure.

Methods
The Barry Caerphilly Growth Study is a follow-up of a randomized, controlled trial undertaken from 1972 to 1974 in 2 small towns in South Wales, United Kingdom. The original trial participants were...
composed of all of the resident pregnant mothers and their offspring, who were followed up until 5 years of age. Women in the supplemented group were provided with milk tokens throughout pregnancy and, subsequently, for their child until the age of 5 years. In the late 1990s, the offspring were recontacted and invited to participate in a (follow-up) study when \( z \) years of age. The Bro Taf Local Research Ethics Committee approved the follow-up study, and subjects provided informed consent.

A total of 1288 women were eligible, and only 37 (2.9%) refused to cooperate, leaving 1251 participants. Of these, 88 women were subsequently excluded from the study because of miscarriage or because they were not pregnant or moved away from the research area, leaving 1163 mothers who were enrolled into the trial. A total of 951 singleton children (88.8%) completed the trial at 5 years (18.2% loss). An analysis of the characteristics of the participants who dropped out in the first 5 years did not reveal evidence of any systematic bias in terms of birth weight or other maternal characteristics (see Reference 12 for more details of the original study).

After birth, the infants were visited at 10 days, 6 weeks, and at 3, 6, 9, and 12 months, and thereafter at 6 monthly intervals (resulting in 14 home visits) until their fifth birthday. Birth weight was obtained from hospital records, and thereafter weight and height were measured by trained study nurses. The follow-up study contacted the adult participants \( z \) years of age and asked them to complete a questionnaire and attend a screening clinic where they were asked to empty their bladder, change into a hospital gown, and rest supine for 10 minutes. Blood pressure was then recorded twice, by 2 trained research nurses, using an Omron Model HEM-705CP sphygmomanometer placed on the left arm, with the subject supine and with the sphygmomanometer at heart level. The first phase was used for systolic blood pressure (SBP) and the fifth phase for diastolic blood pressure (DBP). The second reading was taken after an additional 5-minute interval. The mean of these 2 readings was used for analysis.

### Statistical Analysis

We used 2 different approaches to model the effects of prenatal and postnatal growth on adult blood pressure. Simple linear regression was used to examine the effects of early growth on later blood pressure. Because of the multitude of measurements, we reduced the data by only including measures at birth, 3.0 months, 1.5 years, and 5.0 years. These time points were chosen because we were specifically interested in testing the accelerated early growth hypothesis. For birth weight, internal \( z \) scores were derived for all of the births that took place between 36 and 44 weeks’ gestation and were standardized by sex and gestational age (in weeks). For the other growth measures, internal \( z \) scores were standardized by sex and age at the time of the measurement for all of the children in the original study.

The second approach was more complex, using a within-subject analysis of all 14 childhood measurements in developing a linear spline random-effects model with 2 knots (thus dividing follow-up into 3 time periods, each with its own gradient). This accounts for repeated measures on the same individuals. The 4 between-subject random effects from the spline model are, thus, a within-subject summary of an individual’s growth curve from birth to 5 years, denoting the deviation from the average predicted birth weight and the deviation from the average predicted growth rate (kilograms per year) for each of the 3 time periods. These are defined as “immediate weight velocity” (between birth and 5 months), “infant weight velocity” (between 5 months and 1 year and 9 months), and “childhood weight velocity” (between 1 year and 9 months and 5 years). These variables were converted into \( z \) scores so that the sizes of the coefficients were directly comparable. Analyses of the adult outcome measures were undertaken using linear regression with the 4 random effects (the deviation from the average predicted birth weight and the deviation from the average predicted growth rate for each of the 3 time periods) as exposures. Additional details of this model are reported elsewhere.

We examined the effects of early growth with 4 incremental models to account for potential confounders: (1) adjusting for adult age, sex, room temperature, and observer; (2) as in 1 but with mutual adjustment for all of the growth measures; (3) as in 2 but with the addition of maternal and paternal weight and height and parental social class in childhood; and (4) as in 3 but with the addition of maternal smoking and adult waist:hip ratio, the latter of which may act as an intermediary between earlier growth and adult blood pressure. We choose waist:hip ratio as our measure of adiposity, because it was a stronger predictor of blood pressure than body mass index, waist circumference, and sagittal abdominal diameter.

### Results

Of the 951 subjects who completed the original study, 23 were untraceable or had died or emigrated; 679 (73%) of the remaining 928 agreed to attended the adult follow-up clinic. Male subjects were heavier than female subjects for all 14 of the time points in childhood \( P<0.01 \). They also had higher SBP and DBP \( P<0.001; \) Table 1. We have shown previously that younger maternal age, unclassified social class, and lighter birth weight predicted loss to follow-up (see Reference 14 for detailed analysis).

The strength of association between standardized SBP and DBP with weight at each time point is shown in panel A of the Figure. We used the standardized measures rather than actual values, because the mean and SD of DBP are smaller than those of SBP, so effects look weaker simply because

### Table 1. Basic Descriptive Data on Anthropometric Measures and Adult Blood Pressure by Gender

<table>
<thead>
<tr>
<th>Variable</th>
<th>Men (n=362)</th>
<th>Women (n=318)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>Mean 3.44  SD 0.49 Range 1.99 to 4.86</td>
<td>Mean 3.30  SD 0.51 Range 1.88 to 4.69</td>
</tr>
<tr>
<td>3.0 mo</td>
<td>Mean 6.42  SD 0.73 Range 4.10 to 8.82</td>
<td>Mean 5.83  SD 0.66 Range 3.90 to 7.64</td>
</tr>
<tr>
<td>1.5 y</td>
<td>Mean 12.1  SD 1.3 Range 8.64 to 16.3</td>
<td>Mean 11.3  SD 1.2 Range 7.88 to 14.9</td>
</tr>
<tr>
<td>5.0 y</td>
<td>Mean 19.1  SD 2.3 Range 13.5 to 31.0</td>
<td>Mean 18.6  SD 2.3 Range 11.0 to 26.4</td>
</tr>
<tr>
<td>Adult measures</td>
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<tr>
<td>Age, y</td>
<td>Mean 25  SD 0.7 Range 23 to 27</td>
<td>Mean 25  SD 0.7 Range 23 to 26.8</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>Mean 123.5  SD 11.1 Range 100 to 169</td>
<td>Mean 108.0  SD 9.4 Range 86 to 144</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>Mean 71.5  SD 7.6 Range 55 to 93</td>
<td>Mean 68.3  SD 7.1 Range 53 to 102</td>
</tr>
<tr>
<td>Waist:hip ratio, ( \times 100 )</td>
<td>Mean 83.5  SD 5.1 Range 71.2 to 101.8</td>
<td>Mean 71.2  SD 6.0 Range 60.6 to 95.6</td>
</tr>
</tbody>
</table>
there was no effect with DBP. Ponderal index showed a similar pattern to birth weight, although it appeared more bimodal with a second peak around 3 years, although this could have been a chance fluctuation ($P=0.12$ for SBP). Given the similarity between the weight and ponderal index pattern, we have chosen to only present the detailed models for birth weight.

Table 2 shows the regression coefficients for birth weight and weight at 3.0 months, 1.5 years, and 5.0 years for both SBP and DBP. There was little difference if the intervention arm was included in the model, because this did not predict blood pressure. Gestational age alone did not predict either SBP ($P=0.40$) or DBP ($P=0.17$). Adjustment for the later growth measures increased the inverse association between birth weight and SBP, although this was somewhat attenuated in the final model that also included adult waist:hip ratio as a potential intermediary. All of the associations with DBP were compatible with chance. A further analysis using birth length and height found that only height at 5 years showed a positive association with SBP (model 4 height at 5 years $\beta$ coefficient: 1.93; 95% CI: 0.52 to 3.34; $P=0.007$), whereas birth length showed an association with DBP (model 4: birth length $\beta$ coefficient: $-0.88$; 95% CI: $-1.74$ to $-0.02$; $P=0.05$). We repeated model 2 but also included the trial intervention arm to ensure that this did not alter our results; the $\beta$ coefficients for SBP with birth weight and weight at 3.0 months, 1.5 years, and 5.0 years were $-1.67$, $0.69$, $-0.08$, and $0.99$, respectively, which were almost the same as the results in Table 2. Results for DBP were hardly altered after including the intervention arm into the models.

The correlations among the 4 standardized weight measures were moderately high (between 0.30 and 0.72), but this was much weaker for the birth weight and spline coefficients (between 0.05 and 0.48), with the correlation between birth weight and immediate weight velocity only being 0.07. The spline models revealed different patterns of results (Table 3). Although birth weight remained inversely associated with SBP, immediate postnatal growth between 0 and 5 months, both with and without adjustment for the other growth measures, was associated positively with higher SBP. The same pattern was seen for DBP, but now only immediate postnatal growth had a strong enough effect to provide modest evidence to reject the null hypothesis ($P=0.04$). To compare our results with the Hertfordshire cohort, we also examined the association between weight at 1 year and SBP. This found a weak positive effect that was consistent with chance variation ($\beta$ coefficient for 1 SD change in weight at 1 year: $0.55$ mm Hg; 95% CI: $-0.25$ to 1.35; $P=0.18$).

The results with birth length and height found that immediate height gain (fully adjusted $\beta$ coefficient: 1.50; 95% CI: 0.46 to 2.53; $P=0.005$) and childhood height gain (fully adjusted $\beta$ coefficient: 1.78; 95% CI: 0.45 to 3.12; $P=0.009$) were positively associated with SBP, similar to weight gain and, if anything, even stronger. Only infant height gain predicted DBP ($\beta$ coefficient: 0.73; 95% CI: 0.02 to 1.47; $P=0.05$). There was no evidence of sex differences in the associations between early growth and blood pressure using either method.

they are not on the same scale. There was an inverse association with birth weight, which reversed and became maximally positive at 9 months. Thereafter, the relative size of effect was fairly similar. The associations with DBP were only seen with birth weight and the immediate postnatal period, after which there was no association. The associations with birth length and height were rather different. There was an inverse association with birth length, which was abolished by 6 months and thereafter a gradual increase in effect size.
Table 2. Association Between Birth Weight and Weight in Infancy and Childhood (z Score) With Adult SBP and DBP

<table>
<thead>
<tr>
<th>Variables</th>
<th>Model 1 (n=623)†</th>
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<tbody>
<tr>
<td></td>
<td>β Coefficient</td>
<td>95% CI</td>
<td>P</td>
<td>β Coefficient</td>
<td>95% CI</td>
<td>P</td>
<td>β Coefficient</td>
<td>95% CI</td>
<td>P</td>
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<tr>
<td>SBP, mm Hg</td>
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<tr>
<td>Birth weight*</td>
<td>−0.94</td>
<td>−1.77 to −0.11</td>
<td>0.03</td>
<td>−1.61</td>
<td>−2.60 to −0.61</td>
<td>0.002</td>
<td>−1.47</td>
<td>−2.57 to −0.37</td>
<td>0.009</td>
</tr>
<tr>
<td>Weight at 3.0 mo</td>
<td>0.21</td>
<td>−0.60 to 1.02</td>
<td>0.61</td>
<td>0.70</td>
<td>−0.42 to 1.82</td>
<td>0.22</td>
<td>0.47</td>
<td>−0.79 to 1.72</td>
<td>0.46</td>
</tr>
<tr>
<td>Weight at 1.5 y</td>
<td>0.34</td>
<td>−0.46 to 1.15</td>
<td>0.40</td>
<td>−0.07</td>
<td>−1.35 to 1.21</td>
<td>0.92</td>
<td>0.44</td>
<td>−0.98 to 1.85</td>
<td>0.55</td>
</tr>
<tr>
<td>Weight at 5.0 y</td>
<td>0.77</td>
<td>−0.03 to 1.57</td>
<td>0.06</td>
<td>0.97</td>
<td>−0.24 to 2.19</td>
<td>0.12</td>
<td>0.76</td>
<td>−0.66 to 2.18</td>
<td>0.29</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
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<tr>
<td>Birth weight*</td>
<td>−0.47</td>
<td>−1.06 to 0.11</td>
<td>0.11</td>
<td>−0.81</td>
<td>−1.51 to −0.12</td>
<td>0.02</td>
<td>−0.85</td>
<td>−1.63 to −0.08</td>
<td>0.03</td>
</tr>
<tr>
<td>Weight at 3.0 mo</td>
<td>0.21</td>
<td>−0.35 to 0.77</td>
<td>0.46</td>
<td>0.74</td>
<td>−0.04 to 1.53</td>
<td>0.06</td>
<td>0.56</td>
<td>−0.33 to 1.44</td>
<td>0.22</td>
</tr>
<tr>
<td>Weight at 1.5 y</td>
<td>0.02</td>
<td>−0.55 to 0.58</td>
<td>0.96</td>
<td>−0.18</td>
<td>−1.08 to 0.73</td>
<td>0.70</td>
<td>0.07</td>
<td>−0.93 to 1.07</td>
<td>0.88</td>
</tr>
<tr>
<td>Weight at 5.0 y</td>
<td>0.09</td>
<td>−0.47 to 0.64</td>
<td>0.75</td>
<td>0.11</td>
<td>−0.74 to 0.97</td>
<td>0.79</td>
<td>0.11</td>
<td>−0.89 to 1.11</td>
<td>0.83</td>
</tr>
</tbody>
</table>

For model 1, each growth measure is adjusted for adult age, sex, room temperature, and observer; for each other, model 2 is as 1, but each growth measure is now mutually adjusted for each other; model 3 is as 2 but with the addition of the use of parent heights and weights and parental social class in childhood; and model 4 is as 3 but with the addition of maternal smoking in pregnancy and adult waist:hip ratio.

Table 3. Association Between Birth Weight and Immediate, Infant, and Childhood Weight Velocities (z Score) With Adult SBP and DBP

<table>
<thead>
<tr>
<th>Variables</th>
<th>Model 1 (n=600)</th>
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<tr>
<td></td>
<td>β Coefficient</td>
<td>95% CI</td>
<td>P</td>
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<td>95% CI</td>
<td>P</td>
<td>β Coefficient</td>
<td>95% CI</td>
<td>P</td>
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<tr>
<td>SBP, mm Hg</td>
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</tr>
<tr>
<td>Birth weight*</td>
<td>−0.88</td>
<td>−1.76 to 0.01</td>
<td>0.05</td>
<td>−1.13</td>
<td>−2.22 to −0.05</td>
<td>0.04</td>
<td>−1.17</td>
<td>−2.27 to −0.08</td>
<td>0.04</td>
</tr>
<tr>
<td>Immediate (0 to 5 mo)</td>
<td>1.17</td>
<td>0.35 to 2.00</td>
<td>0.006</td>
<td>1.29</td>
<td>0.36 to 2.23</td>
<td>0.007</td>
<td>1.22</td>
<td>0.28 to 2.17</td>
<td>0.01</td>
</tr>
<tr>
<td>Infant (5 mo and 1 y and 9 mo)</td>
<td>0.43</td>
<td>−0.39 to 1.26</td>
<td>0.30</td>
<td>0.19</td>
<td>−0.84 to 1.23</td>
<td>0.72</td>
<td>0.15</td>
<td>−0.91 to 1.21</td>
<td>0.78</td>
</tr>
<tr>
<td>Child (1 y and 9 mo and 5 y)</td>
<td>1.00</td>
<td>0.15 to 1.84</td>
<td>0.02</td>
<td>1.44</td>
<td>0.31 to 2.57</td>
<td>0.01</td>
<td>1.31</td>
<td>0.16 to 2.46</td>
<td>0.03</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
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</tr>
<tr>
<td>Birth weight*</td>
<td>−0.38</td>
<td>−1.00 to 0.24</td>
<td>0.23</td>
<td>−0.56</td>
<td>−1.33 to 0.21</td>
<td>0.16</td>
<td>−0.57</td>
<td>−1.35 to 0.21</td>
<td>0.15</td>
</tr>
<tr>
<td>Immediate (0 to 5 mo)</td>
<td>0.62</td>
<td>0.04 to 1.21</td>
<td>0.04</td>
<td>0.74</td>
<td>0.06 to 1.41</td>
<td>0.03</td>
<td>0.72</td>
<td>0.04 to 1.39</td>
<td>0.04</td>
</tr>
<tr>
<td>Infant (5 mo and 1 y and 9 mo)</td>
<td>−0.31</td>
<td>−0.89 to 0.26</td>
<td>0.29</td>
<td>−0.27</td>
<td>−1.00 to 0.47</td>
<td>0.47</td>
<td>−0.25</td>
<td>−1.00 to 0.50</td>
<td>0.51</td>
</tr>
<tr>
<td>Child (1 y and 9 mo and 5 y)</td>
<td>0.13</td>
<td>−0.46 to 0.72</td>
<td>0.67</td>
<td>0.59</td>
<td>−0.21 to 1.40</td>
<td>0.15</td>
<td>0.50</td>
<td>−0.32 to 1.32</td>
<td>0.23</td>
</tr>
</tbody>
</table>

For model 1, each growth measure is adjusted for adult age, sex, room temperature, and observer; for each other, model 2 is as 1, but each growth measure is now mutually adjusted for each other; model 3 is as 2 but with the addition of the use of parent heights and weights and parental social class in childhood; and model 4 is as 3 but with the addition of maternal smoking in pregnancy and adult waist:hip ratio.

*All of the measures have been z scored.

Discussion

This is the first study that has modeled detailed growth trajectories over the first 5 years in relation to blood pressure in adult life. No other studies, that we know, have such detailed measures over the first few years of life and over 20 years of follow-up. We have shown that a more sophisticated approach to modeling growth periods was more sensitive in identifying effects on SBP than the conventional approach of adding anthropometric parameters at arbitrary ages, although the findings with DBP were broadly similar. This approach models changes in growth velocity rather than anthropometry.
at 1 time point, which, from an etiologic perspective, is the more relevant exposure. We have specifically identified that rapid postnatal weight and increases in length in the first 5 to 6 months of life may be important for both future SBP and DBP independent of fetal growth, weight gain in later childhood, and adult adiposity. Our associations were present before any adjustment for adult adiposity and cannot be dismissed as mere statistical artifact. Birth weight adjusted for gestational age showed that the well-documented inverse association with blood pressure and childhood weight gain was positively associated with higher SBP. These data suggest that both prenatal and postnatal growth patterns are important and are consistent with both the fetal origins and growth acceleration hypotheses. We can only speculate on the possible pathophysiological mechanism behind these associations, but it has been argued that abnormal patterns of growth, both prenatally and in the immediate postnatal period, may have long-term effects on the ratio of elastin to collagen fibers in the arterial wall. The effect of postnatal growth on DBP is relatively novel and may be of clinical importance, because longitudinal analysis from the Framingham Heart Study has shown that isolated diastolic hypertension is a very strong predictor of new-onset systolic diastolic hypertension.

Several publications have emerged from the long-term follow-up of randomized, controlled trials of infant feeding, although these studies only had prehospital discharge measures at several weeks of age. Preterm infants (130 subjects) randomly assigned to formula milk compared with banked breast milk showed greater weight gain before discharge and had higher mean arterial blood pressure, DBP, and SBP, although the latter was consistent with chance. A similar study recruiting 250 small-for-gestational-age infants, randomly assigned to standard formula, nutrient-enriched formula, or breastfeeding, also found that the nutrient-enriched group had higher mean arterial pressure and DBP, with a weaker effect on SBP. One must be cautious before generalizing the results from preterm and small-for-gestational-age infants to all term births. Other but not all observational cohorts have also found positive associations between childhood growth and later life blood pressure.

The Minneapolis Children’s Blood Pressure Study found that faster rates of weight gain in childhood and adolescence were both associated with increased SBP. The Brompton cohort study found that conditional childhood weight gain, between 1 and 5 years, showed a positive association with SBP but not DBP. Conditional infant weight gain, between birth and 1 year, showed a weak positive association, which was totally attenuated after adjustment for adult body mass index. A Japanese study from Ishikawa found that weight at age 3 years and weight gain from ages 3 to 20 years were positively associated with SBP and DBP, whereas an increase in height from 3 to 20 years was inversely associated with SBP. Two Finnish studies found that weight gain during the first year of life was positively associated with SBP but not DBP at 7 and 31 years of life. A retrospective cohort study of children born between 1934 and 1944 from Helsinki, Finland, found that hypertensive subjects were lighter at birth and caught up to average weight by 6 to 7 years, thereafter being heavier than normotensive subjects, although different patterns were observed for subjects with diagnosed hypertension than with undiagnosed hypertension.

Other studies either show no association or an inverse association between early life changes in anthropometry and later-life blood pressure. There are several possible factors for these divergent findings. There are major differences in the analytic strategies. For example, a simple analysis of weight at 1 year in our data set, as in the Hertfordshire cohort, would find no association between early growth and SBP. In some studies, the effects or early growth are attenuated or even reversed after adjustment for a later measure of growth. For example, the Pelotas cohort in Brazil found that weight at 2 years was positively associated with SBP at 15 years, but after adjustment for weight at 4 and 15 years it can became inversely associated. Finally, there may be genuine heterogeneity in the effects of postnatal growth depending on its social and biological context. So, rapid infant growth may reflect recovery from fetal growth restriction and normalization of body weight within a developing world context or excess growth resulting in infant obesity in a developed world context.

One logical explanation for our associations is that faster postnatal and childhood growth alter an individual’s trajectory or endocrine status so that he or she is more likely to be obese or insulin resistant in later life. In our study, childhood weight gain was a much stronger predictor of adult body mass index than immediate weight gain, and neither predicted waist:hip ratio. It is possible that postnatal growth operates through a different pathway, such as the development of the vascular tree. Greater weight gain in the first 2 weeks of life was associated with worse endothelial function between 13 and 16 years among preterm babies. We have failed previously to find an association between birth weight and arterial stiffness in this cohort, but we did not examine immediate postnatal weight gain.

**Strengths and Limitations**

The study has several important strengths. First, we are unaware of any study with as many as 14 measures of growth between birth and 5 years and long-term follow-up. This has allowed us to differentiate different patterns of growth in early life using more complex spline regression methods rather than growth measures at arbitrary time points. This may identify potential critical or sensitive periods for intervention, which are based on biological growth patterns defined a priori, rather than examining multiple time points in an ad hoc fashion and then choosing those that show the largest association with the outcome. Our approach also allows us to examine within-subject variations and reduces the problem of collinearity between repeated growth measures made over short time periods. It also allows one to better handle missing data at any specific time point, which are dropped in the simpler analysis. However, we did not have growth data between 6 and 24 years of age. In addition, there was some inevitable loss to follow-up, which was associated
with lighter birth weight\(^ {14}\); however, this was relatively small compared with most studies and is unlikely to be related to differences in blood pressure, because the cohort is still young and in good health.

**Perspectives**

These findings suggest that developmental factors acting both prenatally and postnatally may alter future blood pressure. We cannot elucidate the mechanisms underlying these associations. They may reflect a common genetic effect whereby genes that regulate postnatal growth themselves determine blood pressure. They may be the influence of postnatal environmental factors, which could influence an individual’s biological trajectory so that more rapid growth, adaptive in the short-term, could have a maladaptive effect in later life. They could reflect the influence of both genes and environment through epigenetic influences or a gene-environment interaction. Future work needs to explore these possibilities, preferably through an experimental paradigm, e.g., the effect of nutritional supplementation on later blood pressure in humans or animals or by studying known genetic variants that are associated either with blood pressure or growth. This study shows that both birth weight and the immediate postnatal period may be important in determining both SBP and DBP and, hence, the future risk of both essential and isolated systolic hypertension. This highlights the need to consider life course influences on the developmental trajectories of infants, children, and adolescents.

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**Disclosures**

None.

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