

## ORIGINAL ARTICLE

# Weight gain in infancy and markers of cardiometabolic health in young adulthood

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## Funding information

This research was funded by the Academy of Finland (grants 206374, 294834, 251360, 275595, 307996, 322112), the Juho Vainio Foundation, the Finnish Foundation for Cardiovascular Research, the Finnish Ministry of Education and Culture, the Finnish Cultural Foundation, the Sigrid Jusélius Foundation, Special Governmental grants for Health Sciences Research (Turku University Hospital), the Yrjö Jahnsson Foundation, the Finnish Medical Foundation and the Turku University Foundation

## Abstract

**Aim:** We studied whether repeatedly measured weight gain from birth up to age 2 years associated with cardiometabolic health in young adulthood.

**Methods:** Using the data collected in the longitudinal Special Turku Coronary Risk Factor Intervention Project, we investigated in 454 healthy subjects how early weight gain in six age intervals (birth to 7 months, 7–13 months, 13–18 months, 18–24 months, and birth to 13 and 24 months) associated with measures of cardiometabolic health at age 20 years. Linear regression analyses were controlled for (1) child's sex, intervention/control group, gestational age, baseline weight and change in length for each interval, and (2) parents' education, mother's weight before pregnancy, height and weight gain during pregnancy, and father's body mass index at the 7-month visit.

**Results:** Weight gain after the first year of life associated directly, when adjusted for traits of the child and parents, with systolic blood pressure, waist circumference and body mass index at age 20 years. In the fully adjusted analyses, weight gain from birth to 1 year and to 2 years of age associated inversely with insulin and insulin resistance. We found no association between early growth and diastolic blood pressure or serum lipids.

**Conclusion:** Early weight gain during first 2 years of life may predict later markers of cardiometabolic health.

## KEYWORDS

cardiometabolic health, infancy, weight gain

**Abbreviations:** BMI, body mass index; BP, blood pressure; BW, birth weight; CI, confidence interval; CVD, cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; SDS, standard deviation scores; SES, socioeconomic status; STRIP, Special Turku Coronary Risk Factor Intervention Project; WC, waist circumference.

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## 1 | INTRODUCTION

It has been suggested that birth weight (BW) predicts risk for later non-communicable diseases.<sup>1-3</sup> Further studies have shown that not only BW, but also early postnatal growth, may predict later disease risk.<sup>2</sup> Low BW combined with rapid early weight gain is thought to increase the later risk factors for cardiovascular disease (CVD) more than low BW alone.<sup>2,4,5</sup> Similar results have been obtained in studies on infants with high BW, in whom rapid early weight gain also predicted a higher risk for later obesity.<sup>3</sup> Previous reviews have shown a link between rapid postnatal weight gain and increased risk for later obesity and CVD risk factors.<sup>6-8</sup> Rapid early weight gain has also been associated with higher blood pressure (BP) measured in children and adults.<sup>9</sup> Studies on the associations between of early growth with insulin resistance and risk for type 2 diabetes have found contradicting results.<sup>10</sup> There also are indications that childhood socioeconomic status (SES) affects later risk for obesity and later CVD risk.<sup>11</sup>

Only few previous studies can combine early growth data measured repeatedly during the first years of life with several cardiometabolic risk factors measured in early adulthood. To fill this gap in knowledge, we applied longitudinal data from the Special Turku Coronary Risk Factor Intervention Project (STRIP), that is a prospective, randomised, controlled infancy-onset trial that offers unique data to provide evidence on the associations of early weight gain with multiple markers of cardiometabolic health in adulthood. Additional uniqueness of the data is that it is collected prospectively with well-established methods, and it also comprises of a relatively large number of participants who were measured repeatedly. Therefore, leveraging the repeatedly measured STRIP Study data, we investigated the association between early weight gain, from birth to age 2 years, and cardiometabolic health markers measured at the age of 20 years.

## 2 | PATIENTS AND METHODS

### 2.1 | STRIP study design

The STRIP study is a prospective, infancy-onset, randomised controlled trial to prevent atherosclerosis risk factors beginning from age 7 months and continuing to the age of 20 years. The recruitment of 5-month-old infants and their families began in March 1990 at well-baby clinics in Turku, Finland, and continued until June 1992. 1062 infants participated in the study and were subsequently randomly allocated into the intervention group ( $n = 540$ ) or control group ( $n = 522$ ).

The intervention group received individualised dietary counselling at least biannually, beginning from 8 months of age until 20 years of age. The control group was seen biannually until 7 years of age and annually between ages 7 and 20 years. The intervention in the STRIP study consisted of a dietary intervention to improve dietary fat quality and reduce cholesterol intake, as well as to increase

### Key Notes

- Weight gain in early life is directly linked with body mass index, waist circumference and systolic blood pressure in young adulthood.
- Excess weight gain during transition from infant feeding to a diet similar to the family may be of utmost significance.
- Prevention of cardiovascular disease should begin in infancy.

consumption of vegetables, fruit and whole grains. Previous results have shown that the STRIP intervention was successful in decreasing saturated fat intake<sup>12</sup> and improving many cardiometabolic health markers.<sup>13</sup> Better adherence to the dietary targets, regardless of study group allocation, was associated with a decreased intake of saturated fatty acids and a 0.1–0.2 mmol/L decrease in low-density lipoprotein cholesterol (LDL-C).<sup>14</sup> The control group received basic health education given at Finnish baby-well clinics and school health care. Both study groups met the same study personnel and similar measurements were performed on both groups.

Informed consent was obtained from the parents at the beginning of the study and from the children at the ages 15 years and 18 years. The study protocol of the STRIP Study is approved by the local ethics committee and the guidelines of the Declaration of Helsinki are followed accordingly.<sup>12,15</sup>

The present study included all study participants who took part in the study visit at the age of 20 years. Eighteen subjects were excluded from the present analyses because of known conditions that could have influence on growth, blood cholesterol/triglyceride values or insulin measurements (two twin pairs, Down syndrome, familial hypercholesterolemia, type 1 diabetes mellitus, cerebral palsy and other developmental disorders). Finally, data of 454 participants were used. Out of these 235 (51.8%) were female and 219 (48.2%) were male. Of the study population, 45.1% ( $n = 205$ ) belonged to the intervention group and 54.9% to the control group ( $n = 249$ ).

### 2.2 | Measurements of growth and blood pressure

Mother's pre-pregnancy and pregnancy data, and the BW of the infant were obtained from databases maintained by well-baby clinics and maternity hospitals. Father's body mass index (BMI) and parents' SES were collected during 7-month or 13-month study visits. Weight and height of the infant was measured at the 7-month, 13-month, 18-month and 24-month study visits. Measurements collected at the 20-year study visit included BP, weight, height, BMI and waist circumference (WC).

Before the age of 18 months, weight was measured with an infant scale (model 725; Seca, Murrhardt, Germany), and an infant

TABLE 1 Mean (SD) weight gain (g) in different age intervals from birth to 2 years of age

Age interval (n)	All	Boys	Girls	p-Value between boys and girls	Intervention group	Control group	p-Value between groups
Birth–7 months (450)	4896 (799)	<b>5141 (744)</b>	<b>4667 (783)</b>	<0.0001	4953 (815)	4848 (785)	0.16
7–13 months (449)	1774 (542)	1795 (511)	1754 (569)	0.43	1793 (514)	1758 (564)	0.50
13–18 months (425)	1314 (501)	1282 (494)	1344 (506)	0.20	1342 (466)	1290 (528)	0.28
18–24 months (415)	1304 (562)	<b>1219 (519)</b>	<b>1385 (588)</b>	<b>0.002</b>	1287 (542)	1318 (577)	0.57
Birth–13 months (453)	6675 (922)	<b>6943 (886)</b>	<b>6424 (887)</b>	<0.0001	6745 (939)	6617 (907)	0.14
Birth–24 months (440)	9276 (1288)	<b>9436 (1157)</b>	<b>9127 (1387)</b>	<b>0.01</b>	9357 (1321)	9209 (1259)	0.23

Note: *n* referenced to subjects with measurements at 20-years. Bold indicates  $p < 0.05$ .

board (Bekvil; Paljerakene, Helsinki, Finland) was used for the measurement of length before the age of 24 months.

Measurement of weight at the age of 24 months and thereafter was done with an electronic scale (S10; Soehnle, Murrhardt, Germany) to the nearest 0.1 kg. Height was measured to the nearest 0.1 cm with a Harpenden stadiometer (Holtain) from the age of 24 months forwards. Using these measures, BMI was calculated as weight in kilograms divided by height in metres squared ( $\text{kg}/\text{m}^2$ ).

Waist circumference was measured at the age of 20 years with a flexible measuring tape to the nearest 0.5 cm midway between the iliac crest and the lowest rib at the midaxillary line.

Blood pressure was measured at the age of 20 years twice using an oscillometric noninvasive blood pressure monitor (Criticon Dinamap Compact T) after  $\geq 15$  min of rest. Accuracy of the device was regularly tested against a mercury manometer. An appropriate cuff size was chosen according to the subject's right arm. The average of the two measurements was used in statistical analyses.<sup>15–17</sup>

### 2.3 | Laboratory methods

Markers of cardiometabolic health obtained at the 20-year study visit included serum total cholesterol, high-density lipoprotein cholesterol (HDL-C), calculated LDL-C, triglycerides, glucose, insulin and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). All analyses were done from serum samples obtained after an overnight fast and performed at the laboratory of the National Public Health Institute in Turku, Finland.<sup>13</sup>

For serum lipid analyses, the blood samples were low-speed centrifuged after clotting at room temperature and the separated serum was frozen until analysed. Serum total cholesterol and triglyceride concentrations were measured using a fully enzymatic cholesterol oxidase-p-aminophenazone method (Merck, Darmstadt, Germany) with an automatic Olympus AU400 analyser.<sup>15</sup> Serum HDL-C concentration was analysed after precipitation of non-HDL-lipoproteins

with dextran sulphate 500,000.<sup>13</sup> LDL-C concentration was calculated using the Friedewald formula, and none of the participants had triglycerides  $>4.25$  mmol/L ( $>400$  mg/dl).<sup>15</sup>

Serum glucose was measured by a hexokinase method (Glucose Olympus System Reagent, Olympus, Ireland, interassay CV 1.8%). For insulin analyses, the blood samples were centrifuged immediately and 30  $\mu\text{l}$  Trasylol was added to the 0.5-ml serum sample and the samples were frozen until analysed. Serum insulin was measured by radioimmunoassay (Pharmacia Diagnostics, Uppsala, Sweden).<sup>15</sup> Insulin sensitivity was estimated by calculating HOMA-IR (fasting insulin  $\text{mU}/\text{L} \times [\text{fasting glucose (mmol/L)} / 22.5]$ ).<sup>18</sup>

### 2.4 | Statistics

Normally distributed measures are reported with the mean value and standard deviation (SD).

Distributions of the continuous variables were evaluated visually and using the Kolmogorov–Smirnov test. The differences in the amount of weight gain within six age intervals (birth to 7 months, 7–13 months, 13–18 months, 18–24 months and birth to 13 months and 24 months) were analysed using pooled t-test when assumption of equal variances was met and with Satterthwaite test when variances were assumed unequal. The equality of variances was tested with the Levene's test.

Association between early weight gain in different age intervals and cardiovascular health markers at the age of 20 years was studied using linear regression analyses. Non-normally distributed measures were logarithmically transformed prior to the analyses (triglycerides, insulin and HOMA-IR). Weight gain in the different age intervals was converted to standard deviation scores (SDS). The results from the linear regression analyses were presented as beta-value, 95% confidence interval (CI) of the regression line and p-value and as the impact of +1SD excess weight gain in all intervals.

Statistical analyses were first adjusted for traits of the child (sex, STRIP study group, gestational age, baseline weight for each interval

and change in length for each interval; Model 1) and after that additionally for traits of the parents (parents' education, mother's weight before pregnancy, height and weight gain during pregnancy, and father's BMI; Model 2).

Weight gain within all the different age intervals was normally distributed (Table 1).

To investigate whether the associations between early growth and the cardiometabolic markers at the age of 20 years differ in males and females, we introduced a sex\*interaction term to the analyses using mixed model analysis of variance.

Statistical analyses were conducted using SAS statistical software, release 9.4 (SAS Institute Inc.).  $p$ -values  $< 0.05$  were considered statistically significant.

### 3 | RESULTS

The mean increase in weight from birth to age 24 months was 9280 (SD = 1284) grams. There was no significant difference in weight gain in any of the age intervals between the STRIP Study groups (intervention/control). Boys gained more weight than girls from birth to age 7 months, birth to age 13 months and birth to age 24 months, while girls gained more weight than boys from age 18 to 24 months (Table 1).

#### 3.1 | BMI and waist circumference

In all age intervals, direct association between early weight gain and BMI at age 20 years was observed in the analyses adjusted for the child's traits (Model 1). In the fully adjusted analyses (Model 2), the association was significant for BMI in the 13–18 months, the 18–24 months and the birth to 24 months intervals. From birth to 24 months, a +1SD excess weight gain was associated with a 0.98 kg/m<sup>2</sup> (95% CI 0.48 – 1.49 kg/m<sup>2</sup>,  $p < 0.001$ ) higher BMI at age 20 years (Table 2, Model 2).

In all age intervals, a direct association between early growth and WC at age 20 years was observed in the analyses adjusted for the child's traits (Model 1). In the fully adjusted analyses (Model 2), the association was significant in the 13–18 months, the 18–24 months and the birth to 24 months intervals (Table 2). Between birth and 24 months, a +1SD excess weight gain was associated with a 1.62 cm (95% CI 0.40 – 2.84 cm,  $p = 0.01$ ) higher WC at age 20 years (Table 2, Model 2).

#### 3.2 | Blood pressure

There was a direct association between early weight gain and systolic BP at age 20 years, but no significant associations were observed between early growth and diastolic BP.

In the analyses adjusted for the child's traits (Model 1), the association of early weight gain with systolic BP was significant in the 13

to 18 months and the birth to 24 months intervals. In the fully adjusted analyses (Model 2), the association of early weight gain with systolic BP was significant in the age interval 18–24 months. For +1SD excess weight gain during this interval, systolic BP increased by 1.83 mmHg (95% CI 0.30 – 3.36 mmHg,  $p = 0.02$ ) at age 20 years (Model 2). (Table 2).

#### 3.3 | Serum lipids, glucose, insulin and HOMA-IR

No association was found between early weight gain and total cholesterol, HDL-C, LDL-C or triglycerides measured at 20 years of age in models 1 or 2 (Table 3). In the fully adjusted analyses (model 2), early weight gain associated inversely with glucose in the birth to 24 months interval, while insulin and HOMA-IR associated inversely with early weight gain in the birth to 13 months and the birth to 24 months intervals (Table 4).

#### 3.4 | Sex-interaction and sex-specific analyses

A significant sex interaction was observed in seven analyses investigating the associations between early weight gain and the cardiometabolic markers at age 20 years: For BMI in the 7–13 months ( $p < 0.001$ ), 13–18 months ( $p = 0.01$ ) and birth to 13 months ( $p = 0.03$ ) age intervals; for WC in the 7–13 months ( $p < 0.001$ ) and 13–18 months ( $p = 0.02$ ) age intervals; for diastolic BP in the 18–24 months age interval ( $p = 0.002$ ); and finally for glucose in the birth to 13 months age interval ( $p = 0.03$ ). When subsequent sex-specific analyses were performed, the associations of early weight gain with diastolic BP and glucose remained non-significant in both males and females (data not shown). For BMI and WC the association was stronger for females than for males in the sex-specific analyses (data not shown).

### 4 | DISCUSSION

Studies have shown that metabolic measures obtained in childhood correlate with the same measures later in life<sup>19</sup> indicating that measures of BP, serum lipids and BMI in early adulthood can be considered to predict trends on measurements in middle age and later, when metabolic diseases and CVD become symptomatic.

The results in this study indicate that the weight gain during the first two years of life, especially in the 13–18 months and 18–24 months age intervals, is directly associated with BMI, WC and systolic BP measured at 20 years of age. Intriguingly, the transition from infant feeding to a diet similar to the older family members takes place during the second year of life. In addition to the changes in diet, this age interval coincides with increasing physical activity of the child. Excess weight gain in this age interval, where weight increase per month naturally decreases, seems to be of significance for future cardiometabolic health. Increased early weight gain could

**TABLE 2** Associations of early weight gain with BMI, waist circumference and blood pressure (BP) at age 20 years

		Model 1 Beta <sup>a</sup> (CI), <i>p</i> -value	Model 2 Beta <sup>a</sup> (CI), <i>p</i> -value
BMI, kg/m <sup>2</sup>	Birth-7 months	<b>0.68 (0.21 - 1.16), 0.005</b>	0.33 (-0.19 - 0.85), 0.22
	7-13 months	<b>0.52 (0.10 - 0.93), 0.01</b>	0.32 (-0.12 - 0.77), 0.15
	13-18 months	<b>1.03 (0.63 - 1.44), &lt;0.0001</b>	<b>0.78 (0.33 - 1.24), &lt;0.001</b>
	18-24 months	<b>0.67 (0.27 - 1.06), &lt;0.001</b>	<b>0.72 (0.27 - 1.17), 0.002</b>
	Birth-13 months	<b>0.91 (0.44 - 1.38), &lt;0.001</b>	0.49 (-0.03 - 1.00), 0.07
	Birth-24 months	<b>1.41 (0.97 - 1.86), &lt;0.0001</b>	<b>0.98 (0.48 - 1.49), &lt;0.001</b>
Waist circumference, cm	Birth-7 months	<b>1.14 (0.03 - 2.26), 0.04</b>	0.34 (-0.90 - 1.59), 0.59
	7-13 months	<b>1.02 (0.03 - 2.01), 0.04</b>	0.53 (-0.54 - 1.60), 0.33
	13-18 months	<b>2.57 (1.60 - 3.53), &lt;0.0001</b>	<b>2.06 (0.97 - 3.15), &lt;0.001</b>
	18-24 months	<b>1.24 (0.29 - 2.19), 0.01</b>	<b>1.25 (0.14 - 2.35), 0.03</b>
	Birth-13 months	<b>1.55 (0.43 - 2.67), 0.007</b>	0.54 (-0.70 - 1.78), 0.39
	Birth-24 months	<b>2.58 (1.51 - 3.65), &lt;0.0001</b>	<b>1.62 (0.40 - 2.84), 0.01</b>
Systolic BP, mmHg	Birth-7 months	0.67 (-0.74 - 2.09), 0.35	0.18 (-1.56 - 1.91), 0.84
	7-13 months	0.71 (-0.56 - 1.98), 0.27	0.49 (-1.00 - 1.98), 0.52
	13-18 months	<b>1.35 (0.09 - 2.61), 0.04</b>	1.05 (-0.48 - 2.59), 0.18
	18-24 months	1.18 (-0.04 - 2.40), 0.06	<b>1.83 (0.30 - 3.36), 0.02</b>
	Birth-13 months	1.09 (-0.36 - 2.54), 0.14	0.45 (-1.30 - 2.19), 0.61
	Birth-24 months	<b>1.55 (0.16 - 2.95), 0.03</b>	1.19 (-0.54 - 2.93), 0.18
Diastolic BP, mmHg	Birth-7 months	0.22 (-0.74 - 1.17), 0.65	0.25 (-0.90 - 1.41), 0.67
	7-13 months	0.52 (-0.33 - 1.37), 0.23	0.39 (-0.60 - 1.38), 0.44
	13-18 months	0.05 (-0.79 - 0.88), 0.91	0.03 (-0.97 - 1.03), 0.96
	18-24 months	0.17 (-0.64 - 0.98), 0.68	0.37 (-0.63 - 1.37), 0.47
	Birth-13 months	0.64 (-0.32 - 1.61), 0.19	0.47 (-0.68 - 1.62), 0.42
	Birth-24 months	0.44 (-0.51 - 1.38), 0.36	0.52 (-0.63 - 1.67), 0.37

<sup>a</sup>The beta estimate represents association of 1 SD increase in early growth with the outcome variable. Bold indicates *p* < 0.05.

		Model 1 Beta <sup>a</sup> (CI), <i>p</i> -value	Model 2 Beta <sup>a</sup> (CI), <i>p</i> -value
Total cholesterol, mmol/L	Birth-7 months	-0.05 (-0.14 - 0.04), 0.31	-0.04 (-0.15 - 0.07), 0.43
	7-13 months	-0.002 (-0.08 - 0.08), 0.96	-0.03 (-0.12 - 0.07), 0.58
	13-18 months	0.03 (-0.05 - 0.11), 0.53	0.03 (-0.07 - 0.12), 0.55
	18-24 months	0.02 (-0.06 - 0.09), 0.69	-0.03 (-0.12 - 0.06), 0.53
	Birth-13 months	-0.05 (-0.15 - 0.04), 0.27	-0.07 (-0.18 - 0.04), 0.21
	Birth-24 months	-0.02 (-0.11 - 0.07), 0.73	-0.05 (-0.15 - 0.06), 0.40
HDL-C, mmol/L	Birth-7 months	-0.01 (-0.05 - 0.03), 0.55	-0.01 (-0.05 - 0.04), 0.76
	7-13 months	0.02 (-0.01 - 0.05), 0.19	0.04 (-0.0003 - 0.07), 0.052
	13-18 months	-0.01 (-0.04 - 0.02), 0.45	-0.02 (-0.05 - 0.02), 0.44
	18-24 months	0.01 (-0.02 - 0.04), 0.62	0.01 (-0.03 - 0.05), 0.61
	Birth-13 months	0.01 (-0.03 - 0.04), 0.72	0.02 (-0.02 - 0.07), 0.35
	Birth-24 months	0.0004 (-0.04 - 0.04), 0.98	0.01 (-0.04 - 0.05), 0.76
LDL-C, mmol/L	Birth-7 months	-0.02 (-0.10 - 0.06), 0.64	-0.01 (-0.11 - 0.08), 0.77
	7-13 months	-0.02 (-0.09 - 0.05), 0.51	-0.05 (-0.13 - 0.03), 0.22
	13-18 months	0.02 (-0.05 - 0.09), 0.55	0.03 (-0.06 - 0.11), 0.53
	18-24 months	0.01 (-0.06 - 0.08), 0.75	-0.04 (-0.12 - 0.04), 0.33
	Birth-13 months	-0.04 (-0.12 - 0.04), 0.30	-0.06 (-0.15 - 0.04), 0.22
	Birth-24 months	-0.003 (-0.08 - 0.08), 0.95	-0.03 (-0.12 - 0.06), 0.53
Triglycerides <sup>b</sup> , mmol/L	Birth-7 months	-0.04 (-0.09 - 0.02), 0.19	-0.05 (-0.11 - 0.02), 0.14
	7-13 months	0.01 (-0.04 - 0.05), 0.79	-0.02 (-0.07 - 0.04), 0.52
	13-18 months	0.02 (-0.02 - 0.07), 0.34	0.02 (-0.04 - 0.08), 0.49
	18-24 months	-0.01 (-0.05 - 0.04), 0.76	-0.01 (-0.06 - 0.05), 0.83
	Birth-13 months	-0.03 (-0.08 - 0.02), 0.29	-0.06 (-0.12 - 0.01), 0.08
	Birth-24 months	-0.03 (-0.08 - 0.02), 0.26	-0.06 (-0.12 - 0.01), 0.09

**TABLE 3** Associations of early weight gain with total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides at the age of 20 years

<sup>a</sup>The beta estimate represents association of 1 SD increase in early growth with the outcome variable (mmol/L).

<sup>b</sup>Logarithmically transformed values used in the analyses.

be connected to family food consumption and composition, suggesting that the dietary habits in the family start to shape later health early in life.

#### 4.1 | BMI and waist circumference

Our results indicate that increased weight gain during the first two years of life associated with a higher BMI and larger WC at 20 years of age. From birth to age 24 months, the mean weight gain was

9.3 kg (SD 1.3 kg), and for a +1SD excess weight gain, BMI measured at 20 years of age increased by 0.98 kg/m<sup>2</sup> and waist circumference increased by 1.62 cm, indicating an association that is clinically relevant.

Our results are in line with findings from studies focusing on the association between growth in infancy and risk for higher BMI later in life.<sup>8,20</sup> A systematic review found that rapid weight gain during the first year of life is associated with higher odds for later overweight than rapid weight gain from birth to two years.<sup>20</sup> In contrast to these findings, our study found the association between early

**TABLE 4** Associations of early weight gain with serum glucose, serum insulin and HOMA-IR at age 20 years

		Model 1 Beta <sup>a</sup> (CI), <i>p</i> -value	Model 2 Beta <sup>a</sup> (CI), <i>p</i> -value
Glucose, mmol/L	Birth–7 months	–0.03 (–0.08 – 0.02), 0.17	–0.03 (–0.10 – 0.03), 0.27
	7–13 months	0.02 (–0.02 – 0.06), 0.39	0.02 (–0.03 – 0.07), 0.41
	13–18 months	–0.01 (–0.05 – 0.04), 0.81	–0.03 (–0.08 – 0.03), 0.31
	18–24 months	–0.02 (–0.06 – 0.02), 0.35	–0.05 (–0.10 – 0.005), 0.07
	Birth–13 months	–0.02 (–0.07 – 0.03), 0.46	–0.02 (–0.08 – 0.04), 0.58
	Birth–24 months	–0.04 (–0.09 – 0.01), 0.12	<b>–0.07 (–0.13 – –0.004), 0.04</b>
Insulin <sup>b</sup> , mU/L	Birth–7 months	–0.03 (–0.08 – 0.03), 0.37	–0.05 (–0.12 – 0.02), 0.15
	7–13 months	0.002 (–0.05 – 0.05), 0.94	–0.03 (–0.09 – 0.02), 0.25
	13–18 months	0.03 (–0.02 – 0.08), 0.19	0.03 (–0.03 – 0.09), 0.36
	18–24 months	–0.01 (–0.06 – 0.04), 0.59	–0.01 (–0.07 – 0.05), 0.68
	Birth–13 months	–0.02 (–0.08 – 0.04), 0.50	<b>–0.07 (–0.14 – –0.003), 0.04</b>
	Birth–24 months	–0.03 (–0.08 – 0.03), 0.34	<b>–0.08 (–0.14 – –0.01), 0.02</b>
HOMA-IR <sup>b</sup>	Birth–7 months	–0.04 (–0.11 – 0.02), 0.15	–0.07 (–0.14 – 0.001), 0.054
	7–13 months	0.01 (–0.04 – 0.06), 0.69	–0.02 (–0.08 – 0.04), 0.44
	13–18 months	0.03 (–0.03 – 0.08), 0.34	0.01 (–0.05 – 0.08), 0.67
	18–24 months	–0.02 (–0.07 – 0.03), 0.45	–0.02 (–0.09 – 0.04), 0.44
	Birth–13 months	–0.03 (–0.09 – 0.03), 0.37	<b>–0.08 (–0.15 – –0.01), 0.03</b>
	Birth–24 months	–0.04 (–0.10 – 0.02), 0.16	<b>–0.10 (0.17 – –0.03), 0.005</b>

<sup>a</sup>The beta estimate represents association of 1 SD increase in early growth with the outcome variable (mmol/L).

<sup>b</sup>Logarithmically transformed values used in the analyses.

Bold indicates *p* < 0.05.

weight gain and measures indicating higher adiposity at 20 years of age (higher BMI and bigger WC) to be stronger after the first year of life, in the 13–18 months, 18–24 months and the birth to 24 months age intervals.

## 4.2 | Blood pressure

We found a direct association between early weight gain and systolic BP in young adulthood. For a +1SD excess weight gain from 18 to 24 months, systolic BP measured at 20 years of age increased by

1.83 mmHg, indicating an association that is clinically relevant. BW and rapid postnatal growth have previously been associated with increased adult systolic BP.<sup>21</sup>

## 4.3 | Total cholesterol, HDL-C, LDL-C and triglycerides

Some studies have found rapid early growth to predict higher levels of future triglycerides, total cholesterol and LDL-C, and lower levels of HDL-C,<sup>22</sup> while other studies have found no association between

early growth and serum lipids.<sup>23</sup> In this study, we found no association between early growth and any of the serum lipids measured at 20 years of age.

#### 4.4 | Fasting glucose, serum insulin and insulin resistance

Results from previous studies have been contradicting, finding both reduced<sup>24</sup> and increased<sup>25</sup> growth in infancy to predict later insulin resistance. Our results indicate there to be an inverse association between increased growth and later insulin resistance in the fully adjusted analyses, suggesting reduced growth in infancy to predict later insulin resistance. Taken together the findings from our and the previous studies, no firm conclusion can be made on the association between early weight gain and later serum glucose, insulin and insulin resistance.

#### 4.5 | Sex-specific analyses

Sex-specific analyses indicated that the associations of early weight gain with BMI and WC were stronger for females, but the directions of the associations were similar in both sexes. Diluted associations may be due to the decreased number of participants when males and females were analysed separately, combined with a relatively large inter-individual variation in weight gain.

#### 4.6 | Strengths and limitations

The strengths of the STRIP Study are use of well-established methods, long follow-up period from infancy to young adulthood and large number of repeatedly studied participants. Furthermore, the vast majority of the infants were adequate for gestational age. This study focused on the weight gain from birth to two years of age. The age intervals were chosen based on the available data from the STRIP Study, where the first study visit was at the 7 months with the following study visits at the months of 13, 18 and 24. This gave us an opportunity to study how early weight gain during approximately 6-month intervals associated with markers of cardiometabolic health at 20 years of age.

A potential limitation of the STRIP study is the possible selection bias in the recruitment of the subjects, as the participating families might have been more health oriented than the non-participants, possibly affecting the association of early growth with later cardiometabolic health because of health awareness. Also, the extensive 20-year study period inevitably caused loss to follow-up among the participants. During the first study years, the most common reasons for discontinuation were moving away from the Turku area, recurrent infections, and reluctance to have blood sampled.<sup>26</sup> Loss to follow-up has been stable, with no apparent peaks. The characteristics of study participants and who were lost

to follow-up have been compared,<sup>26</sup> and no significant differences in body weight, BMI, serum total cholesterol or saturated fat intake have been found. Thus, a systematic selection bias should not have influenced the present findings. While the intervention conducted in the STRIP study did not affect early weight gain, we chose additionally to control our analyses with belonging to the control or intervention group.

A limitation of this study also is that we did not account for breastfeeding or its duration. Information on the duration of breastfeeding was partly retrospective and not always available. Solid foods were introduced at 3–5 months, and the mean duration of breastfeeding was 5 (SD 4, range 0–12) months in both the intervention and control groups. All infants were weaned and had changed from infant formulas to cows' milk by 1 year of age.<sup>27</sup> Breastfeeding has been suggested to decrease the risk for obesity and for type 2 diabetes, and it seems to protect more from risk of obesity in childhood and adolescence than from obesity in adulthood<sup>28</sup>.

All subjects in the STRIP study are Caucasian; thus, the results may not be generalisable to other ethnicities.

## 5 | CONCLUSIONS

Early weight gain, especially during the second year of life, is linked with markers of cardiometabolic health—BMI, WC, systolic BP, insulin and insulin resistance—in young adulthood. Prevention of CVD should begin in infancy. Investing in nutrition and lifestyle counseling during early childhood, especially during and after weaning, is of importance for later cardiometabolic health.

### ACKNOWLEDGEMENT

The STRIP study children and their parents and grandparents have made this unique study possible—we thank them for their time, continued efforts and commitment to the STRIP throughout the years.

### CONFLICT OF INTEREST

The authors have no conflicts of interest.

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**How to cite this article:** Nummela SR, Salo P, Pahkala K, et al. Weight gain in infancy and markers of cardiometabolic health in young adulthood. *Acta Paediatr*. 2022;111:1603–1611. doi:10.1111/apa.16349