

## ORIGINAL ARTICLE

# Steeper increases in body mass index during childhood correlate with blood pressure elevation in adolescence: a long-term follow-up study in a Japanese community

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The aim of this study was to clarify the relationship between long-term changes in body mass index (BMI) during childhood and adolescent blood-pressure levels in a general Japanese population. We used health report data from 900 Japanese children between 1983 and 2007. After adjusting for baseline BMI and other confounding factors multivariate linear regression analyses were performed to examine the relationship between changes in BMI ( $\Delta$ BMI) over a 6-year period (6–12 years) and blood pressure once children reached ages 14 or 15. Sub-group analyses were also performed to ascertain the relationship between  $\Delta$ BMI and blood pressure at 9th grade for children who had been in the bottom BMI tertile at 1st grade. Endpoint blood-pressure levels in boys (systolic and diastolic) and girls (systolic) from the group whose BMIs increased the most were significantly higher than those from the group whose BMIs increased the least ( $P < 0.05$ , analysis of variance). After adjustment for baseline BMI and school-entrance year, the former group showed higher blood pressure at the endpoint than the latter ( $P < 0.05$ , multiple regression analysis). Further adjustment for baseline blood pressure also showed similar results in a combined-sex analysis ( $n = 592$ ). Higher  $\Delta$ BMI was associated with higher SBP<sub>9</sub> even in children whose BMI was in the lowest tertile at baseline after adjustment for sex and school-entrance year ( $P = 0.02$ , multiple regression analysis). Steeper BMI increases during primary school lead to adolescent increases in blood pressure even if baseline BMI is low. Growth during childhood should be carefully managed.

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## INTRODUCTION

Obesity leads to a variety of chronic conditions, and its prevention is an urgent issue not only in developed countries but also in many emerging ones.<sup>1–3</sup> Some previous studies show that birth weight and obesity in childhood are associated with chronic health conditions in later life, such as hypertension.<sup>4,5</sup> Additionally, adolescent health shows a particularly strong association with chronic health conditions in later life.<sup>6,7</sup> However, little is known about the relationship between childhood and adolescent blood pressure levels in the Japanese population.

We performed an epidemiological study using data from an area in Nagano Prefecture where school-children have undergone annual physical health checks since 1973. We used the records of these examinations to investigate the association between changes in body

mass index (BMI) over a 6-year period during childhood and blood pressure level in adolescence.

## METHODS

### Study area and population

This study was conducted using data from a typical rural area of Nagano Prefecture with a population of ~4600. The target population was all 989 children (517 boys and 472 girls) who entered a certain primary school between 1983 and 1999. Records from 1983 to 2007 were selected to include 9th-grade data from children who had entered the primary school in 1999. Of these, data from 46 6th-grade and 37 9th-grade children were missing because the children changed school, and 6 9th-grade children did not have data for both systolic and diastolic blood pressure (SBP, DBP). Therefore, 900 children (476 boys, 424 girls) had data for health checks from both the 1st and 6th

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grades (ages: 6–7 years and 11–12 years, respectively) and blood-pressure data for the 9th grade (14–15 years).

### Physical check-ups

Japanese schools have been involved in checking and managing child health for over 100 years. The School Health and Safety Act of 1958 requires all Japanese schools to carry out regular physical check-ups within the first 3 months of each new school year (that is, April–June). Mandatory items include a medical interview, standing and sitting height, weight, visual and hearing acuity, visual examination of the oral cavity, investigation of nutritional status and a dental checkup. The school carries out blood-pressure measurements and blood and urine tests in addition to these mandated items.

We used data from children receiving check-ups between 1983 and 2007. Height and weight were measured by a school nurse and rounded to the nearest integer. We converted the childrens' BMIs to BMI s.d. scores (BMI-SDSs) using the LMS method.<sup>8,9</sup> Mean  $\pm$  s.d. of BMI-SDSs of 1st-grade children were  $-0.07 \pm 0.92$  (boys) and  $-0.10 \pm 0.86$  (girls), and those of the 6th-grade children were  $-0.02 \pm 0.99$  (boys) and  $-0.12 \pm 1.00$  (girls). Analysis determined that they were physically representative of Japanese schoolchildren.

Changes in BMI ( $\text{kg m}^{-2}$ ) between the 1st and 6th grade were used as an indicator of change in physical constitution. In the Japanese educational system, primary school lasts from 1st to 6th grade. Therefore, using BMI change during this period is convenient for continuous health management. Blood pressure was measured by nurses using an automated oscillometric sphygmomanometer (ES-H51T3 or ES-H55; Terumo Corporation, Tokyo, Japan) starting in 1991 when children who had entered primary school in 1983 reached 9th grade. At each check-up, blood pressure was measured in accordance with the latest available guidelines provided by the Japanese Society of Hypertension<sup>10</sup> as follows: cuff size was selected based on the circumference of the childrens' upper right arm. Before measurement, children were allowed to micturate and then sit quietly for at least 5 min in a room equipped with tables and chairs, and maintained at comfortable temperature and humidity levels. Blood pressure was measured twice using in right arm at heart level, and the average was recorded, with an interval of at least 1 min separating the two measurements. The guidelines were revised twice between 1991 and 2007 (2000<sup>11</sup> and 2004;<sup>12</sup> however the procedure for measuring blood pressure was not altered. The parents of any child who was overweight or thought to be unhealthy in any way after the check-up were advised to seek medical advice, but no systematic interventions against obesity were implemented during the observation period.

### Statistical analysis

To examine the association between BMI increases during the primary school years and blood pressure levels in the 9th grade, the change in BMI ( $\Delta$ BMI) from 1st to 6th grade was calculated for each subject.  $\Delta$ BMI tertiles were established for each sex, and analysis of variance (ANOVA) and *post-hoc* tests with Bonferroni correction were used to compare height, weight and BMI at 1st grade (BMI<sub>1</sub>), 6th grade, and 9th grade across three groups of children with different degrees of  $\Delta$ BMI (low, moderate and high for the first, second and the third tertile). The relationship between  $\Delta$ BMI and blood pressure in the 9th grade was then analyzed with an ANOVA for each sex. We next used linear regression models to determine whether BMI<sub>1</sub>, school-entrance year and blood pressure at 1st grade were confounding factors. We chose these potential factors because we wanted to know the effects of BMI gain on children with low baseline BMIs and because changing population eating habits may make entry-year relevant. Additionally, blood pressure is well known to track over time. To examine separate effects of  $\Delta$ BMI and 9th-grade weight on 9th-grade blood pressure, we should include BMI at 9th grade in the models. However, results showed that  $\Delta$ BMI and BMI<sub>9</sub> were strongly correlated (Pearson product-moment correlation coefficient, boys:  $r = 0.69$ ,  $P < 0.001$ , girls:  $r = 0.66$ ,  $P < 0.001$ ), and we therefore did not include BMI at 9th grade as a covariate. Model 1 was used for crude analyses and Model 2 included adjustments for BMI<sub>1</sub>. Model 3 adjusted for school-entrance year and the variables from Model 2. Furthermore, Model 4 adjusted for the variables from Model 3 and either 1st-grade systolic or diastolic blood pressure (SBP<sub>1</sub> or

DBP<sub>1</sub>), depending on the outcome of the Model 3 analysis: if the outcome was SBP at 9th grade (SBP<sub>9</sub>), SBP<sub>1</sub> was included in the model as a covariate. Similarly, if the outcome was DBP at 9th grade (DBP<sub>9</sub>), DBP<sub>1</sub> was included. Only 592 subjects (314 boys, 278 girls) had blood pressure data at 1st grade because SBP<sub>1</sub> and DBP<sub>1</sub> data were only available for those who had entered primary school before 1994. We therefore combined data from both sexes and used a multiple regression analysis that adjusted for sex, BMI<sub>1</sub>, school-entrance year and either SBP<sub>1</sub> or DBP<sub>1</sub>. Lastly, we performed a sub-group analysis to ascertain whether the same relationship between  $\Delta$ BMI and blood pressure at 9th grade was observable even among the children who had been slim in 1st grade. Steeper  $\Delta$ BMI would appear desirable in such children so that they could achieve BMIs within the normal range by the time they were in the 6th grade. However, if steeper  $\Delta$ BMI was also found to affect 9th-grade blood pressure in these children, concern would be warranted not only for children in the high baseline BMI group but also for those in the low baseline BMI group as well. BMI<sub>1</sub> was classified into tertiles for each sex, and regression analyses were used to assess the relationship between  $\Delta$ BMI and blood pressure at 9th grade in the subjects belonging to the lowest BMI<sub>1</sub> group. Because the number of subjects was small (152 boys and 139 girls), we combined data from both sexes. In the analysis, we adjusted for sex, school-entrance year and blood pressure at 1st grade.

BMI<sub>1</sub> and blood pressures at 1st grade were categorized into three groups by tertile. Entrance year was categorized into three groups: 1983–1988, 1989–1994 and 1995–1999. All variables were used as dummy variables. When we used BMI<sub>1</sub>, blood pressure at 1st grade, and school-entrance year as continuous variables, multiple regression analysis yielded similar results.

All statistical analyses were done with STATA ver. 10.0 (STATA Corp., College Station, TX, USA). All confidence intervals were estimated at the 95% level, and  $P$ -values  $< 0.05$  were considered statistically significant.

### Ethical considerations

This study was approved by Saku Central Hospital's Ethics Committee (approval number: 31) and the Ethics Committee of Keio University (approval number: 2011-069). All data provided by Saku Central Hospital were anonymized, and the researchers could not access personal information about any of the children.

### RESULTS

Table 1 shows participant characteristics by sex. Because significant sex-related differences were found in 6th grade and 9th grade, subsequent analyses were performed separately for each sex.  $\Delta$ BMI for boys ( $2.7 \pm 2.1$ ) and girls ( $2.6 \pm 1.8$ ) did not significantly differ ( $T$ -test,  $P = 0.30$ ).

Table 2 shows the results of a one-way ANOVA on the relationship between  $\Delta$ BMI and physical growth and blood pressure in boys. SBP<sub>9</sub> and DBP<sub>9</sub> were significantly different between the three groups. The mean SBP<sub>9</sub> of the high and low  $\Delta$ BMI groups differed by  $\sim 4$  mm Hg. BMI, height and weight all differed between the high and low  $\Delta$ BMI groups. Although SBP<sub>1</sub> did not differ statistically between the three groups, DBP<sub>1</sub> was significantly higher in the high- $\Delta$ BMI group. Year of entrance into primary school differed significantly among the  $\Delta$ BMI groups.

In girls, DBP<sub>9</sub>, BH<sub>9</sub>, distribution of primary-school entrance year and blood pressure at 1st grade were not significantly different between the three groups (Table 3). Results for other variables were similar to those found in boys.

The results of univariate and multivariate linear regression analyses using categorized and dummy variables by tertiles are shown in Table 4. Crude coefficients in Model 1 (a univariate linear regression model) showed that a high  $\Delta$ BMI was significantly correlated with higher SBP<sub>9</sub> and DBP<sub>9</sub> in both boys and girls. Even after adjustment for BMI<sub>1</sub> and primary-school entrance year in Model 3, both SBP<sub>9</sub> and DBP<sub>9</sub> were significantly higher in the high  $\Delta$ BMI groups for both sexes. Although Model 4 that adjusted for variables in Model 3 and

**Table 1 Characteristics of subjects**

Variables	Grade	Boys (n = 476)	Girls (n = 424)	P <sup>a</sup>
		Mean ± s.d. or n (%)	Mean ± s.d. or n (%)	
Height (cm)	1st <sup>b</sup>	115.9 ± 4.7	115.2 ± 4.7	0.04
	6th <sup>c</sup>	143.9 ± 6.7	145.5 ± 6.7	<0.001
	9th <sup>d</sup>	164.3 ± 6.5	156.0 ± 5.3	<0.001
Weight (kg)	1st <sup>b</sup>	21.1 ± 3.3	20.7 ± 3.0	0.047
	6th <sup>c</sup>	38.3 ± 8.7	38.5 ± 7.7	0.67
	9th <sup>d</sup>	55.1 ± 10.2	51.0 ± 7.4	<0.001
BMI (kg m <sup>-2</sup> )	1st <sup>b</sup>	15.6 ± 1.6	15.5 ± 1.6	0.26
	6th <sup>c</sup>	18.3 ± 3.0	18.1 ± 2.7	0.18
	9th <sup>d</sup>	20.3 ± 3.1	20.9 ± 2.8	0.002
Change in BMI (ΔBMI)	1st–6th	2.7 ± 2.1	2.6 ± 1.8	0.30
SBP (mm Hg)	1st <sup>e</sup>	95.7 ± 9.8	94.8 ± 9.5	0.28
	6th <sup>f</sup>	108.2 ± 10.6	108.9 ± 11.3	0.30
	9th <sup>d</sup>	115.6 ± 10.4	109.2 ± 10.8	<0.001
DBP (mm Hg)	1st <sup>e</sup>	52.9 ± 9.8	52.5 ± 9.4	0.67
	6th <sup>f</sup>	63.4 ± 10.4	64.6 ± 10.2	0.09
	9th <sup>d</sup>	69.1 ± 8.4	67.2 ± 8.2	<0.001
<i>Year of entrance into primary school</i>				
		186 (39.8%)	170 (40.9%)	
		169 (35.5%)	143 (33.7%)	
		121 (25.4%)	111 (26.2%)	

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

<sup>a</sup>t-test for continuous variables or chi-square test for categorical variables.

<sup>b</sup>The children in grade 1 were 6 or 7 years old.

<sup>c</sup>The children in grade 6 were 11 or 12 years old.

<sup>d</sup>The children in grade 9 were 14 or 15 years old.

<sup>e</sup>SBP and DBP at 1st-grade data were available only on those who entered elementary school before 1994 (n = 314 boys, 278 girls).

<sup>f</sup>SBP and DBP data at 6th grade were available from 894 among 900 children (474 boys and 420 girls).

either SBP<sub>1</sub> or DBP<sub>1</sub> (depending on Model-3 outcome, see Methods) showed no significant association between ΔBMI and SBP<sub>9</sub> in boys (SBP<sub>9</sub>: P = 0.073, DBP<sub>9</sub>: P = 0.04). Also, in Model 4, after adjusting for SBP<sub>1</sub> and DBP<sub>1</sub> as continuous variables, the similar results were shown (SBP<sub>9</sub>: P = 0.089, DBP<sub>9</sub>: P = 0.038 in boys, SBP<sub>9</sub>: P = 0.03, DBP<sub>9</sub>: P = 0.01 in girls). However, when we combined the data for both sexes and adjusted for sex, BMI<sub>1</sub>, school-entrance year and either SBP<sub>1</sub> or DBP<sub>1</sub> (n = 592), we found a significant association between high and low ΔBMI (SBP<sub>9</sub>: P = 0.008, DBP<sub>9</sub>: P = 0.001). In the sub-group analysis, a significant association between ΔBMI and SBP<sub>9</sub> was shown after adjusting for sex and school-entrance year, however, after adding systolic or diastolic blood pressure at 1st grade as covariates, the associations attenuated (Table 5). Multivariate regression analyses yielded similar results when children whose ΔBMI or BMI<sub>9</sub> were above the 90 percentile were excluded.

## DISCUSSION

We showed that children whose BMI increased substantially over a 6-year period during primary school (high ΔBMI group) had higher systolic and diastolic blood pressure in the 9th grade (ages 14–15 years). Interestingly, this relationship was significant even after adjusting for categorized BMI at first grade and categorized school-entrance year, indicating that it applies to children who were slim

**Table 2 Comparison of physical growth and blood pressure in three groups of Japanese school children with different degrees of BMI change between 1st and 6th grade, boys**

Variables	Grade	BMI change group <sup>a</sup>			P*
		Low (n = 158)	Moderate (n = 159)	High (n = 159)	
		Mean ± s.d. or n (%)	Mean ± s.d. or n (%)	Mean ± s.d. or n (%)	
ΔBMI (kg m <sup>-2</sup> )	1st–6th	0.9 ± 0.5	2.1** ± 0.4	5.1** ± 1.9	<0.001
SBP (mm Hg)	9th	113.3 ± 9.7	116.1 ± 10.1	117.5** ± 10.9	0.01
DBP (mm Hg)	9th	67.7 ± 8.1	69.4 ± 8.7	70.3** ± 8.1	0.02
Height (cm)	1st	114.4 ± 4.9	116.0** ± 4.2	117.3** ± 4.5	<0.001
	6th	141.3 ± 6.6	143.8** ± 6.0	146.6** ± 6.4	<0.001
	9th	162.4 ± 7.3	165.0** ± 6.0	165.9** ± 5.8	<0.001
Weight (kg)	1st	20.1 ± 2.5	20.8 ± 3.0	22.4** ± 3.8	<0.001
	6th	32.4 ± 4.4	36.3** ± 5.3	46.2** ± 8.8	<0.001
	9th	48.9 ± 6.4	53.7** ± 6.8	62.7** ± 11.3	<0.001
BMI (kg m <sup>-2</sup> )	1st	15.3 ± 1.3	15.4 ± 1.5	16.2** ± 1.9	<0.001
	6th	16.2 ± 1.3	17.5** ± 1.6	21.3** ± 3.0	<0.001
	9th	18.5 ± 1.7	19.8** ± 2.0	22.7** ± 3.5	<0.001
<i>Year of entrance into primary school</i>					
		74 (39.8)	69 (37.1)	43 (23.1)	0.001
		44 (26.0)	51 (30.2)	74 (43.8)	
		40 (33.1)	39 (32.2)	42 (34.7)	
		(n = 158)	(n = 158)	(n = 158)	
SBP (mm Hg)	6th	104.6 ± 10.8	107.6** ± 10.0	112.3** ± 9.5	<0.001
DBP (mm Hg)	6th	60.6 ± 10.5	64.1** ± 10.2	65.6** ± 9.8	<0.001
		(n = 102)	(n = 109)	(n = 103)	
SBP (mm Hg)	1st <sup>b</sup>	94.5 ± 9.4	94.7 ± 9.4	97.2 ± 10.6	0.75
DBP (mm Hg)	1st <sup>b</sup>	51.3 ± 9.3	52.6 ± 10.0	54.7** ± 10.1	0.048

Abbreviations: ANOVA, analysis of variance; BMI, body mass index; ΔBMI, change in BMI between 1st and 6th grade; DBP, diastolic blood pressure; SBP, systolic blood pressure.

<sup>a</sup>ANOVA and *post-hoc* tests with Bonferroni correction were used to compare the differences between the three BMI change groups.

<sup>b</sup>Data of blood pressure at 1st grade were available only on those who entered elementary school before 1994 (n = 314 boys, 278 girls).

\*P-values for ANOVA or  $\chi^2$ -test.

\*\*P < 0.05 for *post-hoc* tests with Bonferroni correction, using the low group as a reference.

upon primary-school entry. After adjusting for blood pressure at 1st grade, only ΔBMI and SBP<sub>9</sub> in boys failed to show a significant relationship. This might be explained by the fact that 1st-grade blood pressure data were available only from children who entered primary school before 1994 and thus the sample size of the Model 4 analysis was smaller than that used in the other analyses. If blood pressure measurements at 1st grade had continued after 1994, blood pressure at 9th grade might have been statistically different among the three ΔBMI groups because the sample size Model 4 would have been larger. Sub-group analysis focusing on the bottom tertile BMI<sub>1</sub> children showed a statistically significant relationship between ΔBMI and SBP<sub>9</sub> after adjusting for sex and school-entrance year. Although the association was much attenuated by adding blood pressure at 1st grade, the interpretation should be done carefully because this analysis was based on much smaller number of subjects due to the lack of blood pressure data at 1st grade.

Among the three ΔBMI groups, the distribution of school-entrance years was different in boys. However, even after adjusting for the school-entrance year, the correlation between blood-pressure elevation in 9th grade and ΔBMI was statistically significant.

**Table 3 Comparison of physical growth and blood pressure in three groups of Japanese school children with different degrees of BMI change between 1st and 6th grade, girls**

	Grade	BMI change group <sup>a</sup>			P*
		Low (n = 141)	Moderate (n = 141)	High (n = 142)	
		Mean ± s.d. or n (%)	Mean ± s.d. or n (%)	Mean ± s.d. or n (%)	
ΔBMI (kg m <sup>-2</sup> )	1st–6th	0.9 ± 0.6	2.2** ± 0.4	4.5** ± 1.4	<0.001
SBP (mm Hg)	9th	107.2 ± 10.5	108.7 ± 10.1	111.5** ± 11.5	0.003
DBP (mm Hg)	9th	66.1 ± 7.9	67.0 ± 8.4	68.3 ± 8.1	0.070
Height (cm)	1st	114.4 ± 5.2	116.0** ± 4.4	117.3** ± 4.1	<0.001
	6th	141.3 ± 7.0	143.8** ± 6.2	146.6** ± 5.5	<0.001
	9th	162.4 ± 6.0	164.6 ± 5.2	165.9 ± 4.6	0.23
Weight (kg)	1st	20.1 ± 2.7	20.8 ± 2.7	22.4** ± 3.1	<0.001
	6th	32.4 ± 4.7	36.3** ± 5.1	46.2** ± 6.7	<0.001
	9th	48.9 ± 5.7	53.7** ± 5.5	62.7** ± 6.9	<0.001
BMI (kg m <sup>-2</sup> )	1st	15.3 ± 1.4	15.4 ± 1.4	16.2** ± 1.8	<0.001
	6th	16.2 ± 1.4	17.5** ± 1.4	21.3** ± 2.5	<0.001
	9th	18.5 ± 1.9	19.8** ± 1.8	22.7** ± 2.8	<0.001
<i>Year of entrance into primary school</i>					
	1983–1988	62 (36.5)	60 (35.3)	48 (28.2)	0.17
	1989–1994	39 (27.3)	51 (35.7)	53 (37.1)	
	1995–1999	40 (36.0)	30 (27.0)	41 (36.9)	
		(n = 141)	(n = 141)	(n = 138)	
SBP (mm Hg)	6th	105.5 ± 11.5	108.5 ± 9.5	113.0** ± 11.5	<0.001
DBP (mm Hg)	6th	62.4 ± 9.8	64.7 ± 10.1	66.7** ± 10.4	0.002
		(n = 88)	(n = 100)	(n = 90)	
SBP (mm Hg)	1st <sup>b</sup>	94.5 ± 9.4	94.7 ± 9.6	97.2 ± 9.9	0.77
DBP (mm Hg)	1st <sup>b</sup>	51.3 ± 9.5	52.6 ± 9.2	54.7 ± 10.3	0.16

Abbreviations: ANOVA, analysis of variance; BMI, body mass index; ΔBMI, change in BMI between 1st and 6th grade; DBP, diastolic blood pressure; SBP, systolic blood pressure.

<sup>a</sup>ANOVA and *post-hoc* tests with Bonferroni correction were used to compare the differences between the three BMI change groups.

<sup>b</sup>Data of blood pressure at 1st grade were available only on those who entered elementary school before 1994 (n = 314 boys, 278 girls).

\*P-values for ANOVA or  $\chi^2$ -test.

\*\*P < 0.05 for *post-hoc* tests with Bonferroni correction, using the low group as a reference.

In 1994, Uchiyama *et al.*<sup>13</sup> reported that elevated blood pressure in 12- to 15-year-old children led to hypertension in adulthood. Our results are therefore significant as they link adolescent blood pressure to BMI at even younger ages. While BMI naturally increases as children grow, our data show that a steeper BMI gain in childhood was correlated with elevated blood pressure in the future. This relationship was observed even in children who were slim in the 1st grade, which highlights the need to manage weight gain carefully in all children.

Although technically within Japan's normal range for children, the difference in average blood pressure between the high and low ΔBMI groups was 3–4 mm Hg, similar to the calculated amount that the average adult systolic pressure could be lowered with healthy diet, resulting in lower risks of heart attack and stroke-related death.<sup>14</sup> Although evidence linking reduced blood pressure with reduced cerebrocardiovascular disease-related death in adults has not been established, when blood pressure changes from adolescence to adulthood are tracked, the different average blood pressures between each ΔBMI group will be meaningful.

Presently, the cornerstones of blood pressure regulation are thought to be vasomotor tone and balance of sodium and fluid.<sup>15</sup> Both

mechanisms are complex, however, and the causes of essential hypertension are not clear. The relationship between the slope of BMI increase and development of the controlling systems is therefore an interesting topic for future research in hypertension control. Our results indicate that steeper increases in BMI during primary school can be viewed as a predictor of adolescent higher blood pressure.

Although several recent studies in Europe and the United States have investigated associations between cardiovascular disease risk factors in adults and ΔBMI changes in children,<sup>16–21</sup> few similar studies have been carried out in Japanese populations. Moreover, because little is known about the association between steeper ΔBMI in childhood, particularly in those with low BMI at 1st grade, and blood pressure in adolescents of other races, further investigation is needed to conclusively validate these results in diverse populations.

Miura *et al.*<sup>22</sup> reported that low birth weight and slow height gain in childhood are independently associated with elevated blood pressure in adulthood among Japanese. We looked for an association between height gain and blood pressure, and found a significantly positive association only in boys (data not shown). However, because height gain cannot be controlled, we did not include it as a covariate in our models. In contrast, BMI can be controlled with education about appropriate diet and exercise, making it a good target for preventative measures.

Several investigations of cardiovascular risk factors have focused on childhood changes in body weight.<sup>23–26</sup> Changes in both body weight and BMI could be adopted as indices for the tendency towards obesity. However, because changes in BMI also take into account height growth, it estimates this trend more accurately than weight change alone. Moreover, when linking childhood and adult data, using changes in BMI is more comprehensible because BMI is a mainstream measurement in adult examinations. Our data show that between gains in BMI and body weight during primary school, only BMI gain was related to blood pressure at 9th grade in boys and girls. Further investigations are needed to determine which indices' relationships to adolescent blood pressure are more variable.

A strength of this study is that it included all children from a typical local area in Japan, and the lifestyles of these children are likely shared with others living across Japan. Although confirmation of external validity is needed, the possibility of selection bias is low.

The study also has three limitations. First, blood pressure was measured using oscillometric devices. Auscultation is more desirable to measure blood pressure.<sup>27</sup> However, any discrepancy between the two techniques should not be a significant issue because the same method was used throughout the years included in the study, and because data was analyzed using regression analysis and ANOVA. Second, we did not have sufficient information about important potentially confounding factors that might influence blood pressure, such as birth weight and prenatal complications,<sup>28</sup> family history of hypertension,<sup>29</sup> family history of obesity<sup>30</sup> or passive smoking.<sup>31</sup> However, our models included adjustments for BMI<sub>1</sub>, blood pressure at 1st grade and primary school-entrance year, so we believe that the influence of the most important confounding factors was minimized. Lastly, there are no established criteria in Japan for classifying pediatric hypertension and appropriate BMI in relation to general health, so we could not classify children into normal or high blood pressure or BMI groups. This might lead to difficulties in interpreting and applying the study results. Further studies are needed to determine specific values for acceptable BMI increases and blood pressure in childhood.

Here, we found that steeper BMI increases in childhood were correlated with higher blood pressure in adolescence. Because it is

**Table 4 Relationship between BMI change and blood pressure at 9th grade by possible confounding factors**

			Model 1	Model 2	Model 3	Model 4
			476 boys, 424 girls (crude analysis)	476 boys, 424 girls (adjusted for BMI <sub>1</sub> <sup>a,b</sup> )	476 boys, 424 girls (adjusted for BMI <sub>1</sub> and year of entrance <sup>c,b</sup> )	314 boys, 278 girls (adjusted for BMI <sub>1</sub> , year of entrance <sup>c</sup> and BP <sub>1</sub> <sup>a,b,d</sup> )
BMI change group			Crude coefficients (95% CI)	Adjusted coefficients (95% CI)	Adjusted coefficients (95% CI)	Adjusted coefficients (95% CI)
Boys	SBP	Low	Ref	Ref	Ref	Ref
		Moderate	2.76 (0.50,5.02)	2.81 (0.55,5.07)	2.89 (0.65,5.13)	2.17 (-0.48,4.83)
		High	4.17 (1.90,6.43)	3.68 (1.37,5.98)	3.91 (1.58,6.23)	2.56 (-0.25,5.37)
	DBP	Low	Ref	Ref	Ref	Ref
		Moderate	1.67 (-0.16,3.51)	1.70 (-0.14,3.53)	1.74 (-0.09,3.58)	1.76 (-0.57,4.08)
		High	2.64 (0.80,4.47)	2.48 (0.60,4.36)	2.66 (0.76,4.57)	2.59 (0.12,5.07)
Girls	SBP	Low	Ref	Ref	Ref	Ref
		Moderate	1.42 (-1.09,3.92)	1.36 (-1.15,3.87)	1.45 (-1.07,3.96)	0.15 (-2.72,3.01)
		High	4.29 (1.79,6.80)	4.24 (1.66,6.82)	4.47 (1.89,7.06)	3.41 (0.40,6.42)
	DBP	Low	Ref	Ref	Ref	Ref
		Moderate	0.91 (-1.00,2.81)	0.91 (-1.00,2.82)	0.88 (-1.04,2.80)	0.63 (-1.81,3.06)
		High	2.22 (0.32,4.12)	2.34 (0.38,4.30)	2.36 (0.39,4.33)	3.16 (0.62,5.70)

Abbreviations: BH, body height; BMI, body mass index; BMI<sub>1</sub>, BMI at 1st grade; BP, blood pressure; BP<sub>1</sub>, blood pressure at 1st grade; CI, confidence interval; DBP, diastolic blood pressure; Ref, reference group; SBP, systolic blood pressure.

<sup>a</sup>BMI<sub>1</sub> and BP<sub>1</sub> are divided into three groups by tertile.

<sup>b</sup>BMI<sub>1</sub>, BP<sub>1</sub> and year of entrance were used as dummy variables.

<sup>c</sup>Year of entrance into primary school are divided into three groups (the year 1983–1988, 1989–1994, 1995–1999).

<sup>d</sup>When the outcome was SBP at 9th grade (SBP9), SBP at 1st grade was included in the model as a covariate. Similarly, when the outcome was DBP at 9th grade (DBP9), DBP at 1st grade was included. In Model 4, BP1 data were available only on those who entered elementary school before 1994.

**Table 5 Relationship between BMI change and blood pressure at 9th grade by possible confounding factors among low BMI group at 1st grade children**

			291 (152 boys and 139 girls)	291 (152 boys and 139 girls)	291 (152 boys and 139 girls)	192 (106 boys and 86 girls)
n			Crude analysis	Adjusted for sex	Adjusted for sex and year of entrance <sup>a,b</sup>	Adjusted for sex, year of entrance <sup>a,b</sup> and BP <sub>1</sub> <sup>c,d</sup>
BMI change group			Crude coefficients (95% CI)	Adjusted coefficients (95% CI)	Adjusted coefficients (95% CI)	Adjusted coefficients (95% CI)
Boys and girls	SBP	Low	Ref	Ref	Ref	Ref
		Moderate	3.67 (0.92,6.42)	3.65 (1.02,6.28)	3.66 (1.03,6.29)	1.77 (-1.35,4.89)
		High	3.26 (0.06,6.46)	3.42 (0.36,6.49)	3.58 (0.50,6.66)	1.52 (-1.97,5.02)
	DBP	Low	Ref	Ref	Ref	Ref
		Moderate	1.87 (-0.27,4.01)	1.87 (-0.27,4.00)	1.89 (-0.24,4.02)	1.94 (-0.81,4.70)
		High	2.09 (-0.40,4.58)	2.13 (-0.35,4.62)	2.35 (-0.14,4.85)	2.59 (-0.50,5.68)

Abbreviations: BH, body height; BMI, body mass index; BMI<sub>1</sub>, BMI at 1st grade; BP<sub>1</sub>, blood pressure at 1st grade; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; Ref, reference group; SBP, systolic blood pressure.

<sup>a</sup>Year of entrance into primary school are divided into three groups (the year 1983–1988, 1989–1994, 1995–1999).

<sup>b</sup>Year of entrance and BP<sub>1</sub> were used as dummy variables.

<sup>c</sup>BP<sub>1</sub> are divided into three groups by tertile.

<sup>d</sup>When the outcome was SBP at 9th grade (SBP9), SBP at 1st grade was included in the model as a covariate. Similarly, when the outcome was DBP at 9th grade (DBP9), DBP at 1st grade was included. SBP and DBP at 1st grade data were available only on those who entered elementary school before 1994 (n = 106 boys, 86 girls).

unclear whether a steeper BMI increase in childhood leads to adult hypertension, continuation of this study in the same individuals into adulthood would be beneficial.

**CONFLICT OF INTEREST**

The authors declare no conflicts of interest.

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