Weight Gain Trajectories from Birth to Adolescence and Cardiometabolic Status in Adolescence

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Objective To assess the influence of the trajectory of weight gain from birth to adolescence on cardiovascular and metabolic risk. We studied childhood body mass index (BMI) trajectories from birth to age 14 years and cardiometabolic risk factors at age 14 years.

Study design In total, 410 children with weight and height measurements were assessed from birth throughout childhood, from the Childhood Asthma Prevention Study, a prospective community-based cohort. BMI trajectory groups were determined by latent basis growth mixture models. Of these subjects, 190 had detailed cardiometabolic risk factors assessed at age 14 years.

Results Three BMI trajectory groups were identified; normal BMI, "early rising" excess BMI from 2 years, and "late rising" excess BMI from 5 years. Differences were found between normal and excess BMI in children at 14 years of age. In addition, children with an early rising BMI trajectory had statistically significantly higher central adiposity and a more atherogenic lipoprotein profile at age 14 years than children with a late rising BMI trajectory ($P < .05$). No differences between BMI trajectory groups in vascular structure or function was identified at age 14 years.

Conclusions Earlier onset of an elevated BMI trajectory persisting from birth to age 14 years results in an unfavorable cardiometabolic risk profile at age 14 years, including central adiposity and more atherogenic lipoproteins, independent of achieved BMI. *(J Pediatr 2019;208:89-95)*.

Several studies have shown an association between childhood obesity, cardiovascular risk factors,[1-4] and cardiovascular disease in adult life.[5,6] These studies have largely utilized cross-sectional measurements of childhood weight status. Body mass index (BMI) growth trajectories from birth to adolescence could provide more information on adiposity and its association with cardiometabolic risk than single cross-sectional measurements.

In terms of later cardiovascular health, previous studies have examined associations between early life growth, in the first 18 months,[7-9] and prepubertal[1] and adolescent measures of adiposity.[10,11] Information concerning growth trajectories throughout childhood into adolescence, however, have not been well described. Adolescent cardiometabolic profiles are associated with those in adulthood,[12,13] but there is little evidence as to whether the timing of obesity onset and the pattern of BMI change from birth to adolescence might determine an individual's metabolic profile or anthropometry in adolescence. Similarly, there is little evidence about whether obesity onset and pattern in childhood results in functional changes in the vasculature in adolescents, as has been shown in adults.[10,11,14]

The primary aim of this study was to determine if differing patterns of BMI change from birth to age 14 years are associated with metabolic profile and cardiovascular structure and function at age 14 years. We hypothesized that an earlier onset of an elevated BMI in childhood results in more adverse cardiometabolic status in adolescence. In addition, we sought to investigate those factors

AIX	Augmentation index
Apo	Apolipoprotein
BMI	Body mass index
CIMT	Carotid intima-media thickness
ER	Early rising
HDL	High density lipoprotein
LDL	Low density lipoprotein
LR	Late rising
PWV	Pulse wave velocity

associated with BMI trajectories that might influence cardio-metabolic health in adolescence.

Methods

We analyzed data from the Childhood Asthma Prevention Study. This study was a randomized controlled 2 × 2 factorial trial investigating the effects of house dust mite avoidance and omega-3 fatty acid supplementation from birth (gestation of ≥36 weeks) to age 5 years on the incidence of asthma during this period. Participants were recruited from antenatal clinics in Western and South-Western Sydney from 1997 to 2000. Details of the study design and outcomes of the randomized controlled trial have been previously reported.[15-18] The total number of participants in the study was 616 at enrollment, of whom 410 had BMI growth trajectory data, 220 (lost to follow-up) and 190 (retained cohort) had detailed cardiometabolic measures at age 14 years. Fourteen years of age was considered as adolescence in this cohort as it was after the onset of puberty in 100% of female subjects and 97% of male subjects. Data on the BMI growth trajectory to age 11.5 years have been previously reported.[19] Participants were invited to participate in an assessment of vascular structure at age 8 and 14 years. The results at age 8 years have been previously reported.[7,20,21] This study was approved by the Human Research and Ethics Committees of The Children's Hospital at Westmead, the South Western, Western and Central Sydney Area Health Services and the University of Sydney.[15]

Birth weight and length were recorded from hospital records; details of measurements can be found in the **Appendix** (available at www.jpeds.com). BMI (kg/m²) and waist circumference to height ratio were calculated. BMI z score was calculated using the US Centers for Disease Control and Prevention growth references.[22] Early life weight gain was calculated as the residual of the height change from 0 to 18 months of age as previously described.[23]

BMI trajectory groups were determined from all available weight and height measurements from birth to age 14 years. Growth trajectory models were identified using a latent basis growth mixture model, separately for boys and girls, as previously described in this cohort.[19] Growth mixture modeling allows identification of (latent) classes that are defined by their patterns of change over time. Each individual is assigned a probability of belonging to each class, and individuals are assigned to the class for which they have the highest probability of membership. To determine the optimum number of classes, we assessed model convergence, fit indices (Bayesian information criterion; adjusted Bayesian information criterion; Akaike information criterion); entropy, class size, and interpretability. Based on model fit statistics and visualisation of expected mean plots, 3 BMI trajectory classes had the greatest discriminatory power for boys and girls. These were (1) normal BMI from birth to age 14 years; (2) early rising (ER) BMI, with the increase in BMI commencing in approximately the first 2 years of life; and (3) late rising (LR) BMI trajectory, with the BMI increasing

between the ages of 2 and 5 years (**Figure**). Further details of the trajectory modeling can be found in the **Appendix** (Methods section). The resultant trajectory classes for each sex were similar, thus, sexes were combined by class allocation. The combined trajectory groups and those 190 subjects with data for cardiometabolic variables at age 14 years consisted of 112 (59%) in the normal group, 17 (9%) in the ER group, and 61 (32%) in the LR group. The ER group was characterized by a rising trajectory above the 90th centile for BMI before 2.5 years of age and persistence of BMI at or above the 90th centile to age 14 years. The LR group was characterized by a later increase in BMI from approximately 5 years of age onward. The normal group was characterised by tracking along the 50th centile from age 2 to 14 years. In this cohort at the age of 14 years, the mean BMI (kg/m²) in each trajectory group was 27 (ER), 25 (LR), and 20 (normal).

Nonfasting, peripheral venous blood samples were collected at age 14 years for measurement of total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, triglycerides, apolipoprotein (Apo) A1 and Apo B, and asymmetric dimethylarginine by standard enzymatic assays. Non-HDL cholesterol was calculated as total cholesterol minus HDL cholesterol. Apo B/A1 ratio was also recorded.

Measures of vascular structure and function were made at age 14 years. Carotid intima-media thickness (CIMT) was measured by obtaining longitudinal views of the right and left common carotid artery on ultrasound (GE Vivid 9, GE Healthcare, Silverwater, New South Wales, Australia). Augmentation index (AIX) was measured by applanation tonometry (Sphygmacor; Atcor Medical, Sydney, Australia) and standardized to a heart rate of 75 bpm, as previously
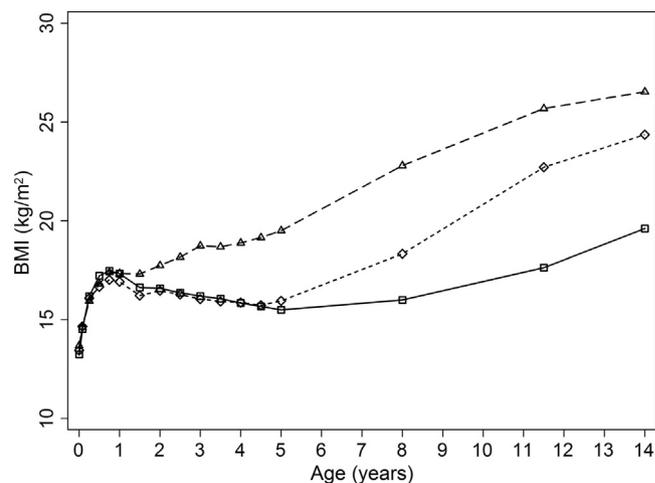

Figure. BMI trajectory groups birth to age 14 years. Triangles are the ER BMI trajectory group; Diamonds are the LR BMI trajectory group; Squares are the normal BMI trajectory group. The dashed, short dash, and solid lines represent the expected mean BMI value at each time point in age of the participants for the ER, LR, and normal groups, respectively.

described.[24] Carotid to radial and carotid to dorsalis pedis pulse wave velocity (PWV) measurements were recorded in meters per second by applanation tonometry (Sphygmacor; Atcor Medical), as previously described.[24] Details of measurements are available in the Appendix.

Other measures were recorded by self-reported questionnaires, interview, or from hospital records, as previously described.[15-18] Socioeconomic status was assessed by proxy of paternal education and maternal education (tertiary and nontertiary education). Details of data collection for all other parameters are available in the Appendix.

Baseline characteristics were assessed for differences between each growth trajectory group. Number and percentage for categorical variables and mean and SD for continuous variables are reported. χ^2, Fischer exact, and multinomial logistic regression coefficients were used to test differences in characteristics between groups. Multivariable linear regression models were used to assess the relationship between trajectory groups (normal, LR, and ER), and the outcomes: BMI, waist circumference, waist to height ratio, BMI z score, lipid levels, and cardiovascular measures at age 14 years. The multivariable linear regression models were also adjusted for maternal BMI and maternal waist circumference as these variables were found to be significant predictors of trajectory group in univariate analyses. Models adjusting for birth weight were not considered as this variable is included in the growth trajectory model from birth to age 14 years. Models were further adjusted for BMI z score at age 14 years to assess the impact of achieved BMI. Multinomial logistic regression was used to assess dietary intake across trajectory groups. All outcome variables were normally distributed except for triglyceride levels, which were log transformed due to the skewed distribution. The Student t test was used to assess the difference in metabolic and cardiovascular outcomes at age 14 years between normal and elevated BMI groups (LR and ER combined). Log triglycerides was separately assessed for male and female subjects because of a significant sex interaction, no other sex interaction was found for any other cardiometabolic outcomes at age 14 years. No other model contained a significant sex interaction, so results were not stratified by sex. All statistical analyses were performed using SPSS v 23(SPSS Inc, Chicago, Illinois), except for growth mixture models in M-Plus v 7.3 (Muthén & Muthén, Los Angeles, CA).

Results

Of the 616 participants in the study, 410 participants had growth trajectory data up to age 14 years and 190 returned for cardiometabolic testing at age 14 years. Compared with those without growth data, those with growth data were more likely to have parents with tertiary education (Table I; available at www.jpeds.com). Compared with those with growth data alone, those who returned for cardiometabolic testing at age 14 years were more likely to be male, to have been breastfed for at least 6 months, and to have mothers with tertiary education and who

did not smoke during pregnancy (Table II; available at www.jpeds.com). In the retained cohort, these variables were not associated with vascular or metabolic outcomes measured at age 14 years. The characteristics of the BMI trajectory groups are outlined in Table III. Birth weight was significantly higher in the LR group compared with normal (LR 3570 g [519], normal 3450 g [472], P = .03). Maternal BMI and maternal waist circumference when participants were age 8 years showed a graded increase from normal to LR to ER. Maternal waist circumference was also higher in the ER group compared with the LR group (ER 99.29 cm [(22.65], LR 91.59 cm [15.39], P = .027). There was no difference across the 3 BMI trajectory groups in diet intake of macronutrients including carbohydrate, protein, fat, and total energy intake at either age 18 months (Table IV; available at www.jpeds.com) or age 3 years, and there was no difference across trajectory groups in compliance of omega-3 supplementation (data not shown). There was no difference across BMI trajectory groups in age at Tanner stage 2, considered as a marker for the onset of puberty. Mean age in boys 11.5 years (1.01) and girls 11.2 years (0.61) (data not shown).

As expected, those in the elevated BMI trajectory groups had higher BMI, BMI z score, waist circumference, and waist to height ratio at age 14 years. Participants in this elevated BMI group also had a lower HDL and Apo A1, higher Apo B/A1 ratio, and systolic blood pressure. Log triglycerides were also higher in boys (Table V). AIX was significantly lower in the elevated BMI group, however, when adjusted for height, this significance was lost, P = .08.

Those adolescents in the LR and ER groups had a high BMI at age 14 years compared with the normal BMI trajectory group. There was also a graded elevation in systolic blood pressure, non-HDL cholesterol, Apo B and B/A1 ratio, and reduction in HDL and Apo A1 across the BMI trajectory groups at age 14 years (Table VI). Levels of non-HDL cholesterol, Apo B, and B/A1 ratio, as well as waist circumference and systolic blood pressure remained significant after adjustment for BMI z score at age 14 years (Table VI). Comparison between the ER and LR groups shows that the ER group had evidence of more central adiposity as reflected in a significantly higher waist circumference (mean difference 5.31, 95% CI 0.42-10.21, P = .033) and waist/height ratio (mean difference 3.33, 95% CI 0.42-6.24, P = .025). Mean BMI was also higher in the ER group (mean difference 2.18, 95% CI 0.37-3.99, P = .018) compared with LR, although BMI z score was not. A more atherogenic lipoprotein profile was evident in the ER group compared with the LR group, with higher total cholesterol (mean difference 0.4, 95% CI 0.02-0.78, P = .038); non-HDL cholesterol (mean difference 0.45, 95% CI 0.086- 0.82, P = .015), Apo B (mean difference 0.12, 95% CI 0.015-0.23, P = .025) and Apo B/A1 ratio (mean difference 0.11, 95% CI 0.023-0.2, P = .014) (Table VII; available at www.jpeds.com). All differences in lipoprotein levels between the 2 elevated trajectory groups remained after adjusting for BMI z score at age 14 years

Table III. Characteristics of BMI growth trajectory groups

Variables	Number	Normal n = 246	LR n = 122	ER n = 42	P
Gestational age (wk)	410	39.61 (1.256)	39.56 (1.213)	39.38 (1.481)	.54
Birth weight(g)	410	3450 (472)	3570 (519)	3580 (436)	.04
Ponderal index (kg/m^3)	407	0.026 (0.003)	0.027 (0.003)	0.027 (0.003)	.20
Maternal BMI at 8 y (kg/m^2)	398	27 (6.4)	29 (6.8)	32 (10.5)	<.001
Maternal waist circumference at 8 y (cm)	376	86.95 (15.15)	91.59 (15.39)	99.29 (22.65)	<.001
Paternal BMI at 8 y (kg/m^2)	376	28 (4.6)	29 (6.3)	30 (7.7)	.06
Family history of premature CVS disease <55 y	408				1.0
Yes		53 (22%)	26 (21%)	9 (21%)	
No		191 (78%)	96 (79%)	33 (79%)	
Diet group	410				.81
Control		118 (48%)	63 (52%)	20 (48%)	
Active		128 (52%)	59 (48%)	22 (52%)	
Sex	410				.05
Female		132 (54%)	50 (41%)	24 (57%)	
Male		114 (46%)	72 (59%)	18 (43%)	
Breastfeeding duration	410				.39
≥6 mo		97 (39%)	57 (47%)	16 (38%)	
<6 mo		149 (61%)	65 (53%)	26 (62%)	
Smoking in pregnancy	410				.11
Yes		52 (21%)	27 (22%)	15 (36%)	
No		194 (79%)	95 (78%)	27 (64%)	
Paternal education	405				.13
Tertiary		124 (51%)	61 (51%)	14 (34%)	
Nontertiary		120 (49%)	59 (49%)	27 (66%)	
Maternal education	410				.82
Tertiary		127 (52%)	59 (48%)	22 (52%)	
Nontertiary		119 (48%)	63 (52%)	20 (48%)	
TV h per weekday	305				.26
1		70 (39%)	27 (30%)	12 (36%)	
2		98 (54%)	50 (56%)	19 (58%)	
3		10 (5%)	12 (13%)	1 (3%)	
4		4 (2%)	1 (1%)	1 (3%)	
Mother born in Australia	410				.06
Yes		180 (73%)	92 (75%)	24 (57%)	
No		66 (27%)	30 (25%)	18 (43%)	
Father born in Australia	410				.16
Yes		176 (72%)	84 (69%)	24 (57%)	
No		69 (28%)	38 (31%)	18 (43%)	

Tertiary education is defined as any form of education above the high school level. Nontertiary education includes any level of education up to the completion of high school. Continuous variables expressed as mean (SD) and categorical variables expressed as number (percentage). Statistical significance at P = .05 level. χ^2, Fisher exact, and multinomial logistic regression were used as appropriate depending on the variable type, to assess differences among groups.

(**Table VII**). There was no difference in HDL cholesterol between ER and LR groups. After adjustment for maternal BMI and waist circumference, significant differences remained across trajectory groups for central adiposity and lipoprotein profiles. Differences between the 2 elevated trajectory groups in lipoprotein levels and central adiposity remained after adjusting for both maternal waist circumference and maternal BMI (**Table VIII** and **Table IX**; available at www.jpeds.com).

Measures of vascular structure and function did not show significant differences across the 3 groups including diastolic blood pressure, CIMT, carotid to radial PWV and carotid to dorsalis pedis PWV, and AIX (**Table VI**). Measures of vascular structure and function did not show significant differences between the 2 elevated BMI trajectory groups (**Table VII**).

Discussion

Recent studies have looked at trajectory groups of BMI with different numbers and profiles of trajectories over childhood including early childhood[1,8] and later childhood through to adolescence.[25,26] Two studies have followed a cohort from birth to age 14 years with focus on 1 outcome[27-29] as distinct from our study of a wide number of cardiometabolic markers.

We found increased birth weight, maternal BMI, and waist circumference to be associated with elevated growth trajectory groups. Maternal waist circumference remained different between the ER and later rising trajectories of growth. There was no significant difference across growth trajectories of other socioeconomic or early life environmental factors. The association of few early life environmental factors with BMI trajectory groups is in keeping with a recently published study showing an association between maternal body habitus, gestational age, and birth weight with increasing obesity trajectory.[1] Silventoinen et al previously showed early life environmental factors to be associated with obesity in childhood which disappeared by adolescence.[30] This is in keeping with our findings.

Adolescents with accelerated BMI trajectories had unfavorable anthropometry, with increased central adiposity

Table V. Metabolic and vascular outcomes in normal and combined elevated BMI trajectory groups (ER and LR)

Variables	n	Normal n = 112	Elevated BMI trajectory group n = 78	P
Waist circumference (cm)	190	68.13 (5.77)	81.84 (12.71)	<.001
Waist/height ratio (cm/m²)	190	41.94 (3.29)	49.74 (7.67)	<.001
BMI (kg/m²)	190	19.67 (2.53)	25.06 (4.41)	<.001
BMI z score	190	0.034 (0.96)	1.25 (0.72)	<.001
Total cholesterol (mmol/L)	190	4.34 (0.68)	4.33 (0.75)	.97
LDL (mmol/L)	176	2.45 (0.57)	2.45 (0.6)	.94
HDL (mmol/L)	176	1.37 (0.26)	1.22 (0.2)	<.001
Non-HDL (mmol/L)	176	2.96 (0.65)	3.11 (0.75)	.175
Ln triglycerides boys (mmol/L)	96	−0.13 (0.41)	0.28 (0.45)	<.001
Ln triglycerides girls (mmol/L)	80	0.12 (0.39)	0.17 (0.58)	.64
Apo A (mmol/L)	174	1.41 (0.20)	1.34 (0.17)	.009
Apo B (mmol/L)	174	0.73 (0.17)	0.78 (0.23)	.079
Apo B/A1 ratio	174	0.53 (0.14)	0.6 (0.19)	.006
ADMA	152	0.73 (0.25)	0.69 (0.16)	.38
SBP (mm Hg)	186	111 (8.61)	119 (9.95)	<.001
DBP (mm Hg)	186	65 (6.67)	66 (6.5)	.5
CIMT mean of max (mm)	188	0.64 (0.077)	0.65 (0.066)	.37
AIX_75 (%)	181	−26.7 (13.12)	−31.12 (12.66)	.025
PWV C_R (m/s)	181	7.62 (1.32)	7.56 (1.12)	.76
PWV C_DP (m/s)	178	5.99 (0.66)	6.06 (0.65)	.45

ADMA, asymmetric dimethylarginine; *AIX_75*, AIX adjusted for heart rate 75 beats per minute; *DBP*, diastolic blood pressure; *Ln*, Log; *PWV C_DP*, carotid to dorsalis pedis PWV; *PWV C_R*, carotid to radial PWV; *SBP*, systolic blood pressure.
Results are presented as mean (SD). *P* significant at .05 level from Student *t* test. The breakdown per elevated BMI trajectory groups compared with normal for triglycerides is for male subjects: normal 50 (52%) and LR/ER combined 46 (48%) and for female subjects: normal 50 (62.5%) and LR/ER combined 30 (37.5%).

and more atherogenic lipoprotein expression at age 14 years. Huang et al reported that low birth weight and accelerated growth in childhood, and persistent accelerated growth from normal birth weight, to be associated with hypertension in adolescence,[27] and sustained elevated or rising BMI trajectories were associated with higher insulin resistance in adolescence.[28] Furthermore, upward crossing centiles of growth measured from age 5 to 15 years have been shown to have higher LDL, triglycerides, and blood pressure after

adjusting for weight at age 15 years.[26] Our cohort demonstrates the importance of an earlier BMI rise in terms of a negative effect on anthropometry and lipoproteins in adolescence.

In our cohort, we demonstrated that ER in BMI was associated with increased central adiposity compared with LR in BMI. The development of central adiposity is associated with poor metabolic outcomes, with cardiovascular disease in adulthood[3,6] and with abnormal lipoprotein

Table VI. Comparison across BMI trajectory groups of metabolic and vascular outcomes

Variables	n	Normal n = 112	LR n = 61	ER n = 17	P	P*
Metabolic variables						
Waist circumference (cm)	190	68 (5.77)	81 (12.68)	86 (12.27)	<.001	.002
Waist/height ratio (cm/m)	190	42 (3.3)	49 (7.8)	52 (6.8)	<.001	.19
BMI (kg/m²)	190	19.67 (2.53)	24.59 (4.64)	26.77 (2.98)	<.001	n/a
BMI z score	190	−0.034 (0.96)	1.157 (0.74)	1.595 (0.49)	<.001	n/a
Height (m)	190	1.63 (0.079)	1.65 (0.078)	1.64 (0.078)	.16	n/a
Total cholesterol (mmol/L)	176	4.34 (0.68)	4.24 (0.72)	4.64 (0.79)	.116	.013
LDL (mmol/L)	176	2.45 (0.57)	2.38 (0.60)	2.68 (0.58)	.17	.031
HDL (mmol/L)	176	1.37 (0.26)	1.24 (0.20)	1.18 (0.20)	<.001	.12
non-HDL (mmol/L)	176	2.96 (0.65)	3.01 (0.72)	3.46 (0.76)	.02	.027
Ln triglycerides boys (mmol/L)	96	−0.13 (0.41)	0.25 (0.46)	0.43 (0.38)	<.001	.38
Ln triglycerides girls (mmol/L)	80	0.12 (0.39)	0.09 (0.51)	0.35 (0.73)	.34	.18
Apo A1 (mmol/L)	174	1.41 (0.20)	1.34 (0.17)	1.31 (0.19)	.024	.26
Apo B (mmol/L)	174	0.73 (0.17)	0.76 (0.23)	0.88 (0.22)	.016	.018
Apo B/A1 ratio	174	0.53 (0.14)	0.57 (0.19)	0.69 (0.20)	.001	.028
ADMA	155	0.73 (0.25)	0.70 (0.17)	0.66 (0.12)	.55	.88
Vascular variables						
SBP (mm Hg)	186	111 (8.61)	119 (10.09)	117 (9.61)	<.001	.027
DBP (mm Hg)	186	65 (6.67)	66 (6.48)	65 (6.74)	.78	.45
CIMT mean of max (mm)	188	0.64 (0.077)	0.64 (0.065)	0.67 (0.066)	.25	.43
AIX_75 (%)	181	−26.7 (13.12)	−31.74 (11.52)	−28.91 (16.34)	.056	.17
PWV C_R (m/s)	181	7.62 (1.32)	7.65 (1.08)	7.23 (1.21)	.45	.50
PWV C_DP (m/s)	178	5.99 (0.66)	6.1 (0.66)	5.9 (0.59)	.42	.37

Data expressed as mean (SD). *P* value from Wald test from multivariable linear regression model.
The breakdown per BMI trajectory group for triglycerides is for male subjects: normal 50 (52%), LR 38 (40%), and ER 8(8%); and for female subjects: normal 50 (63%), LR 21(26%), and ER 9 (11%).
*P from Wald test from multivariable linear regression model additionally adjusted for BMI z score at age 14 years.

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profiles in adolescence.[31] However, the relationship between the BMI trajectory with anthropometry in adolescence has not been previously well described.

Rapid early life weight gain 0-18 months is associated with obesity in children age 8 years,[7] and in adolescents,[32] without accounting for the tracking of growth throughout the remainder of childhood. Furthermore, there is some evidence that early adiposity rebound (the onset of increasing BMI after early childhood nadir, usually around 5-6 years of age), is associated with an increased risk of obesity in adult life[33] and adolescence.[34] Similarly, the strongest association from 0 to 10 years of age in BMI change measured at age 15 years was a BMI change between 2 and 5 years of age in girls and 5 and 5.5 years of age in boys.[35] Our study suggests that the earlier the onset of excess adiposity, before 5 years of age, the more likely is central adiposity by adolescence.

We have found the earlier onset of elevated BMI trajectory around 2 years of age to be associated with an increased total cholesterol, non-HDL, Apo B, and Apo B/A1 ratio compared with a later rising trajectory of BMI. Studies have shown earlier onset of adiposity rebound to be associated with lower HDL cholesterol, higher triglycerides and Apo B at 12 years of age[36] and increased incidence of diabetes and glucose intolerance in young adults.[37] Early childhood interval changes in BMI have also been shown to attenuate later relationships of interval BMI change with cardiovascular risk factors at 15 years of age.[35] It has been previously shown that an increase in HDL of 0.0259 mmol/L can decrease coronary artery disease risk in men and women by 2%-3%.[38] Thus, a difference between normal and each elevated BMI trajectory group of 0.19 mmol/L (ER) and 0.14 mmol/L (LR) is likely clinically relevant. Similarly, a 10% reduction in total cholesterol has been shown to reduce coronary artery disease risk by up to 50% at age 40 years,[39] and, thus, the mean increase of 9% between ER and LR groups at age 14 years, as well as the mean increase of 7% from normal to ER groups in LDL may be clinically relevant to future coronary disease risk. It is well established that obesity in childhood and adolescence tracks to adulthood,[40] and an adverse metabolic profile in adolescence both in cross-sectional studies[5,6,11,41,42] and growth trajectory models throughout childhood[1] results in adult obesity and cardiovascular disease and mortality. However, in those that are able to return to a normal weight status, their cardiovascular risk in adulthood appears to be reduced.[3] What is not established is whether structural and functional changes have already begun in adolescence in this group of overweight individuals with worse metabolic profiles.

Measures of vascular structure and function in our cohort at 14 years of age included CIMT, PWV, and AIX. There was no difference across BMI trajectory groups, nor between the 2 elevated BMI trajectory groups in any of these markers of subclinical atherosclerosis at age 14 years. This is in keeping with recently published data by Hanvey et al suggesting the phenotype of structural and functional change is not being expressed this early in life.[29] This suggests, that there is a

point at which we can potentially reverse the trajectory of cardiovascular risk.

Weaknesses of this study include the significant loss to follow-up of subjects in adolescence. However, the retained cohorts are representative of the whole cohort other than for some evidence of a higher socioeconomic status by proxy. The potential bias of a higher socioeconomic population cannot be ruled out in this study because those lost to follow-up were of lower socioeconomic status, a factor potentially related to increased BMI. A further weakness may be considered a lack of fasting lipoprotein measures, which is likely to have resulted in a skewed distribution of triglyceride levels, which are less reliable in their interpretation. However, nonfasting measures in adults and in children have been used to determine cardiovascular risk.[43] Finally, our community-based sample is relatively small and so confirmation in larger cohorts should be considered.

The trajectory of elevated BMI from birth through age 14 years influences body habitus and metabolic profile at age 14 years, with a negative impact of early onset of elevated BMI from approximately 2 years of age. The determinants of these growth trajectories include birth weight and maternal adiposity. ∎

Data Statement

Data sharing statement available at www.jpeds.com.

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Table I. Comparison of participants with BMI growth trajectory data and the original participants in the study lost to follow-up

Variables	N	Lost to follow-up Original study participants	N	Participants with BMI trajectory data	P
	206		410		
Gestational age (wk)	201	39.55 (1.26)	410	39.57 (1.27)	.81
Birth weight (g)	202	3490 (497.4)	410	3496 (485.8)	.89
Maternal BMI at 8 y (kg/m^2)	17	26.62 (4.34)	398	28.37 (7.15)	.13
Paternal BMI at 8 y (kg/m^2)	17	27.78 (4.10)	376	28.54 (5.54)	.47
Diet group	206		410		
Control		102 (49.5%)		201 (49%)	.91
Active		104 (50.5%)		209 (51%)	
Sex	206		410		
Female		98 (48%)		206 (50%)	.53
Male		108 (52%)		204 (50%)	
Breastfeeding duration	170		410		
≥6 mo		57 (33.5%)		170 (41.5%)	.07
<6 mo		113 (66.55)		240 (58.5%)	
Smoking in pregnancy	206		410		
Yes		56 (27%)		94 (23%)	.25
No		150 (73%)		316 (77%)	
Paternal education	206		410		<.001
Tertiary		66 (32%)		199 (49%)	
Nontertiary		140 (68%)		211 (51%)	
Maternal education	206		410		<.001
Tertiary		68 (33%)		208 (51%)	
Nontertiary		138 (67%)		202 (49%)	
TV h per weekday	46		305		
1		11 (24%)		109 (35.7%)	.21
2		29 (63%)		167 (54.8%)	
3		6 (13%)		23 (7.5)	
4		0 (0%)		6 (2%)	
Mother born in Australia	206		410		
Yes		161 (78%)		296 (72%)	.11
No		45 (22%)		114 (28%)	
Father born in Australia	206		410		
Yes		137 (66.5%)		284 (69%)	.49
No		69 (33.5%)		126 (31%)	

Tertiary education is defined as any form of eduaction above the high school level. Nontertiary education includes any level of education up to the completion of high school. Values expressed as mean (SD) or number (percentage). P value from χ^2 and Student t test significant at .05 level.

Table II. Comparison of participants with growth trajectory data alone and those with both growth trajectory data and cardiometabolic measures at age 14 years

Variables	N	Lost to follow-up	N	Retained cohort	P
Gestational age (wk)	220	39.55 (1.27)	190	39.61 (1.27)	.63
Birth weight (g)	220	3520 (476)	190	3470 (497)	.25
Maternal BMI at 8 y (kg/m^2)	209	28.57 (7.46)	189	28.15 (6.79)	.56
Paternal BMI at 8 y (kg/m^2)	196	28.57 (5.85)	180	28.51 (5.20)	.91
Early weight gain 0-18 mo (residual of height, m, 18 mo)	210	0.01 (1.107)	185	−0.01 (1.023)	.89
Diet group	220		190		.82
Control		109 (49.5%)		92 (48.4%)	
Active		111 (50.5%)		98 (51.6%)	
Sex	220		190		.023
Female		122 (55.5%)		84 (44.2%)	
Male		98 (44.5%)		106 (55.8%)	
Breastfeeding duration	220		190		.04
≥6 mo		81 (36.8%)		89 (46.8%)	
<6 mo		139 (63.2%)		101 (53.2%)	
Smoking in pregnancy	220		190		.044
Yes		59 (26.8%)		35 (18.4%)	
No		161 (73.2%)		155 (81.6%)	
Paternal education	216		189		.069
Tertiary		97 (44.9%)		102 (54%)	
Nontertiary		119 (55.1%)		87 (46%)	
Maternal education	220		190		.007
Tertiary		98 (44.5%)		110 (57.9%)	
Nontertiary		122 (55.5%)		80 (42.1%)	
TV h per weekday	116		189		.19
1		49 (42.2%)		60 (31.7%)	
2		60 (51.7%)		107 (56.6%)	
3		6 (5.2%)		17 (9%)	
4		1 (0.9%)		5 (2.6%)	
Mother born in Australia	220		190		.36
Yes		163 (74%)		133 (70%)	
No		57 (26%)		57 (30%)	
Father born in Australia	220		190		.87
Yes		152 (69%)		132 (70%)	
no		68 (31%)		57 (30%)	

Tertiary education is defined as any form of education above the high school level. Nontertiary education includes any level of education up to the completion of high school. Values expressed as mean (SD) or number (percentage). P value from χ^2 and Student t test significant at .05 level.

Table IV. Dietary intake 18 months and BMI trajectory groups

Variables	Normal	LR Mean and SD	ER	P	P adjusted for total energy intake
Protein (intake/100 g)	0.38 (0.103)	0.41 (0.111)	0.41 (0.216)	.057	.33
Fat (intake/100 g)	0.42 (0.116)	0.44 (0.111)	0.44 (0.149)	.32	.75
Carbohydrate (intake/100 g)	1.25 (0.306)	1.32 (0.376)	1.28 (0.465)	.25	.75
Energy intake	4.25 (0.904)	4.48 (1.065)	4.42 (1.4)	.15	

Mean (SD). P value significant at .05 level from multinomial logistic regression model.

Table VII. Mean difference between elevated BMI trajectory groups and metabolic outcomes

Variables	N	Mean difference of ER group to LR group	95% CI Lower	95% CI Upper	P value	P* value
Waist circumference (cm)	78	5.31	0.42	10.21	.033	.22
Waist/height ratio (cm/m)	78	3.33	0.42	6.24	.025	.077
BMI (kg/m²)	78	2.18	0.037	3.99	.018	n/a
BMI z score	78	0.44	−0.021	0.9	.06	n/a
Height (m)	78	−0.01	−0.05	0.03	.72	n/a
Total cholesterol (mmol/L)	76	0.4	0.02	0.78	.038	.048
LDL (mmol/L)	76	0.3	−0.1	0.61	.06	.11
HDL (mmol/L)	76	−0.05	−0.18	0.07	.41	.73
non-HDL (mmol/L)	76	0.45	0.086	0.82	.015	.028
Ln triglycerides boys (mmol/L)	46	0.18	−0.14	0.5	.27	.74
Ln triglycerides girls (mmol/L)	30	0.25	−0.11	0.61	.17	.071
Apo A (mmol/L)	75	−0.03	−0.13	0.073	.57	.84
Apo B (mmol/L)	75	0.12	0.15	0.23	.025	.0072
Apo B/A1 ratio	75	0.11	0.023	0.2	.014	.0075
ADMA	64	−0.04	−0.17	0.09	.53	.70
Vascular variables						
SBP (mm Hg)	76	−1.83	−6.75	3.08	.47	.16
DBP (mm Hg)	76	−0.36	−3.9	3.18	.84	.54
CIMT mean of max (mm)	77	0.028	−0.01	0.066	.16	.20
AIX_75 (%)	73	2.83	−4.29	9.95	.44	.42
PWV C_R (m/s)	73	−0.43	−1.11	0.26	.22	.29
PWV C_DP (m/s)	72	−0.2	0.57	0.17	.29	.33

ADMA, asymmetric dimethylarginine; *AIX_75*, AIX adjusted for heart rate 75 beats per minute; *DBP*, diastolic blood pressure; *PWV C_DP*, carotid to dorsalis pedis PWV; *PWV C_R*, carotid to radial PWV; *SBP*, systolic blood pressure.
Data expressed as mean difference and 95% CI with LR group as the reference group. *P* value from pairwise comparisons of LR to ER groups from multivariable linear regression model.
P value from comparison of LR to ER groups; model additionally adjusted for BMI z score at age 14 years.

Table VIII. Comparison across BMI trajectory groups of metabolic and vascular outcomes adjusted for maternal BMI

Variables	Normal n = 111	LR n = 61	ER n = 17	P	Comparison of LR with ER group P*
Metabolic variables					
Waist circumference (cm)	68.34 (90.84)	80.42 (1.13)	85.78 (2.15)	<.001	.027
Waist/height ratio (cm/m²)	42.08 (0.50)	48.86 (0.68)	0.52 (1.28)	<.001	.02
BMI (kg/m²)	19.78 (0.30)	24.46 (0.41)	26.67 (0.77)	<.001	.012
BMI z score	0.006 (0.079)	1.13 (0.11)	1.58 (0.20)	<.001	.051
Height (m)	1.62 (0.007)	1.65 (0.01)	1.64 (0.019)	.15	.72
Total cholesterol (mmol/L)	4.34 (0.07)	4.24 (0.091)	4.64 (0.17)	.116	.038
LDL (mmol/L)	2.46 (0.058)	2.37 (0.075)	2.67 (0.139)	.165	.06
HDL (mmol/L)	1.37 (0.023)	1.24 (0.03)	1.19 (0.056)	<.001	.41
non-HDL (mmol/L)	2.98 (0.068)	3.00 (0.88)	3.45 (0.16)	.025	.015
Ln triglycerides boys (mmol/L)	−0.12 (0.060)	0.25 (0.068)	0.43 (0.15)	<.001	.27
Ln triglycerides girls (mmol/L)	0.12 (0.065)	0.09 (0.10)	0.33 (0.15)	.41	.198
Apo A (mmol/L)	1.41 (0.019)	1.34 (0.024)	1.31 (0.046)	.038	.58
Apo B (mmol/L)	0.73 (0.02)	0.76 (0.025)	0.88 (0.049)	.024	.026
Apo B/A1 ratio (%)	0.53 (0.016)	0.57 (0.021)	0.68 (0.04)	.002	.014
Vascular variables					
SBP (mm Hg)	111 (0.88)	119 (1.19)	117 (2.22)	<.001	.47
DBP (mm Hg)	65 (0.63)	66 (0.86)	65 (1.60)	.77	.84
CIMT mean of max (mm)	0.64 (0.0068)	0.65 (0.0092)	0.67 (0.017)	.18	.16
AIX_75 (%)	−26.71 (1.25)	−31.70 (1.71)	−28.86 (3.22)	.062	.44
PWV C_R (m/s)	7.62 (0.12)	7.64 (0.16)	7.21 (0.31)	.43	.35
PWV C_DP (m/s)	5.98 (0.06)	6.1 (0.086)	5.9 (0.17)	.41	.29

Data expressed as mean (SD). *P* value from Wald test from multivariable linear regression model.
P value from pairwise comparisons of LR with ER groups.

Table IX. Comparison across BMI trajectory groups of metabolic and vascular outcomes adjusted for maternal waist circumference

Variable	Normal n = 107	LR n = 56	ER n = 15	P	Comparison of LR with ER group P*
Metabolic variables					
Waist circumference (cm)	68.23 (0.85)	80.45 (1.17)	86.91 (2.27)	<.001	.011
Waist/height ratio (cm/m^2)	42.01 (0.51)	48.92 (0.70)	52.67 (1.36)	<.001	.014
BMI (kg/m^2)	19.73 (0.32)	24.63 (0.44)	26.78 (0.85)	<.001	.024
BMI z score	−0.02 (0.082)	1.15 (0.11)	1.60 (0.22)	<.001	.068
Height (m)	1.62 (0.008)	1.65 (0.01)	1.65 (0.02)	.18	.94
Total cholesterol (mmol/L)	4.33 (0.071)	4.23 (0.093)	4.64 (0.18)	.12	.038
LDL (mmol/L)	2.45 (0.06)	2.37 (0.078)	2.69 (0.15)	.18	.064
HDL (mmol/L)	1.37 (0.024)	1.25 (0.031)	1.18 (0.06)	.001	.3
non-HDL (mmol/L)	2.96 (0.069)	2.98 (0.090)	3.47 (0.17)	.022	.012
Ln triglycerides boys (mmol/L)	−0.12 (0.059)	0.20 (0.07)	0.43 (0.14)	<.001	.16
Ln triglycerides girls (mmol/L)	0.095 (0.062)	0098 (0.093)	0.36 (0.17)	.31	.17
Apo A (mmol/L)	1.41 (0.02)	1.35 (0.025)	1.32 (0.049)	.09	.54
Apo B (mmol/L)	0.73 (0.020)	0.75 (0.026)	0.89 (0.052)	.019	.019
Apo B/A1 ratio (%)	0.53 (0.017)	0.56 (0.022)	0.69 (0.043)	.003	.009
Vascular variables					
SBP (mm Hg)	111 (0.90)	119 (1.26)	117 (2.39)	<.001	.58
DBP (mm Hg)	64 (0.65)	65 (0.91)	65 (1.73)	.83	.97
CIMT mean of max (mm)	0.64 (0.007)	0.64 (0.010)	0.67 (0.019)	.26	.2
AIX_75 (%)	−26.62 (1.29)	−31.56 (1.81)	−27.57 (3.50)	.08	.31
PWV C_R (m/s)	7.59 (0.12)	7.64 (0.16)	7.2 (0.31)	.44	.21
PWV C_DP (m/s)	6.00 (0.064)	6.10 (0.090)	6.02 (0.18)	.63	.67

Data expressed as mean (SD); *P* value from Wald test from multivariable linear regression model.
P from pairwise comparisons of LR with ER groups.