Supplementary material

Infant weight growth velocity patterns and general and abdominal adiposity in school-age children. The Generation R Study

Infant weight growth and adiposity at school-age

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Included in the Online Supplementary Material:

Table S4. Associations of infant weight growth velocity patterns with childhood adiposity outcomes adjusted for age and sex only (N=5,126).

Table S5. Interaction with standard deviation score birth weight and gestational age at birth.

Table S6. Associations of infant weight growth velocity patterns with adiposity outcomes stratified by gestational age at birth or SDS birth weight (N=5,126).

Peak weight velocity

PWV was derived from postnatal growth data using the Reed1 model for boys and girls separately using the previously described procedure (1, 2). The Reed1 model was chosen since it showed a better fit to the early growth data than the Kouchi, Carlberg, and Count models, and it showed an equally good fit to the Reed2 model which has one more parameter than the Reed1 model (3). The difference compared with the simpler models, for example, the Count model, is that the Reed1 model allows the velocity to peak after birth, whereas other models force it to peak at birth. In the first couple of weeks after birth, weight may drop up to 10% in normal individuals. The PWV is thus usually not in the first weeks after birth, but slightly later. Therefore, the Reed1 model is more realistic (especially for weight) and more flexible. The Reed1 model was fitted by sex on all weight measurements taken at 0-3 years of age, including birth weight. We assumed both a fixed and a random component for all our parameters in the model. For each person, the first derivative of the fitted distance curve was taken to obtain the weight velocity curve. Subsequently, the maximum of this curve was taken to obtain the PWV in infancy. The Reed1 model is a four-parameter extension of the three-parameter Count model and its functional form is (3, 4) : $Y = A + Bt + Cln(t) + D/t$

Since this model is not defined at birth (t=0), it was modified for this study in the same way as in Simondon et al. (5): $Y = A + Bt + Cln(t+1) + D/(t+1)$ where t, postnatal age; Y, weight reached at age t and A, B, C, and D the function parameters. Of the function parameters, A is related to the baseline weight at birth, B to the linear component of the growth velocity, C to the decrease in the growth velocity over time, and D to the inflection point that allows growth velocity to peak after birth rather than exactly at birth. The Reed1 model is linear in its constants (4).

Adiposity peak

For BMIAP, a cubic mixed effects model was previously fitted on log(BMI) from 14 days to 1.5 years, using sex as a covariate (1). Modelization of BMI growth was performed from the age of 14 days onward, since children may lose up to 10% of their body weight in the first 2 weeks of life. When fitting the model, age was centralized to 0.75 years. In addition to fixed effects, we included random effects for the constant and the slope in the model. An autoregressive within person correlation structure between measurements was assumed. Then, BMI was derived for each individual at the point where the curve reaches its maximum, i.e. at infant adiposity peak.

References

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2. Sovio U, Bennett AJ, Millwood IY, Molitor J, O'Reilly PF, Timpson NJ, et al. Genetic determinants of height growth assessed longitudinally from infancy to adulthood in the northern Finland birth cohort 1966. *PLoS Genet* 2009; **5**: e1000409.
3. Berkey CS, Reed RB. A model for describing normal and abnormal growth in early childhood. *Hum Biol* 1987; **59**: 973-987.
4. L. HRM. Parametric models for postnatal growth. In: Eds RC Hauspie NCLM (ed). In Methods in Human Growth Research, pp 205-233: Cambridge: Cambridge University press, 2004.
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Figure S1. Flow chart of participants in study

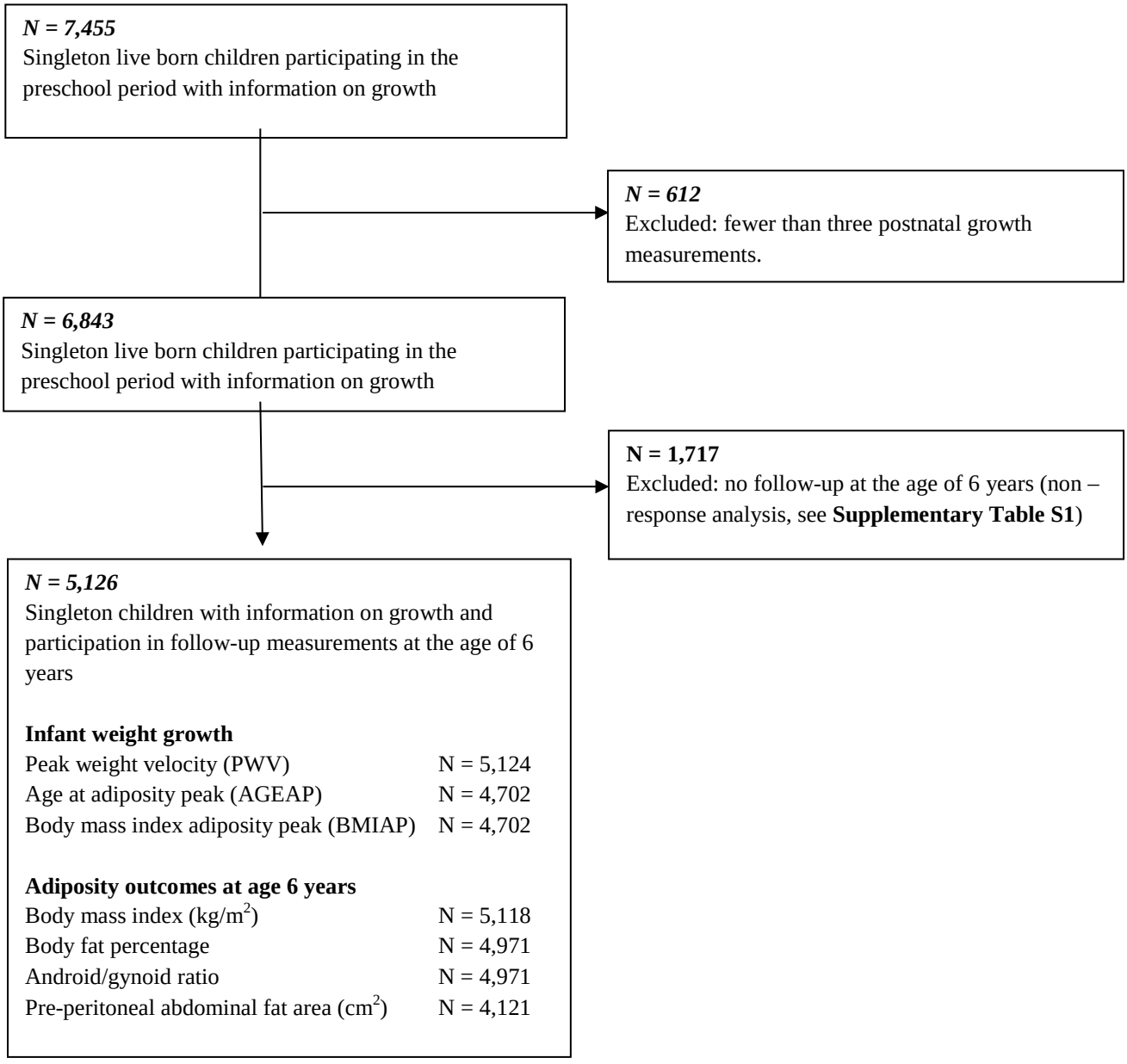

Table S1. Non-response Analysis (N=6,843)

	Eligible for present study (N=6,843)	**Included in analysis Yes (N=5,126)**	**Included in analysis No (N=1,717)**	***P value***
Maternal characteristics				
Age (years)	31.1 (23.1, 36.7)	31.5 (24.0, 36.9)	29.5 (21.6, 35.9)	<0.01
Height (cm)	167.7 (7.4)	168.0 (7.4)	166.9 (7.6)	<0.01
Missing	*8.6*	*8.6*	*8.6*	
Weight (kg)	66.3 (12.3)	66.4 (12.2)	65.7 (12.7)	0.07
Missing	*24.5*	*23.8*	*26.6*	
BMI (kg/m^2)	22.6 (19.4, 29.1)	22.6 (19.4, 28.9)	22.4 (19.1, 29.4)	0.94
Missing	*24.6*	*23.9*	*26.6*	
Parity (%)				<0.01
0	55.7	56.9	52.1	
>= 1	44.3	43.1	47.9	
Missing	*2.6*	*2.5*	*3.0*	
Marital status (%)				<0.01
No partner	12.1	10.8	16.3	
Married/living together	87.9	89.2	83.7	
Missing	*8.9*	*6.9*	*14.0*	
Educational level (%)				
Primary	8.9	7.6	13.3	<0.01
Secondary	42.4	41.1	46.4	<0.01
Higher	48.7	51.3	40.2	<0.01
Missing	*8.3*	*6.6*	*13.6*	
Smoking during pregnancy (%)				<0.01
Ever	16.1	14.9	20.1	
Never	83.9	85.1	79.9	
Missing	*12.6*	*11.5*	*15.6*	
Alcohol consumption (%)				<0.01
Ever	54.8	57.7	54.0	
Never	45.2	42.3	46.0	
Missing	*19.5*	*19.1*	*20.4*	
Folic acid supplement use (%)				<0.01
No	24.4	21.7	32.6	
Yes	75.6	78.3	67.4	
Missing	*30.2*	*29.3*	*32.7*	
Maternal complications (%)				
Gestational diabetes, Yes	0.8	0.7	1.0	0.31
Gestational hypertension, Yes	3.8	3.6	2.8	<0.05
Preeclampsia, Yes	1.9	1.7	2.5	0.06

Paternal characteristics				
Age (y)	33.1 (26.5, 39.7)	33.2 (27.0, 40.2)	32.0 (24.7, 38.6)	<0.01
Missing	*30.6*	*28.2*	*37.9*	
Height (cm)	182 (7.8)	182.1 (7.8)	181.4 (7.7)	<0.01
Missing	*30.7*	*28.2*	*37.9*	
Weight (kg)	83.9 (12.9)	84.0 (12.8)	82.3 (13.1)	0.15
Missing	*30.8*	*28.3*	*38.0*	
BMI (kg/m^2)	25.2 (21.2, 29.4)	24.9 (21.2, 29.4)	25.0 (21.2, 29.4)	0.35
Missing	*30.8*	*28.3*	*38.1*	
Infant characteristics				
Gestational age (weeks)	40.1 (38.0, 41.7)	40.1 (38.0, 41.7)	40.0 (38.0, 41.7)	0.20
Birth weight (g)	3439 (548)	3447 (543)	3414 (562)	<0.05
Ethnicity (%)				<0.01
Dutch or European	65.8	68.0	58.5	
Non- European	34.2	32.0	41.5	
Missing	*3.8*	*1.5*	*10.4*	
Duration of breastfeeding	3.5 (0.0, 12,0)	3.6 (0.5, 10.8)	2.5 (0.0, 10.5)	<0.01
Age at introduction of solid foods (%)				
< 4 months	8.3	8.0	9.8	0.12
4 – 5 months	61.3	61.0	62.7	0.40
5 – 6 months	26.4	26.8	24.2	0.14
> 6 months	3.9	4.1	3.3	0.29
Missing	*42.2*	*37.2*	57.2	
PWV (kg/year)	12.3 (2.2)	12.2 (2.1)	12.5 (2.2)	<0.01
AGEAP (years)	0.7 (0.7, 0.8)	0.7 (0.7, 0.8)	0.7 (0.7, 0.8)	0.22
BMIAP (kg/m^2)	17.6 (16.6, 18.7)	17.6 (16.6, 18.7)	17.6 (16.6, 18.6)	0.09

Abbreviations; N: number. BMI: body mass index, PWV: peak weight velocity, AGEAP: age at adiposity peak, BMIAP: body mass index at adiposity peak. Values are means (standard deviation), percentages or medians (90% range) for variables with skewed distribution. Non-imputed data. P-value (included in analysis: yes versus no) was estimated by using One-Way Anova test and Chi-square tests.

Table S2. Correlation coefficients between infant weight growth and childhood adiposity outcomes (N=5,126)

	Infant weight growth measures			Childhood adiposity measures			
	PWV (kg/year)	AGEAP (years)	BMIAP (kg/m2))	BMI (kg/m^2)	Body fat percentage	Android/gynoid fat mass ratio	Pre-peritoneal abdominal fat area (cm^2)
PWV (cm/year)	**1**	-	-	-	-	-	-
AGEAP (years)	-0.02	**1**	-	-	-	-	
BMIAP (kg/m2)	0.68**	-0.21**	**1**	-	-	-	-
BMI (kg/m^2)	0.33**	0.03	0.46**	**1**	-	-	-
Body fat percentage	0.08**	0.04**	0.12**	0.69**	**1**	-	-
Android/gynoid fat mass ratio	0.14**	0.02	0.15**	0.61**	0.65**	**1**	-
Pre-peritoneal abdominal fat area (cm^2)	0.11**	0.02	0.09**	0.57**	0.63**	0.54**	**1**

Abbreviations; N: number, PWV: peak weight velocity, AGEAP: age at adiposity peak, BMIAP: body mass index at adiposity peak, BMI: body mass index.

*P value <0.05, ** P value <0.01.

Table S3. Associations of infant weight growth velocity patterns with adiposity outcomes in absolute values (N=5, 126)

	Absolute difference in childhood body fat outcomes (95% Confidence Interval)			
	BMI (kg/m^2)	Body fat percentage	Android/gynoid fat mass ratio	ln Pre-peritoneal abdominal area (cm^2)
Total group				
PWV (kg/year)	0.31 (0.29, 0.34)**,***	0.54 (0.47, 0.62)** ,***	0.004 (0.003, 0.005)** ,***	0.03 (0.02 0.04)** ,***
AgeBMIAP (years)	3.42 (2.22, 4.61)** ,***	6.80 (3.38, 10.21)** ,***	0.04 (-0.01, 0.08) ,***	0.24 (-0.12, 0.59)
BMIAP (kg/m^2)	1.00 (0.93, 1.06)**	1.60 (1.41, 1.80)**	0.01 (0.01, 0.02)** ,***	0.07 (0.05, 0.09)**
Boys				
PWV (kg/year)	0.27 (0.24, 0.30)**	0.49 (0.39, 0.59)**	0.00 (0.00, 0,00)	0.03 (0.02, 0.04)**
AgeBMIAP (years)	1.68 (0.05, 3.31)*	1.81 (-2.88, 6.51)	-0.03 (-0.09, 0.03)	-0.14 (-0.62, 0.34)
BMIAP (kg/m2)	0.96 (0.87, 1.05)*	1.56 (1.29, 1.83)**	0.01 (0.01, 0.01)**	0.07 (0.04, 0.10)**
Girls				
PWV (kg/year)	0.36 (0.33, 0.41)	0.63 (0.51, 0.75)**	0.01 (0.00, 0.01)**	0.04 (0.03, 0.05)**
AgeBMIAP (years)	5.2 (3.45, 7.02)**	11.77 (6.78, 16.75)**	0.10 (0.03, 0.17)**	0.60 (0.08, 1.13)*
BMIAP (kg/m2)	1.03 (0.94, 1.12)**	1.65 (1.37, 1.93)**	0.02 (0.01, 0.02)**	0.07 (0.04, 0.10)**

Abbreviations: BMI: body mass index, PWV: peak weight velocity, AGEAP: age at adiposity peak, BMIAP: body mass index at adiposity peak; Values are linear regression coefficients (95% confidence interval) based on multiple linear regression models and reflect the change in outcome in each infant weight growth characteristics;

Model adjusted for age, sex (total group), age mother, body mass index before pregnancy, parity, marital status, education mother, smoking during pregnancy, use of alcohol during pregnancy, folic acid supplement use, gestational diabetes and gestational hypertensive disorders, paternal body mass index, standard deviation score birth weight, ethnicity child, number of postnatal measurements, duration of breastfeeding, age at introduction of solid foods and watching television. Analyses with fat mass were additionally adjusted for height of the child.

* P value<0.05, ** P value <0.01, *** P values for interaction with sex <0.05.

Table S4. Associations of infant weight growth velocity patterns with childhood adiposity outcomes (SDS) adjusted for age and sex only (N=5,126)

	SDS difference in childhood body fat outcomes (95% Confidence Interval)			
	BMI	Body fat percentage	Android/gynoid fat mass ratio	Pre-peritoneal abdominal fat area
Total group				
PWV (1 SDS = 2.1 kg/year)				
Model 1	0.39 (0.36, 0.41)**	0.31 (0.28, 0.34)**	0.19 (0.16, 0.22)**	0.23 (0.19, 0.26)**
Model 2	0.37 (0.34, 0.40)**	0.21 (0.18, 0.24)**	0.14 (0.10, 0.17)**	0.13 (0.10, 0.17)**
AGEAP (1 SDS = 0.04 years)				
Model 1	0.03 (0.01, 0.06)*	0.04 (0.01, 0.06)**	0.02 (-0.01, 0.05)	0.01 (-0.02, 0.04)
Model 2	0.08 (0.06, 0.11)**	0.05 (0.03, 0.08)**	0.03 (-0.01, 0.06)	0.02 (-0.01, 0.05)
BMIAP (1 SDS = 0.8 kg/m^2)				
Model 1	0.48 (0.46, 0.51)**	0.25 (0.22, 0.28)**	0.17 (0.14, 0.20)**	0.14 (0.11, 0.17)**
Model 2	0.45 (0.43, 0.48)**	0.24 (0.21, 0.27)**	0.17 (0.10, 0.17)**	0.11 (0.08, 0.15)**

Abbreviations: N: number, SDS: standard deviation scores, BMI: body mass index, PWV: peak weight velocity, AGEAP: age at adiposity peak, BMIAP: body mass index at adiposity peak. Values are linear regression coefficients (95% CI) based on multiple linear regression models and reflect the change in outcome per SD increase in each infant weight growth characteristics. Model 1 adjusted for age, sex. Model 2 is additionally adjusted age mother, body mass index before pregnancy, parity, marital status, education mother, smoking during pregnancy, use of alcohol during pregnancy, folic acid use, gestational diabetes and gestational hypertensive disorders, paternal body mass index, standard deviation score birth weight, ethnicity child, number of postnatal measurements, duration of breast feeding, age at introduction of solid foods and watching television. Analyses with fat mass were additionally adjusted for height of the child.

* P value <0.05, ** P value <0.01.

Table S5. Interaction with standard deviation score birth weight and gestational age at birth

Interaction term	P-value
Gestational age at birth*PWV	
BMI (SDS)	NI
Body fat percentage (SDS)	NI
Android/gynoid fat mass ratio (SDS)	NI
Pre-peritoneal abdominal fat area (SDS)	NI
Gestational age at birth*AGEAP	
BMI (SDS)	0.021
Body fat percentage (SDS)	NI
Android/gynoid fat mass ratio (SDS)	0.016
Pre-peritoneal abdominal fat area (SDS)	NI
Gestational age at birth*BMIAP	
BMI (SDS)	NI
Body fat percentage (SDS)	NI
Android/gynoid fat mass ratio (SDS)	NI
Pre-peritoneal abdominal fat area (SDS)	NI
SDS birth weight*PWV	
BMI (SDS)	0.008
Body fat percentage (SDS)	NI
Android/gynoid fat mass ratio (SDS)	NI
Pre-peritoneal abdominal fat area (SDS)	NI
SDS birth weight*AGEAP	
BMI (SDS)	0.001
Body fat percentage (SDS)	0.047
Android/gynoid fat mass ratio (SDS)	0.005
Pre-peritoneal abdominal fat area (SDS)	NI
SDS birth weight*BMIAP	
BMI (SDS)	NI
Body fat percentage (SDS)	NI
Android/gynoid fat mass ratio (SDS)	NI
Pre-peritoneal abdominal fat area (SDS)	NI

Abbreviations: BMI: body mass index, SDS: standard deviation scores, NI: no significant interaction.

Table S6. Associations of infant weight growth velocity patterns with adiposity outcomes stratified by gestational age at birth or SDS birth weight (N=5,126)

	SDS difference in childhood body fat outcomes (95% Confidence Interval)			
	BMI	Body fat percentage	Android/gynoid fat mass ratio	Pre-peritoneal abdominal fat area
AGEAP (N=4,702)				
Preterm (≤ 37 weeks)	0.09 (-0.03, 0.20)	NI	0.03 (-0.00, 0.06)	NI
Term (> 37 weeks)	0.05 (0.03, 0.08)**	NI	0.12 (-0.01, 0.25)	NI
PWV (N=5,120)				
Small for gestational age	0.43 (0.34, 0.52)**	NI	NI	NI
Appropriate for gestational age	0.36 (0.33, 0.39)**	NI	NI	NI
Large for gestational age	0.34 (0.27, 0.41)**	NI	NI	NI
AGEAP (N=4,700)				
Small for gestational age	0.17 (0.09, 0.25)**	0.14 (0.06, 0.22)**	0.10 (0.00, 0.19)	NI
Appropriate for gestational age	0.06 (0.03, 0.09)**	0.05 (0.02, 0.08)**	0.03 (-0.00, 0.06)	NI
Large for gestational age	0.02 (-0.06, 0.11)	-0.02 (-0.08, 0.10)	-0.03 (-0.13, 0.06)	NI

Abbreviations: N: number, SDS: standard deviation scores; BMI: body mass index, PWV: peak weight velocity, AGEAP: age at adiposity peak, BMIAP: body mass index at adiposity peak, NI: no significant interaction. Values are linear regression coefficients (95% confidence interval) based on multiple linear regression models and reflect the change in outcome in each infant weight growth characteristics; Model adjusted for age, sex, age mother, body mass index before pregnancy, parity, marital status, education mother, smoking during pregnancy, use of alcohol during pregnancy, folic acid supplement use, gestational diabetes and gestational hypertensive disorders, paternal body mass index, standard deviation score birth weight, ethnicity child, number of postnatal measurements, breast feeding, age at introduction of solid foods and watching television. Analyses with fat mass were additionally adjusted for height of the child.

* P value<0.05, ** P value<0.01.